NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 431

TOXICOLOGY AND CARCINOGENESIS STUDIES OF BENZYL ACETATE

(CAS NO. 140-11-4)

IN F344/N RATS AND B6C3F$_1$ MICE

(FEED 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

STUDIES OF

BENZYL ACETATE

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IN F344/N RATS AND B6C3F$_1$ MICE

(FEED STUDIES)

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P.O. Box 12233
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CONTRIBUTORS

National Toxicology Program
Evaluated and interpreted results and reported findings

K.M. Abdo, Ph.D.
C.J. Alden, Ph.D.
G.A. Boorman, D.V.M., Ph.D.
D.A. Bridge, B.S.
S.L. Eustis, D.V.M., Ph.D.
T.J. Goehl, Ph.D.
R.A. Griesemer, D.V.M., Ph.D.
J.R. Hailey, D.V.M.
J.K. Haseman, Ph.D.
G.N. Rao, D.V.M., Ph.D.
C.C. Shackelford, D.V.M., M.S., Ph.D.
B.A. Schwetz, D.V.M., Ph.D.
D.B. Walters, Ph.D.
K.L. Witt, M.S., Oak Ridge Associated Universities

Southern Research Institute
Conducted studies, evaluated pathology findings

J.D. Prejean, Ph.D., Principal Investigator
D.R. Farnell, D.V.M., Ph.D.
H.D. Giles, D.V.M., Ph.D.
J.S. Heath, D.V.M.

Experimental Pathology Laboratories, Inc.
Provided pathology quality assurance

J.F. Hardisty, D.V.M., Principal Investigator
S. Botts, M.S., D.V.M.
B.F. Hamilton, D.V.M., Ph.D.

Dynamac Corporation
Prepared quality assurance audits

S. Brecher, Ph.D., Principal Investigator

NTP Pathology Working Group
Evaluated slides, prepared pathology report on rats (29 May 1991)

T.M. Monticello, D.V.M., Ph.D., Chair
Pathology Associates, Inc.
M.A. Bryant, D.V.M.
U.S. Army Medical Reserves Instructor
B.F. Hamilton, D.V.M., Ph.D.
Experimental Pathology Laboratories, Inc.
M.P. Jokinen, D.V.M.
National Toxicology Program
M.M. McDonald, D.V.M., Ph.D.
National Toxicology Program
S. Qureshi, B.V.Sc., Ph.D.
Sandoz, Ltd.
C.C. Shackelford, D.V.M., M.S., Ph.D.
National Toxicology Program
A. Steber (observer)
University of Wisconsin

Evaluated slides, prepared pathology report on mice (15 August 1991)

P.K. Hildebrandt, D.V.M., Chair
PATHCO, Inc.
S. Botts, M.S., D.V.M.
Experimental Pathology Laboratories, Inc.
M.P. Jokinen, D.V.M.
National Toxicology Program
J.R. Hailey, D.V.M.
National Toxicology Program
M.M. McDonald, D.V.M., Ph.D.
National Toxicology Program
K.T. Morgan, B.V.Sc., M.R.C.V.S., Ph.D.
Chemical Industry Institute of Toxicology
E. Sander, M.D. (observer)
Bayer AG
C.C. Shackelford, D.V.M., M.S., Ph.D.
National Toxicology Program

Biotechnical Services, Inc.
Prepared Technical Report

D.D. Lambright, Ph.D., Principal Investigator
G.F. Corley, D.V.M.
P.S. Keightley, B.A.
T.A. King-Hunter, B.S.H.S.
H.S. Lindsay, B.A.

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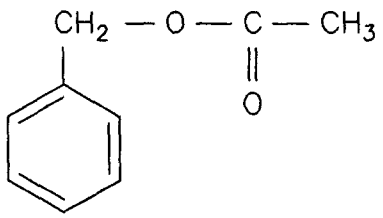
ABSTRACT



BENZYL ACETATE

CAS No. 140-11-4

Chemical Formula: $C_9H_{10}O_2$ Molecular Weight: 150.17

Synonyms: acetic acid benzyl ester, acetic acid phenyl methyl ester, (acetoxymethyl)benzene, acetoxytoluene, benzyl ethanoate, phenylmethyl acetate

Benzyl acetate is used as a flavoring agent in foods, as a fragrance in soaps and perfumes, as a solvent for cellulose acetate and nitrate, and as a component of printing inks and varnish removers. The NTP previously studied the toxicology and carcinogenicity of this chemical in F344/N rats and B6C3F$_1$ mice using the gavage route of administration and corn oil as a vehicle. Benzyl acetate increased the incidences of pancreatic acinar cell adenomas in male rats and the incidences of hepatocellular adenomas and forestomach neoplasms in male and female mice. Because of the confounding effect of corn oil on the incidences of pancreatic neoplasms and because of controversy over the use of the gavage route of administration, the NTP decided to restudy benzyl acetate using the dosed feed route of administration. In these repeat studies, male and female F344/N rats and B6C3F$_1$ mice received benzyl acetate (at least 98% pure) in feed for 13 weeks and 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium*, cultured Chinese hamster ovary cells, L5178Y mouse lymphoma cells, *Drosophila melanogaster*, and mouse bone marrow and peripheral blood cells.

13-WEEK STUDY IN RATS

Groups of 10 male and 10 female F344/N rats were fed diets containing 0, 3,130, 6,250, 12,500, 25,000, or 50,000 ppm (0, 230, 460, 900, 1,750, or 3,900 mg/kg body weight for males and 0, 240, 480, 930, 1,870, or 4,500 mg/kg for females) benzyl acetate for 13 weeks. Nine male and nine female rats receiving 50,000 ppm benzyl acetate died or were killed moribund between weeks 2 and 8 of the study. The mean body weight gain and the final mean body weight of 25,000 ppm males were significantly lower ($P \leq 0.01$) than those of the control group. Feed consumption by exposed rats, except the 25,000 and 50,000 ppm males and 50,000 ppm females, was similar to that by the controls. The reduced feed consumption by 25,000 and 50,000 ppm males and 50,000 ppm females may have been due to toxicity or decreased palatability. Tremors and ataxia occurred only in the 50,000 ppm rats. These findings were first observed on day 15 in nine males and six females and continued until the end of the study. Cholesterol levels in 12,500 and 25,000 ppm females and triglyceride levels in 25,000 ppm females were lower than those in the controls.

Chemical-related lesions occurred in the brain, kidney, tongue, and skeletal muscles of the thigh. Necrosis of the brain involving the cerebellum and/or hippocampus, degeneration and regeneration of the renal tubule epithelium, and degeneration and sarcolemma nuclear hyperplasia of the tongue and skeletal muscles occurred in most male and female

50,000 ppm rats. This effect was observed in the 1,000 mg/kg group in the previous gavage study (NTP, 1986).

13-WEEK STUDY IN MICE

Groups of 10 male and 10 female B6C3F$_1$ mice were fed diets containing 0, 3,130, 6,250, 12,500, 25,000, or 50,000 ppm (0, 425, 1,000, 2,000, 3,700, or 7,900 mg/kg body weight for males and 0, 650, 1,280, 2,980, 4,300, or 9,400 mg/kg for females) benzyl acetate. One 50,000 ppm male mouse died and one 50,000 ppm female mouse was killed moribund before the end of the study. Mean body weight gains and final mean body weights of all exposed male and female mice were significantly lower than those of the controls and the mean body weight gains decreased with increased exposure level. Feed consumption by 3,130 ppm males and all exposed females was lower than that by the controls. Tremors occurred only in females and were first observed on day 16 in three females receiving 50,000 ppm, day 94 in one female receiving 25,000 ppm, and day 93 in one female receiving 12,500 ppm. The tremors continued until the end of the study.

Necrosis of the brain involving the hippocampus occurred in four 50,000 ppm mice, one male and three females. Hepatocellular necrosis also occurred in the male with brain lesions. On reexamination of the previous 13-week gavage study (NTP, 1986), a similar lesion was seen in the brain of one 1,000 mg/kg female mouse; none were seen in 1,000 mg/kg male mice. The lesion was less severe than that described in the present dosed feed study. The highest dose used in the gavage study was 1,000 mg/kg compared to an estimated high dose of 7,200 mg/kg for the feed study.

2-YEAR STUDY IN RATS

The doses selected for the 2-year feed study of benzyl acetate in F344/N rats were based on lower survival, mean body weights, and feed consumption, and on increased incidences of histopathologic brain lesions in 50,000 ppm male and female rats in the 13-week study. Groups of 60 male and 60 female F344/N rats were fed diets containing 0, 3,000, 6,000, or 12,000 ppm benzyl acetate for 2 years.

Survival, Body Weights, Feed and Compound Consumption, and Clinical Pathology

Survival of exposed rats was similar to that of the controls. The mean body weights of the 12,000 ppm males and exposed females were approximately 5% lower than those of the controls throughout most of the study. The feed consumption by 12,000 ppm males was slightly lower than that by the controls. Dietary levels of 3,000, 6,000, and 12,000 ppm benzyl acetate were estimated to result in average daily consumption levels of 130, 260, and 510 mg/kg body weight (males) and 145, 290, and 575 mg/kg (females). No biologically significant changes in hematology or clinical chemistry parameters were found that could be attributed to benzyl acetate administration.

Pathology Findings

No compound-related increased incidences of neoplasms or nonneoplastic lesions occurred in male or female F344/N rats receiving benzyl acetate for as long as 2 years.

2-YEAR STUDY IN MICE

The doses selected for the 2-year feed study of benzyl acetate in B6C3F$_1$ mice were based primarily on lower body weight gains and lower final mean body weights of exposed mice in the 13-week study. Groups of 60 male and 60 female B6C3F$_1$ mice were fed diets containing 0, 330, 1,000, or 3,000 ppm benzyl acetate for 2 years.

Survival, Body Weights, Feed and Compound Consumption, and Clinical Pathology

Survival of all exposed mice, except the 3,000 ppm females, was similar to that of the control groups. Survival of 3,000 ppm females was significantly higher than that of the control group. Throughout the 2-year study, the mean body weights of 1,000 and 3,000 ppm males and females were 2% to 14% lower than those of the control groups. Dietary levels of 330, 1,000, and 3,000 ppm benzyl acetate were estimated to result in average daily consumption levels of 35, 110, and 345 mg/kg (males) and 40, 130, and 375 mg/kg (females). No biologically significant changes in hematology or clinical chemistry parameters were observed in mice receiving 330, 1,000, or 3,000 ppm benzyl acetate.

Pathology Findings

No increase in neoplasm incidence in mice could be attributed to benzyl acetate administration in feed. This contrasts with the previous finding that administration of benzyl acetate in corn oil by gavage once daily 5 days a week for as long as 2 years was carcinogenic to mice, causing increased incidences of hepatocellular neoplasms and forestomach neoplasms. The contrast in results between the two studies may be due to differences in the dose levels used (highest dose: gavage, 1,000 mg/kg a day; feed, 360 mg/kg a day).

Dose-related increased incidences or severities of nonneoplastic nasal lesions occurred in the most posterior portions of the nasal cavity in all exposed groups. The lesions occurred in the majority of the exposed mice and consisted of atrophy and degeneration, primarily of the olfactory epithelium, cystic hyperplasia of the nasal submucosal glands, pigmentation of the mucosal epithelium, and exudate accumulation.

GENETIC TOXICOLOGY

Benzyl acetate was not mutagenic in *Salmonella typhimurium* strains TA98, TA100, TA1535, or TA1537, with or without exogenous metabolic activation (S9). However, a positive response was observed for benzyl acetate, with and without S9, in the mouse lymphoma assay for induction of trifluorothymidine resistance in L5178Y cells. No significant increases in the frequencies of sister chromatid exchanges or chromosomal aberrations occurred in cultured Chinese hamster ovary cells treated with benzyl acetate *in vitro*, with or without S9, and no increases in either sister chromatid exchanges or chromosomal aberrations occurred in bone marrow cells of male mice treated *in vivo* by intraperitoneal injection. No increase in sex-linked recessive lethal germ cell mutations occurred in male *Drosophila melanogaster* administered benzyl acetate in feed or by injection. Tests of benzyl acetate for induction of micronucleated erythrocytes in bone marrow and peripheral blood of mice were also negative.

CONCLUSIONS

Under the conditions of these 2-year feed studies, there was *no evidence of carcinogenic activity** of benzyl acetate in male or female F344/N rats receiving 3,000, 6,000, or 12,000 ppm; however, rats may have tolerated higher doses. There was *no evidence of carcinogenic activity* of benzyl acetate in male or female $B6C3F_1$ mice receiving 330, 1,000, or 3,000 ppm.

Nasal lesions associated with benzyl acetate exposure in male and female mice included nasal mucosa atrophy and degeneration (primarily of the olfactory epithelium), cystic hyperplasia of the nasal submucosal gland, and luminal exudate and pigmentation of the nasal mucosal epithelium.

In previous 2-year gavage studies, benzyl acetate increased the incidence of acinar cell adenomas of the exocrine pancreas in male F344/N rats; the gavage vehicle may have been a contributing factor. There was no evidence of carcinogenic activity in female F344/N rats receiving 250 or 500 mg/kg a day. There was some evidence of carcinogenic activity in male and female $B6C3F_1$ mice, indicated by the increased incidences of hepatocellular adenomas and squamous cell neoplasms of the forestomach.

* Explanation of Levels of Evidence of Carcinogenic Activity is on page 9. A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on page 11.

Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of Benzyl Acetate

Male F344/N Rats	Female F344/N Rats	Male B6C3F$_1$ Mice	Female B6C3F$_1$ Mice
Doses			
0, 3,000, 6,000, or 12,000 ppm in feed (approximately 130, 260, or 510 mg/kg)	0, 3,000, 6,000, or 12,000 ppm in feed (approximately 145, 290, or 575 mg/kg)	0, 330, 1,000, or 3,000 ppm in feed (approximately 35, 110, or 345 mg/kg)	0, 330, 1,000, or 3,000 ppm in feed (approximately 40, 130, or 375 mg/kg)
Body weights			
12,000 ppm group slightly lower than control	Exposed groups slightly lower than control	1,000 and 3,000 ppm groups lower than control	1,000 and 3,000 ppm groups lower than control
2-Year survival rates			
27/50, 34/50, 30/50, 33/50	30/50, 30/50, 37/50, 28/50	39/50, 43/50, 41/50, 39/50	29/50, 28/50, 37/50, 44/50
Nonneoplastic effects			
None	None	Nose: mucosa atrophy (30/50, 49/50, 50/50, 50/50); mucosa degeneration (31/50, 50/50, 50/50, 50/50); glands, cystic hyperplasia (22/50, 43/50, 47/50, 50/50); exudate (8/50, 18/50, 38/50, 26/50); mucosal pigmentation (0/50, 45/50, 50/50, 50/50)	Nose: mucosa atrophy (41/50, 48/50, 49/50, 50/50); mucosa degeneration (48/50, 48/50, 50/50, 50/50); glands, cystic hyperplasia (39/50, 45/50, 49/50, 50/50); exudate (15/50, 26/50, 36/50, 43/50) mucosal pigmentation (0/50, 46/50, 48/50, 48/50)
Neoplastic effects			
None	None	None	None
Level of evidence of carcinogenic activity			
No evidence	No evidence	No evidence	No evidence
Genetic toxicology			
Salmonella typhimurium gene mutation:		Negative in strains TA98, TA100, TA1535, and TA1537 with or without S9	
Mouse lymphoma gene mutations:		Positive with and without S9	
Sister chromatid exchanges			
Cultured Chinese hamster ovary cells *in vitro*:		Negative with or without S9	
Mouse bone marrow *in vivo*:		Negative	
Chromosomal aberrations			
Cultured Chinese hamster ovary cells *in vitro*:		Negative with or without S9	
Mouse bone marrow *in vivo*:		Negative	
Sex-linked recessive lethal mutations			
Drosophila melanogaster:		Negative when administered in feed or by injection	
Micronuclei induction			
Mouse bone marrow *in vivo*:		Negative	
Mouse peripheral blood *in vivo*:		Negative when administered in feed for 13 weeks	

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 benzyl acetate 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.

Curtis D. Klaassen, Ph.D., Chair
Department of Pharmacology and Toxicology
University of Kansas Medical Center
Kansas City, KS

Paul T. Bailey, Ph.D.
Environmental and Health Sciences Laboratory
Mobil Oil Corporation
Princeton, NJ

Louis S. Beliczky, M.S., M.P.H.
Department of Industrial Hygiene
United Rubber Workers International Union
Akron, OH

Arnold L. Brown, M.D.
University of Wisconsin Medical School
Madison, WI

Gary P. Carlson, Ph.D., Principal Reviewer
Department of Pharmacology and Toxicology
Purdue University
West Lafayette, IN

Kowetha A. Davidson, Ph.D.
Health and Safety Research Division
Oak Ridge National Laboratory
Oak Ridge, TN

Harold Davis, D.V.M., Ph.D., Principal Reviewer
Medical Research Division
American Cyanamid
Pearl River, NY

Daniel S. Longnecker, M.D.*
Department of Pathology
Dartmouth Medical School
Lebanon, NH

Louise Ryan, Ph.D.
Division of Biostatistics
Dana-Farber Cancer Institute
Boston, MA

Ellen K. Silbergeld, Ph.D.*
University of Maryland Medical School
Baltimore, MD

Robert E. Taylor, Ph.D.
Department of Pharmacology
Howard University College of Medicine
Washington, DC

Matthew J. van Zwieten, D.V.M., Ph.D.
Department of Safety Assessment
Merck, Sharp & Dohme Research Laboratories
West Point, PA

Jerrold M. Ward, D.V.M., Ph.D.
Frederick Cancer Research Development Center
National Cancer Institute
Frederick, MD

Lauren Zeise, Ph.D.*
Reproductive and Cancer Hazard Assessment Section
California Environmental Protection Agency
Berkeley, CA

* Did not attend

SUMMARY OF TECHNICAL REPORTS REVIEW SUBCOMMITTEE COMMENTS

On December 1, 1992, the draft Technical Report on the toxicology and carcinogenesis studies of benzyl acetate 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. K.M. Abdo, NIEHS, introduced the toxicology and carcinogenesis studies of benzyl acetate by discussing the uses and rationale for study, describing the experimental design, reporting on survival and body weight effects, and commenting on compound-related nonneoplastic lesions in male and female $B6C3F_1$ mice. Benzyl acetate was studied previously by the NTP using the gavage route with corn oil as the vehicle. Because of the confounding effect of corn oil on the increased incidence of pancreatic neoplasms in male rats, the NTP decided to restudy the chemical using the dosed feed route. Dr. J. Yuan, NIEHS, reported on pharmacokinetic studies designed to compare the internal dose for the feed route with that for the gavage route. The pharmacokinetic studies demonstrated that blood levels of the major metabolite of benzyl acetate, benzoic acid, were up to 300 times greater after gavage administration than after administration in the feed. The proposed conclusions for the current and previous studies were *no evidence of carcinogenic activity* of benzyl acetate in male or female F344/N rats, and *no evidence of carcinogenic activity* of benzyl acetate in male or female $B6C3F_1$ mice.

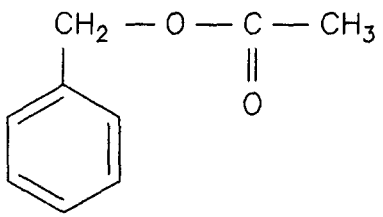
Dr. Davis, a principal reviewer, agreed in principle with the proposed conclusions. He thought a maximum tolerated dose (MTD) was not achieved in rats. Based on lack of mortality or clinical signs and only a modest effect on weight gain at 25,000 ppm in the 13-week studies, he suggested that the highest dose in the 2-year studies should have been between 25,000 and 50,000 ppm. Dr. Abdo agreed that rats could have tolerated a higher dose, but during dose selection there was concern about reduced feed consumption. Dr. Davis requested that this information be added to the report.

Dr. Carlson, the second principal reviewer, agreed with the proposed conclusions, and also felt that the MTD was not reached in the rat studies. He asked whether it was true that nasal lesions did not occur in previous studies or whether they were just not looked for. Dr. C.C. Shackelford, NIEHS, said there was no evidence of nasal lesions in the previous NTP study.

Dr. van Zwieten asked whether the rationale for repeating this as a feed study included reasons other than the corn oil effects noted in the first study. Dr. Abdo cited forestomach irritation as a reason, as well as the fact that human exposure to benzyl acetate is more often through dermal contact or by ingestion of contaminated food. Dr. Davis asked for staff comment on the importance of reaching the MTD. Dr. G.A. Boorman, NIEHS, said it was quite important, particularly when trying to compare effects in studies involving different routes of chemical administration such as this. Dr. Klaassen criticized the analytical method used for measuring blood levels of benzoic acid and also wondered whether the toxicology of benzoic acid was being studied instead of benzyl acetate. Dr. T.J. Goehl, NIEHS, said the method was sensitive down to 1 μg/mL of benzoic acid and can also detect benzyl alcohol and hippuric acid; however, benzoic acid is the major component after either gavage or feed administration. Dr. B.A. Schwetz, NIEHS, said an important point in giving perspective to both studies is that the metabolism of benzyl acetate in rodents is probably quite similar to that in humans.

Dr. Davis moved that the Technical Report on benzyl acetate be accepted with the revisions discussed and with the conclusions as written for male and female rats and mice, *no evidence of carcinogenic activity*. Dr. Carlson seconded the motion and then offered an amendment that the statement be added to the conclusions that higher doses could have been tolerated in the 2-year rat studies. Mr. Beliczky seconded the amendment, which was accepted by six yes votes (Mr. Beliczky, and Drs. Brown, Carlson, Davis, Taylor, and Ward) to four no votes (Drs. Bailey, Davidson, Ryan, and van Zwieten). The original motion by Dr. Davis as amended by Dr. Carlson was then accepted unanimously with ten votes.

INTRODUCTION



BENZYL ACETATE

CAS No. 140-11-4

Chemical Formula: $C_9H_{10}O_2$ Molecular Weight: 150.17

Synonyms: acetic acid benzyl ester, acetic acid phenyl methyl ester, (acetoxymethyl)benzene, acetoxytoluene, benzyl ethanoate, phenylmethyl acetate

CHEMICAL AND PHYSICAL PROPERTIES

Benzyl acetate is a colorless liquid with a pear-like odor (*Merck Index*, 1983). The boiling point of benzyl acetate is 215.5° C, the melting point is −51.3° C, the density is 1.0550 at 20° C (Weast, 1985), and the vapor pressure is 1 mmHg at 45° C (Sax, 1984). Benzyl acetate is essentially insoluble in water but is miscible with alcohol or ether (*Merck Index*, 1983). Benzyl acetate is prepared by reacting sodium acetate with benzyl chloride in the presence of triethylamine as a catalyst (Hennis *et al.*, 1967). Benzyl acetate can also be prepared by acetylating benzyl alcohol or by reacting benzaldehyde and acetic acid in the presence of zinc dust (Furia and Bellanca, 1975).

USE AND HUMAN EXPOSURE

Benzyl acetate is used as a flavoring agent in chewing gum (760 ppm), candy (34 ppm), pudding (23 ppm), baked goods (22 ppm), ice cream (14 ppm), and non-alcoholic beverages (7.8 ppm) (Furia and Bellanca, 1975). Other consumer products containing benzyl acetate include soap (500 to 3,600 ppm), detergent (50 to 360 ppm), lotions (150 to 1,500 ppm) and perfume (5,400 to 30,000 ppm) (Opdyke, 1973). Benzyl acetate is also used as a solvent for cellulose acetate and nitrate (*Merck Index*, 1983) and as a component of printing inks and varnish removers (Hawley, 1981). United States production of benzyl acetate in 1980 was approximately 1.4 million pounds (USITC, 1981) and one million pounds were imported in 1983 (USITC, 1984).

Benzyl acetate occurs naturally in the flowers of jasmine, hyacinth, gardenia, ylang-ylang, and alfalfa. Benzyl acetate concentrations range from 85,000 to 251,000 ppm in jasmine absolute to 262,000 ppm in ylang-ylang essential oils to a trace in extract of clover flowers. Concentrations occurring in fruits range from 3,000 ppm in volatile extracts of mushrooms to 0.06 to 0.10 ppm in passion fruit pulp to trace amounts in quince, apples and apple products, and grapes (IARC, 1986).

The potential for human exposure is great. Exposure can occur in the workplace, through the use of perfumes and other consumer goods, and through the consumption of fruits and processed foods containing the chemical. From a survey conducted from 1981 to 1983, NIOSH has estimated that 275,805 males and 133,630 females in the United States may have been exposed to benzyl acetate (NIOSH, 1991).

REGULATORY STATUS

Benzyl acetate is approved by the U.S. Food and Drug Administration for use as a flavoring agent for foods (U.S. FDA, 1984). The Joint Food and Agricultural Organization/World Health Organization temporarily approved a daily intake (expressed as total benzoic acid) of 0 to 5 mg/kg body weight (World Health Organization, 1986). No threshold limit has been established, although benzyl acetate can be an irritant when inhaled.

ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION

Experimental Animals

Benzyl acetate is absorbed from the gastrointestinal tract, lung, and skin of various species (Snapper *et al.*, 1925; von Oettingen, 1960; Abdo *et al.*, 1985; Chidgey and Caldwell, 1986; Chidgey *et al.*, 1986, 1987; McMahon *et al.*, 1989). Benzyl acetate is excreted as metabolites primarily in the urine after oral or percutaneous administration (Abdo *et al.*, 1985; Chidgey *et al.*, 1987). Benzyl acetate is hydrolyzed to benzyl alcohol, oxidized to benzoic acid, and excreted as hippuric acid and benzyl mercapturic acid (Clapp and Young, 1970).

Male F344/N rats given a single oral dose of 5, 50, or 500 mg/kg body weight and male B6C3F$_1$ mice given a single oral dose of 10, 100, or 1,000 mg/kg body weight of radioactively labeled benzyl acetate in corn oil excreted 90% of the radioactivity in the urine (NTP, 1986). None was detected in the adipose tissue, blood, kidney, liver, lung, muscle, skin, or stomach. The major metabolite isolated in the urine was hippuric acid, and 95% to 99% of the excreted dose was in this form. Other urinary metabolites found were mercapturic acid and benzyl alcohol. The results were similar in studies of male rats given 500 mg/kg body weight and mice given 1,000 mg/kg body weight of benzyl acetate in corn oil by gavage once daily, 5 days a week for 2 weeks (Abdo *et al.*, 1985). Neither the size of the dose nor the frequency of dosing had any effect on the absorption, metabolism, or excretion of benzyl acetate. No evidence of saturation of absorption, distribution, metabolism, or excretion pathways of this chemical occurred in either species at these doses. The percutaneous absorption and disposition of [methylene-^{14}C]benzyl acetate was studied in F344 rats by applying benzyl acetate (100, 250, or 500 mg/kg body weight) either neat or as a 50% solution in ethanol over a shaved area (6.25, 12, or 18 cm^2) on the back of the animal (Chidgey *et al.*, 1987). Twenty-four hours after administration, 28% to 48% of the dose was recovered from the application site, a similar proportion was absorbed and excreted in the urine, and less than 4% remained in the carcass. The amount recovered in the urine was 95% of the absorbed chemical. Benzyl acetate absorption per unit area of skin increased with concentration. The dermal absorption of the chemical in the ethanol vehicle was similar to that of the neat chemical. In both cases, 95% of the urinary ^{14}C was in hippuric acid, the major urinary metabolite.

Chidgey and Caldwell (1986) studied the influence of vehicle and dose on plasma pharmacokinetics and benzyl acetate metabolism in rats. [Methylene-^{14}C]benzyl acetate was given in a single oral dose of 5, 250, or 500 mg/kg body weight as the neat chemical, in corn oil, or in propylene glycol. Peak plasma concentrations occurred earliest in animals given the chemical neat. With propylene glycol as a vehicle, peak concentrations were delayed and absorption was lower. At a dose of 250 or 500 mg/kg body weight of benzyl acetate in corn oil, the peak plasma level was half that when benzyl acetate was given neat and remained at that level for as long as 8 hours. At a dose of 5 mg/kg of benzyl acetate, plasma concentrations were the same as those when the chemical was given neat, regardless of the vehicle used. At doses of 250 or 500 mg/kg of benzyl acetate, the major plasma metabolite was benzoic acid and was accompanied by smaller amounts of hippuric acid and traces of benzyl alcohol. At a dose of 5 mg/kg, the major metabolite was hippuric acid, with smaller amounts of benzoic acid. At this dose level, an additional plasma metabolite (benzylmercapturic acid) occurred when propylene glycol was used as the vehicle. Urinary metabolites occurring were hippuric acid (66% of dose), benzoic acid (2% of dose), and benzylmercapturic acid (1% of dose).

A similar profile of metabolites was observed in the toxicokinetic studies of Yuan *et al.* (1993). After gavage administration of benzyl acetate in corn oil at 500 mg/kg (rats) and 1,000 mg/kg (mice), high benzoic acid plasma concentrations were observed. In contrast, much lower benzoic acid plasma concentrations were found after dosed feed administration at about 615 mg/kg per day for rats and about 850 mg/kg per day for mice. Although the daily doses of benzyl acetate were comparable, bolus

gavage administration effectively saturated the benzoic acid elimination pathway while dosed feed administration did not. In contrast, hippuric acid plasma concentrations were similar after both gavage and dosed feed administration due to the depletion of the glycine supply pool.

The influence of age on the distribution of ^{14}C-benzyl acetate in male F344 rats (age 3 to 4, 9, or 25 months) and male C57BL/6N mice (age 2, 13, or 25 months) was studied by McMahon *et al.* (1989). A single oral dose of 5 or 500 mg/kg was used for rats and 10 mg/kg benzyl acetate was used for mice. Hippuric acid formation from benzyl acetate in rats and mice was not affected by age or dose. In contrast, minor routes of excretion (biliary and fecal) were influenced by age. Irrespective of age or dose, 95% of the administered benzyl acetate was excreted as hippuric acid, whereas the percentage of the dose excreted in the urine as benzylmercapturic acid increased with age (0.1% for a 3- to 4-month-old rat compared to 0.2% for a 25-month-old rat). Plasma levels of this metabolite were higher in 500 mg/kg rats than in the 5 mg/kg rats. Fecal excretion of benzyl acetate declined with age in rats and was associated with an age-related decline in biliary excretion and higher plasma levels of benzyl acetate. In mice, urinary excretion of benzyl acetate was lower and fecal excretion was higher in 25-month-old animals than in 2- or 13-month-old animals.

Humans

No information on the absorption, distribution, metabolism, or excretion of benzyl acetate in humans was found in the literature.

TOXICITY

Experimental Animals

The reported oral LD_{50} for benzyl acetate was 2,490 mg/kg body weight for Osborne-Mendel rats (Jenner *et al.*, 1964) and 2,640 mg/kg for rabbits (Graham and Kuizenga, 1945). Mice and cats exposed to benzyl acetate by inhalation for 7 to 13 hours (mice, 1.3 mg/L; cats, 1.5 mg/L) experienced central nervous system depression and death (von Oettingen, 1960). Urine flow in dogs and rabbits increased 180% 2 hours after intraperitoneal injection of 0.4 mg/kg of benzyl acetate (Gruber, 1924).

The National Toxicology Program previously reported 14-day, 13-week, and 2-year gavage studies of benzyl acetate administered in corn oil by gavage to male and female F344/N rats and $B6C3F_1$ mice (NTP, 1986). In the 14-day study, all rats given 2,000 or 4,000 mg/kg died by day 5 of the study. No deaths or signs of toxicity occurred in rats given doses of 250, 500, or 1,000 mg/kg of benzyl acetate. In the 13-week study, deaths occurred in the high-dose (1,000 mg/kg) rat group; surviving males had a final mean body weight 12% lower than the control group. Tremors, ataxia, and lethargy occurred in male and female rats given doses of 1,000 mg/kg and in females given doses of 500 mg/kg. No chemical-related lesions occurred in rats of either sex.

In the NTP 14-day mouse study, all 2,000 mg/kg males died; no chemical-related deaths occurred in females. Chemical-related clinical findings included ataxia in 2,000 mg/kg males and labored breathing and hyperactivity in 2,000 mg/kg females. In the 13-week mouse study, the doses ranged from 62.5 to 1,000 mg/kg of benzyl acetate for males and 125 to 2,000 mg/kg for females. Chemical-related deaths occurred in females given doses of 2,000 mg/kg; none occurred in dosed males. Clinical findings in high-dose male and female mice included tremors, inactivity, labored breathing, and depressed body temperature. No chemical-related gross or microscopic lesions occurred in either male or female mice.

Humans

Benzyl acetate produces respiratory tract irritation and narcotic effects in humans, and continued exposure to benzyl acetate at an ambient concentration of 50 ppm results in kidney damage (*Handbook of Organic Industrial Solvents*, 1961; Opdyke, 1973). When ingested, benzyl acetate can cause generalized intestinal irritation (Clayton and Clayton, 1981).

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Experimental Animals

Sperm morphology and vaginal cytology of F344/N rats and $B6C3F_1$ mice fed diets containing 0, 3,300, 6,250, 12,500, 25,000, or 50,000 ppm of benzyl acetate for as long as 13 weeks were evaluated. The reports on these studies conducted by Environmental Health Research and Testing are on file at NIEHS. No

chemical-related effects on sperm morphology occurred in rats or mice. A significant dose-related decrease in body weight and a significant lengthening of the estrous cycle occurred in female mice. This effect did not occur in female rats. The lengthening of the estrous cycle observed in exposed female mice may be related to reduced body weights. Gulati *et al.* (unpublished) reported that diet restriction resulting in a 30% reduction in body weight relative to *ad libitum* fed controls caused a lengthening of the estrous cycle in mice.

Humans

No information on the reproductive and developmental toxicity of benzyl acetate in humans was found in the literature.

CARCINOGENICITY

Experimental Animals

In 2-year studies (NTP, 1986), F344/N rats were given benzyl acetate in corn oil by gavage at doses of 0, 250, or 500 mg/kg body weight and B6C3F$_1$ mice were given doses of 0, 500, or 1,000 mg/kg body weight. In male rats, benzyl acetate administration was associated with increased incidences of acinar cell adenomas of the pancreas (control, 22/50; low-dose, 27/50; high-dose, 37/50). There was no evidence of carcinogenic activity of benzyl acetate in female rats. Benzyl acetate administration to male and female mice caused increased incidences of hepatocellular neoplasms and marginally increased incidences of squamous cell neoplasms of the forestomach. Because the increases were mainly for benign neoplasms and the effect was observed only at the highest dose, the results were considered to provide some evidence of carcinogenicity of benzyl acetate in mice.

Other studies suggest that the use of a corn oil vehicle may have been a contributing factor in the increased incidence of pancreatic adenomas in benzyl acetate dosed male rats. A review of data from several NTP studies indicated that the incidences of pancreatic hyperplasia and adenomas in corn oil vehicle control male rats were significantly higher than those occurring in untreated controls (Boorman and Eustis, 1984). Longnecker *et al.* (1986) observed that corn oil given by gavage or in the diet in the presence or absence of benzyl acetate to azaserine-treated Lewis rats enhanced development (number and size) of pancreatic acinar cell foci. Azaserine, a pancreatic carcinogen, was given to rats as a single injection of 30 mg/kg body weight on day 14 of the study. Corn oil (5 mL/kg body weight) was given either by gavage once daily, 5 days a week for 4 months, or continuously in the diet for 4 months. A significant linear response occurred between the number and volume of acinar cell foci and the amount of corn oil given, regardless of the route of administration. Benzyl acetate given in corn oil by gavage at a dose of 500 mg/kg or in the diet at 9,000 ppm did not affect development of pancreatic acinar cell foci in azaserine-treated male Lewis or F344 rats. In a more recent study (Longnecker *et al.*, 1990) of male F344 rats, no damage to pancreatic acinar cell DNA occurred 1 hour after an intraperitoneal injection of benzyl acetate (1,500 mg/kg) dissolved in dimethyl sulfoxide. Additionally, a concentration of 8,000 ppm in the diet stimulated the growth of azaserine-induced acinar cell foci at the end of 6 months, and F344 rats fed benzyl acetate (8,000 ppm) for 2 years without azaserine pretreatment showed a low but significantly increased incidence of anaplastic changes and pancreatic desmoplasia at the end of 2 years. These results suggest that benzyl acetate is a weak promoter of carcinogen-induced and spontaneous preneoplastic pancreatic foci. In the azaserine study, male rats (20 per dose group) received two intraperitoneal injections of azaserine (30 mg/kg) at ages 16 and 23 days and were then fed AIN-76 diet with or without benzyl acetate. In the 2-year study, groups of 25 male rats not pretreated with azaserine were fed AIN-76 diet with or without benzyl acetate.

Humans

No information on the carcinogenicity of benzyl acetate in humans was found in the literature.

GENETIC TOXICITY

Benzyl acetate has been tested in a variety of genetic toxicity assays and most results have been negative. The compound did not inhibit growth due to DNA damage in *Bacillus subtilis* (Oda *et al.*, 1978) or induce mutations in any of several standard *Salmonella typhimurium* test strains, with or without S9 (Florin *et al.*, 1980; Mortelmans *et al.*, 1986). Treatment with benzyl acetate without S9, however, did induce mitotic chromosome loss in a diploid strain of *Saccharomyces cerevisiae* (Zimmermann *et al.*, 1989). Benzyl acetate induced mutations in mouse lymphoma cells with and without S9 (Caspary *et al.*, 1988; McGregor *et al.*, 1988). Gene mutations

at the TK locus in human TK6 lymphoblastoid cells increased in frequency after benzyl acetate treatment with S9 (Caspary *et al.*, 1988). No increases in sister chromatid exchanges or chromosomal aberrations occurred in cultured Chinese hamster ovary cells treated with benzyl acetate, with or without S9 (Galloway *et al.*, 1987). *In vivo*, unscheduled DNA synthesis was not induced in hepatocytes (Mirsalis *et al.*, 1989) or pancreatic cells (Steinmetz and Mirsalis, 1984) of male rats administered benzyl acetate by gavage.

Mutagenicity information is available for three metabolites of benzyl acetate: benzyl alcohol, benzoic acid, and hippuric acid. The results were negative in the majority of the assays in which the three compounds were tested. Benzyl alcohol did not induce mutations in *S. typhimurium* (Florin *et al.*, 1980; Ishidate *et al.*, 1984; Mortelmans *et al.*, 1986) or inhibit growth in DNA repair-deficient strains of *Escherichia coli* (Fluck *et al.*, 1976) or *B. subtilis* (Oda *et al.*, 1978); a questionable response was reported in the mouse lymphoma cell mutation assay of benzyl alcohol (McGregor *et al.*, 1988). Chromosomal aberrations were not induced in mammalian cells treated with benzyl alcohol *in vitro* (Waters *et al.*, 1982; Ishidate *et al.*, 1984) nor were micronuclei induced in mouse bone marrow cells after treatment with benzyl alcohol *in vivo* (Hayashi *et al.*, 1988).

Benzoic acid, the second metabolite for which mutagenicity information is available, did not induce mutations in *S. typhimurium* (Cotruvo *et al.*, 1977; Simmon and Kauhanen, 1978; Ishidate *et al.*, 1984; Zeiger *et al.*, 1988) or *E. coli* (Kikuchi *et al.*, 1977) or sister chromatid exchanges in mammalian cells *in vitro* (Oikawa *et al.*, 1980; Tohda *et al.*, 1980; Jansson *et al.*, 1988). Benzoic acid produced weakly positive results in a test for induction of chromosomal aberrations in cultured Chinese hamster lung cells *in vitro* (Ishidate *et al.*, 1984). The third metabolite, hippuric acid, did not produce positive results in *S. typhimurium* gene mutation tests (Milvy and Garro, 1976; Wang, 1977; Wiessler *et al.*, 1983).

STUDY RATIONALE

The carcinogenicity of benzyl acetate was previously examined by the NTP in 2-year corn oil gavage studies in F344/N rats and B6C3F$_1$ mice (NTP, 1986). However, because of the potential confounding effect of corn oil on the incidence of pancreatic acinar cell adenomas in rats and because of the questions about the use of gavage administration, the NTP decided to reexamine the carcinogenicity of benzyl acetate by using dosed feed. Gavage was chosen as the route of administration in the previous studies because of the volatility and instability of benzyl acetate when mixed with feed. To minimize losses in these dosed feed studies, the feed was changed daily.

MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF BENZYL ACETATE

Benzyl acetate was obtained in two lots (8743-84 and 845585) from Givaudan Corporation (Clifton, NJ). Identity and purity analyses were conducted by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO), and confirmed by the study laboratory (Appendix I).

Both lots of the chemical, a clear, colorless liquid, were identified as benzyl acetate by infrared, nuclear magnetic resonance, and ultraviolet/visible spectroscopy. The purity of each lot was found to be at least 98% by elemental analyses, Karl Fischer water analysis, titrations for free acid and ester, thin-layer chromatography, and gas chromatography. Thin-layer chromatography indicated one major spot. Gas chromatography indicated a major peak and one impurity with an area of approximately 0.4% (8743-84) or 0.21% (845585) relative to the major peak.

Stability studies performed at the analytical chemistry laboratory indicated that benzyl acetate was stable as a bulk chemical for 2 weeks at temperatures as high as 60° C. The stability of the bulk chemical was monitored periodically by the study laboratory using infrared and ultraviolet spectroscopy and gas chromatography; no change in purity was observed.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

Dose formulations for the 13-week and 2-year studies were prepared weekly by mixing benzyl acetate with feed (Table I1). The dose formulations were stored at −20° C in sealed, double plastic bags for no longer than 13 days. Details of preparation and storage of dose formulations are presented in Table I1.

Periodic analyses of the dose formulations of benzyl acetate were conducted at the study laboratory and the analytical chemistry laboratory using gas chromatography. The stability of 330 ppm dose formulations stored in the dark at −20° C was established for at least 3 weeks. Dose formulations were analyzed four times for the 13-week studies and approximately every 6 to 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 I2 and I3). The results of periodic referee analysis performed by the analytical chemistry laboratory indicated agreement with the results obtained by the study laboratory (Table I4). To minimize losses in these dosed feed studies, the feed was changed daily. With the feed available in open feeders for 24 hours, the benzyl acetate concentration remained within 10% of the target concentration.

13-WEEK STUDIES

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Frederick Cancer Research Facility (Frederick, MD). At receipt, the rats were an average of 30 days old and the mice were an average of 29 days old. The rats and mice were quarantined for 13 days before dosing began. During this time, five male and five female rats and mice 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 control animals of each species and sex using the protocols of the NTP Sentinel Animal Program (Appendix L).

Groups of 10 male and 10 female rats and mice were fed diets containing 0, 3,130, 6,250, 12,500, 25,000, or 50,000 ppm (0, 230, 460, 900, 1,750, or 3,900 mg/kg for male rats and 0, 240, 480, 930, 1,870, or 4,500 mg/kg for female rats; 0, 425, 1,000, 2,000, 3,700, or 7,900 mg/kg for male mice and 0, 650, 1,280, 2,980, 4,300, or 9,400 mg/kg for female mice) benzyl acetate for 13 weeks. The appropriate feed was supplied every 1 to 2 days. Feed and water were available *ad libitum*. Feed consumption was recorded daily by cage. Rats were housed five per cage and mice were housed individually. Clinical findings were recorded once weekly. The animals were weighed at the beginning of the studies, weekly, and at the end of the studies. Further details of study design and animal maintenance are summarized in Table 1.

At the end of 11 weeks, blood was collected from the orbital sinus of rats for hematology and clinical chemistry analyses. At the end of the 13-week study, blood was collected from the heart of mice for hematology and clinical chemistry analyses. The clinical pathology parameters measured are listed in Table 1. A necropsy was performed on all animals. The brain, right kidney, liver, pancreas, prostate gland, seminal vesicle, spleen, right testis, thymus, and uterus (rats) of rats and mice were weighed. Pancreas samples from all control rats and mice, from exposed male and female rats except the 50,000 ppm group, and from all exposed male and female mice were collected for assays of levels of pancreatic enzymes, including amylase, lipase, carboxypeptidase, chymotrypsin, and ribonuclease. Liver samples from female rats fed diets of 0, 25,000, or 50,000 ppm benzyl acetate for 13 weeks were collected for electron microscopic evaluation of peroxisomes. Tissues for light 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 control, 25,000, and 50,000 ppm rats. The testis and epididymis of 6,250 and 12,500 ppm male rats were also examined. A complete histopathologic examination was performed on all control, 25,000 ppm females, and all 50,000 ppm mice. Table 1 lists the tissues and organs routinely examined.

2-YEAR STUDIES

Study Design

Groups of 60 male and 60 female rats were fed diets containing 0, 3,000, 6,000, or 12,000 ppm benzyl acetate for as long as 103 weeks. Groups of 60 male and 60 female mice were fed diets containing 0, 330, 1,000, or 3,000 ppm benzyl acetate for as long as 103 weeks. Ten male and ten female rats and mice per exposure group were evaluated after 15 months of chemical exposure.

Source and Specification of Animals

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Simonsen Laboratories, Inc. (Gilroy, CA), for use in the 2-year studies. Rats were quarantined for 12 days, and mice were quarantined for 11 days before the beginning of the studies. During this time, five rats and five mice of each sex were selected for parasite evaluation and gross observation of disease. Serology samples were collected for viral screening. Rats were approximately 41 days old and mice were approximately 40 days old at the beginning of the 2-year studies. The health of the animals was monitored during the studies according to the protocols of the NTP Sentinel Animal Program (Appendix L).

Animal Maintenance

Rats were housed five per cage and mice were housed individually. Feed and water were available *ad libitum*. Feed consumption was measured daily per cage for 5 days once every 4 weeks (Appendix J). 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 K.

Clinical Examinations and Pathology

All animals were observed twice daily. Animals were weighed and clinical findings were recorded weekly for the first 13 weeks, every 4 weeks thereafter, and at the end of the study. Blood was collected from the retroorbital sinus of rats and mice at the 15-month interim evaluations to determine hematology and clinical chemistry parameters. The clinical pathology parameters are listed in Table 1. The brain, right kidney, and liver were weighed at the 15-month interim evaluations. The pancreas of male rats was assayed for pancreatic enzyme (amylase, lipase, and carboxypeptidase) levels at the 15-month interim evaluation.

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 μm, and stained with hematoxylin and eosin for microscopic examination. Complete histopathologic examinations were performed on all animals. 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.

The quality assessment report and slides were submitted to the NTP Pathology Working Group (PWG) chair, who reviewed the selected 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, pancreas, and testis in male rats, uterus in female rats, nose in male and female mice, and ovary and uterus in 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).

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 found dead of other than natural causes were censored from the survival analyses; 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, A4, B1, B4, C1, C4, 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 fit of the model was not significantly enhanced. The exposed 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 exposed group with controls and a test for an

overall dose-related 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 these studies 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 exposed 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 and hematology 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-related 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-related trend (Dunnett's or Dunn's test). Average severity values were analyzed for significance using the Mann-Whitney U test (Hollander and Wolfe, 1973).

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 benzyl acetate was assessed by testing the ability of the chemical to induce mutations in various strains of *Salmonella typhimurium* and mouse lymphoma cells, sister chromatid exchanges and chromosomal aberrations in cultured Chinese hamster ovary cells and mouse bone marrow, induction of sex-linked recessive lethal mutations in *Drosophila melanogaster*, and micronuclei in mouse bone marrow and peripheral blood. The protocols for these studies and the results are given in Appendix E.

The genetic toxicity studies of benzyl acetate 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 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 chemical-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 Feed Studies of Benzyl Acetate

13-Week Studies	2-Year Studies
Study Laboratory Southern Research Institute (Birmingham, AL)	Same as 13-week studies
Strain and Species Rats: F344/N Mice: B6C3F$_1$	Same as 13-week studies
Animal Source Frederick Cancer Research Facility (Frederick, MD)	Simonsen Laboratories, Inc. (Gilroy, CA)
Time Held Before Studies 13 days	Rats: 12 days Mice: 11 days
Average Age When Studies Began Rats: 43 days Mice: 42 days	Rats: 41 days Mice: 40 days
Date of First Dose Rats: 30 April 1985 Mice: 14 May 1985	Rats: 9 September 1986 Mice: 25 August 1986
Duration of Dosing 13 weeks	103 weeks
Date of Last Dose Rats: 30 July to 2 August 1985 Mice: 12-14 August 1985	Rats: 29 August 1988 Mice: 14 August 1988
Necropsy Dates Rats: 30 July to 2 August 1985 Mice: 13-15 August 1985	Rats 15-month interim: 8-10 December 1987 Terminal: 6-12 September 1988 Mice 15-month interim: 23-25 November 1987 Terminal: 22-26 August 1988
Average Age at Necropsy 19 weeks	110 weeks
Size of Study Groups 10 males and 10 females	60 males and 60 females
Method of Distribution Animals were grouped by weight and assigned to cages and the cages assigned to exposure groups using tables of random numbers.	Same as 13-week studies

TABLE 1
Experimental Design and Materials and Methods in the Feed Studies of Benzyl Acetate
(continued)

13-Week Studies	2-Year Studies
Animals per Cage Rats: 5 Mice: 1	Same as 13-week studies
Method of Animal Identification Toe clip	Same as 13-week studies
Diet NIH-07 open formula meal rat and mouse diet (Zeigler Brothers, Inc., Gardners, PA), available *ad libitum*	Same as 13-week studies
Maximum Storage Time for Feed 120 days after milling	Same as 13-week studies
Water Automatic watering system (Edstrom Industries, Waterford, WI), available *ad libitum*	Same as 13-week studies
Cages Polycarbonate (Lab Products, Inc., Maywood, NJ), changed twice weekly (rats) or weekly (mice)	Same as 13-week studies
Bedding BetaChips®, hardwood chips (Northeastern Products, Inc., Warrensburg, NY), changed twice weekly (rats) or weekly (mice)	Same as 13-week studies through 12 February 1987, then Sani-Chips (P.J. Murphy Forest Products Corp., Montville, NJ)
Cage Filters Spun-bonded polyester (Andico, Birmingham, AL), changed once every 2 weeks	Same as 13-week studies
Racks Stainless steel (Lab Products, Inc., Maywood, NJ), changed once every 2 weeks	Same as 13-week studies
Animal Room Environment Temperature: 23.6° ± 3° C (rats), 22.2° ± 3° C (mice) Relative humidity: 46% to 65% (rats), 39% to 59% (mice) Fluorescent light: 12 hours/day Room air: minimum of 10 changes/hour	Temperature: 21.9° ± 0.4° C (rats), 22.6° ± 0.6° C (mice) Relative humidity: 45.4% to 54% (rats), 45% to 52.6% (mice) Fluorescent light: 12 hours/day Room air: minimum of 10 changes/hour
Exposure Levels 0, 3,130, 6,250, 12,500, 25,000, or 50,000 ppm in feed, available *ad libitum*	Rats: 0, 3,000, 6,000, or 12,000 ppm in feed, available *ad libitum* Mice: 0, 330, 1,000, or 3,000 ppm in feed, available *ad libitum*

TABLE 1
Experimental Design and Materials and Methods in the Feed Studies of Benzyl Acetate
(continued)

13-Week Studies	2-Year Studies
Type and Frequency of Observation	
Observed twice daily. Animals weighed initially, weekly, and at end of study. Clinical observations recorded once weekly. Feed consumption recorded daily by cage.	Observed twice daily. Clinical observations and animal weights recorded initially, weekly during first 13 weeks of study, every 4 weeks thereafter, and at end of study. Feed consumption measured daily per cage for 5 days once every 4 weeks.
Method of Sacrifice	
Carbon dioxide asphyxiation (rats) or carbon dioxide anesthesia followed by perfusion (rats) or ether anesthesia followed by thoracotomy (mice)	Carbon dioxide anesthesia followed by thoracotomy for interim evaluation; carbon dioxide asphyxiation for terminal evaluation
Necropsy	
Necropsy was performed on all animals. Organs weighed were brain, right kidney, liver, pancreas, prostate gland, seminal vesicle, spleen, right testis, thymus, and uterus (rats).	Necropsy was performed on all animals. Organs weighed were brain, right kidney, and liver.
Clinical Pathology	
Blood was collected from the orbital sinus (rats) or heart (mice). Pancreas samples from all control and exposed male and female rats except the 50,000 ppm group and all control and exposed mice were collected. Liver samples from control, 25,000 and 50,000 ppm female rats were collected. ***Hematology:*** hematocrit, hemoglobin, erythrocytes, mean erythrocyte volume, mean erythrocyte hemoglobin, mean erythrocyte hemoglobin concentration, platelets, reticulocytes, and leukocyte count and differential ***Clinical chemistry:*** cholesterol and triglyceride ***Pancreatic enzyme analyses:*** amylase, lipase, carboxypeptidase, chymotrypsin, and ribonuclease ***Morphometric analyses:*** liver peroxisomes by electron microscopy (female rats)	Blood was collected from the retroorbital sinus of rats and mice. Pancreas samples (interim evaluation male rats) were collected. ***Hematology:*** hematocrit, hemoglobin, erythrocytes, mean erythrocyte volume, mean erythrocyte hemoglobin, mean erythrocyte hemoglobin concentration, platelets, reticulocytes, and leucocyte count and differential ***Clinical chemistry:*** cholesterol, triglyceride, alkaline phosphatase, creatine kinase, and sorbitol dehydrogenase ***Pancreatic enzyme analyses:*** amylase, lipase, and carboxypeptidase
Histopathology	
Complete histopathologic examinations were performed on all control, 25,000, and 50,000 ppm rats, and on all control, 25,000 ppm females, and all 50,000 ppm mice. In addition to gross lesions, tissue masses, and associated lymph nodes, the tissues examined included: adrenal gland, bone (including marrow), brain, esophagus, gallbladder (mice), heart, kidney, large intestine (cecum, colon, and rectum), liver, lung, mammary gland, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial or clitoral gland (rats), prostate gland, salivary gland, skin, small intestine, spleen, stomach (forestomach and glandular), testis with epididymis and seminal vesicle, thigh muscle, thymus, thyroid gland, tongue, trachea, urinary bladder, and uterus. The testis with epididymis of 6,250 and 12,500 ppm male rats were also examined.	Complete histopathologic examinations were performed on all animals. In addition to gross lesions, tissue masses, and associated lymph nodes, the tissues examined included: adrenal gland, brain, esophagus, femur (including marrow), gallbladder (mice), heart, kidney, large intestine (cecum, colon, and rectum), liver, lung, mammary gland, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial or clitoral gland (rats), prostate gland, salivary gland, skeletal muscle, skin, small intestine, spleen, stomach (forestomach and glandular), testis with epididymis and seminal vesicle, thymus, thyroid gland, tongue, trachea, urinary bladder, and uterus.

RESULTS

RATS

13-WEEK STUDY

Nine male and nine female rats receiving 50,000 ppm benzyl acetate died or were killed moribund between weeks 2 and 8 of the study (Table 2). One 12,500 ppm female died under anesthesia during blood collection at the end of the study. The mean body weight gain and the final mean body weight of 25,000 ppm male rats were significantly lower than those of the control. The final mean body weight of 25,000 ppm males was 10% lower than that of the control group, whereas the final body weights of the surviving 50,000 ppm male and female were less than half those of the controls. Final mean body weights of males and females of other exposed groups were similar to or slightly lower than those of the controls. Feed consumption by exposed rats was similar to controls in all groups except 25,000 and 50,000 ppm

TABLE 2
Survival, Mean Body Weights, and Feed Consumption of Rats in the 13-Week Feed Study of Benzyl Acetate

Dose (ppm)	Survival[a]	Mean Body Weights[b] (g)			Final Weight Relative to Controls (%)	Feed Consumption[c]
		Initial	Final	Change		
Male						
0	10/10	131 ± 2	349 ± 5	219 ± 4		17.8
3,130	10/10	131 ± 2	352 ± 5	222 ± 6	101	17.8
6,250	10/10	127 ± 3	348 ± 8	221 ± 9	100	17.7
12,500	10/10	130 ± 3	342 ± 6	212 ± 7	98	17.1
25,000	10/10	129 ± 2	315 ± 8**	186 ± 6**	90	15.8
50,000	1/10[d]	127 ± 3	128[e]	–[e]	36	10.2
Female						
0	10/10	104 ± 2	199 ± 2	95 ± 2		11.8
3,130	10/10	105 ± 2	196 ± 3	91 ± 2	98	11.6
6,250	10/10	104 ± 2	194 ± 4	90 ± 3	97	11.5
12,500	9/10[f]	106 ± 2	191 ± 3	85 ± 3*	96	11.1
25,000	10/10	105 ± 2	189 ± 5	84 ± 4**	95	11.0
50,000	1/10[g]	102 ± 2	93[e]	–[e]	47	9.0

* 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 studies.
[c] The average feed consumption during weeks 2 through 13 is expressed as grams per animal per day. Feed consumption was not calculated for week 1.
[d] Week of death: 2, 3, 4, 4, 4, 5, 6, 7, 8
[e] No statistic calculated due to high mortality.
[f] Week of death: 13
[g] Week of death: 2, 2, 3, 3, 3, 4, 4, 4, 5

males and 50,000 ppm females. The reduced feed consumption by 25,000 and 50,000 ppm males and 50,000 ppm females may have been due to decreased palatability and/or toxicity. Clinical findings related to toxicity observed in the 50,000 ppm rats included tremors, ataxia, and urine stains. These findings were first observed on day 15 of the study in nine males and six females and continued until the end of the study.

Slight differences in organ weights were observed and were considered secondary to the reduced body weights (Table F1). Excluding the data from the 50,000 ppm males and females (only one survivor in each group), hematology values for all exposed groups were similar to those of the control groups (Table G1). The clinical chemistry evaluations showed significantly lower cholesterol levels in 12,500 and 25,000 ppm female rats (Table G1) than in the controls. No chemical-related differences occurred in the cholesterol or triglyceride levels in exposed males.

No chemical-related differences in the activity of pancreatic enzymes in the homogenate of pancreata of rats were found (Table H1). No evaluations of the highest exposure group were made due to reduced survival. The amylase and carboxypeptidase A activities increased with exposure level and chymotrypsin activity decreased with exposure level in males. Since these enzymes are produced by pancreatic acinar cells, and since no chemical-related increase in the incidence of pancreatic acinar cell hyperplasia was observed, the differences in activities observed in these enzymes were not considered to be related to benzyl acetate administration.

In the evaluation of hepatic peroxisomes in female rats, significant increases in volume, surface, and numerical densities of peroxisomes in rat liver occurred in the 25,000 ppm group (Table 3). Compared to control values, 25,000 ppm females had a 1.6-fold increase in peroxisomal volume, a 2.0-fold increase in surface density, and a 2.9-fold increase in numerical density.

In exposed female rats, peroxisomes were identified by the cytochemical localization of catalase activity. The hepatocytes of control females had typical morphology and contained mostly spherical peroxisomes with little variation in size. The hepatocytes of 25,000 ppm females had typical morphology; however, the number, size, and shape of the peroxisomes varied considerably. In the livers of two female rats receiving 25,000 ppm, numerous bizarrely shaped degenerating peroxisomes occurred.

The diffusion of electron-dense reaction products was visible through the peroxisomal membrane. The peroxisomes apparently degenerated through autophagic vacuoles. A higher magnification examination of hepatocytes in exposed female rats showed a close spatial relationship between a smooth endoplasmic reticulum and peroxisomes. The limiting membrane of the peroxisomes appeared to be intact, although in some of the peroxisomes, diffusion of catalase was visible. Membrane continuity between peroxisome

TABLE 3
Morphometric Analysis of Hepatic Peroxisomes for Female Rats in the 13-Week Feed Study of Benzyl Acetate[a]

Dose (ppm)	0	25,000	50,000
n	10	10	1[b]
Volume density (% cytoplasm)	1.04 ± 0.05	1.65 ± 0.12***	3.10
Surface density ($\mu m^2/\mu m^3$)	0.114 ± 0.004	0.231 ± 0.011***	0.300
Numerical density (μm^{-3})	0.140 ± 0.013	0.404 ± 0.040***	0.341

***Significantly different (P≤0.001) from the control group by Student's *t*-test
[a] Mean ± standard error
[b] No standard errors were calculated for groups with high mortality.

and microperoxisome was also observed. Peroxisomes in the proximity of lipid droplets and mitochondria were apparent.

The principal nonneoplastic lesions associated with exposure of rats to benzyl acetate in feed for 13 weeks occurred in the brain, kidney, tongue, and skeletal muscles of the thigh (Table 4). Necrosis of the brain involving the cerebellum and/or the hippocampus occurred in all 50,000 ppm male and female rats but did not occur in any of the 25,000 ppm rats. The lesions were consistent in location, primarily involved the granular layer of the cerebellum and the pyramidal layer of the hippocampus, and were characterized by degeneration and extensive necrosis of neurons and glial cells (Plates 1 and 2). The necrosis was moderate or marked in severity in all 50,000 ppm male rats and in most females and mild in a few females. The severity of the lesion increased with length of exposure to benzyl acetate. The Purkinje cells of one female rat were markedly vacuolated. Concretions suggestive of mineral deposits were associated with cerebellar necrosis in three males and one female of the 50,000 ppm groups. The concretions appeared as localized or focal aggregates of roughly spherical basophilic structures (Plate 3). This lesion was mild to marked in severity and occurred in those rats with the longest exposure to benzyl acetate. On reexamination, similar lesions were observed in the brain of male and female 1,000 mg/kg rats in the previous NTP 13-week benzyl acetate gavage study; however, these lesions were less severe than those observed in the present dosed feed study. The lesions consisted of hippocampal necrosis with a higher incidence and greater severity in males than in females (males, 8/8; females, 4/10).

Renal tubule degeneration and regeneration occurred in seven male and eight female rats in the 50,000 ppm groups (Table 4). The changes occurred primarily in the outer cortex of the kidney, with the severity ranging from minimal to moderate. Renal tubule degeneration was characterized by slightly basophilic cells with vacuolated cytoplasm lining the renal tubules, which in some instances had dilated lumina (Plate 4). Karyorrhectic nuclei occasionally occurred in renal tubule epithelial cells, denoting minimal necrosis. Renal tubule regeneration was characterized by increased numbers of mitotic figures in the renal tubule epithelial cells of some rats. These degenerative and regenerative renal lesions did not occur in 25,000 ppm rats. Nephropathy, a spontaneous kidney change primarily occurring in male rats, occurred in nine control male rats and in four 25,000 ppm males and was minimal in severity. Nephropathy did not occur in any 50,000 ppm males and may have been masked by the chemical-related renal tubule degeneration and regeneration.

Degeneration and sarcolemma nuclear hyperplasia occurred in the skeletal muscles of the thigh and in the tongue of most 50,000 ppm male and female rats (Table 4). Degeneration was characterized by randomly arranged muscle fibers with increased basophilia, loss of cross-striations, and faint vacuolation. The severity of the lesion varied from mild to marked, and in some of the more severe cases, the degenerated muscle fibers had increased eosinophilia and marked dissolution with the infiltration of mixed inflammatory cells (Plates 5 and 6). Accompanying the degenerative changes were increased numbers (proliferation) of the sarcolemmal nuclei of mild to marked severity (Plate 5). In one 50,000 ppm female, diffuse infiltration of mast cells and neutrophils into the tongue musculature occurred. Mild chronic inflammation of the tongue of one male and one 25,000 ppm female was focal in nature and probably spontaneous. No chemical-related skeletal muscle or tongue lesions occurred in the 25,000 ppm groups.

Testicular changes related to chemical exposure occurred in male rats receiving 12,500, 25,000, and 50,000 ppm dosed feed. The lesions were characterized by mild or moderate aspermatogenesis in two 50,000 ppm male rats and atrophy of seminiferous tubules in two 25,000 ppm and one 12,500 ppm rats. In one 25,000 ppm rat, the seminiferous tubule atrophy was marked in severity and included atypical cells (enlarged, degenerated spermatozoa) in the corresponding epididymis and mild interstitial cell hyperplasia. The seminiferous tubule atrophy was minimal in severity in one 12,500 ppm rat. No testicular lesions occurred in the 6,250 ppm or lower exposure levels.

Several changes in 50,000 ppm rats were considered indirectly related to chemical exposure. These changes included depletion of the cellular components of the bone marrow, thymus (atrophy), and splenic lymphoid follicles, zymogen granule depletion and increased basophilia of the pancreatic acinar cells

(cytoplasmic alteration), minimal to mild erosions of the glandular stomach, secretory depletion of the seminal vesicles, and immature/hypoplastic uterus. These changes are frequently observed in rodents and are usually caused by debilitation, stress, age, or poor nutrition. Although ultrastructural changes of liver peroxisomes occurred in 25,000 ppm female rats, no chemical-related lesions were found in the livers of either sex using light microscopy.

Dose Selection Rationale

Dietary concentrations selected for the 2-year study in rats were 0, 3,000, 6,000, or 12,000 ppm benzyl acetate. The 25,000 and 50,000 ppm levels were considered too high for males and females because of the reduced mean body weights of and feed consumption by rats receiving 25,000 and 50,000 ppm and the low survival and microscopic lesions that occurred in 50,000 ppm rats in the 13-week study.

TABLE 4
Selected Incidences of Nonneoplastic Lesions in Rats in the 13-Week Feed Study of Benzyl Acetate[a]

Dose (ppm)	0	25,000	50,000
Male			
Brain (Cerebellum/Hippocampus)	10	10	9
Necrosis	0	0	9**(3.5)
Concretions	0	0	3 (3.0)
Kidney	10	10	9
Renal Tubule Degeneration	0	0	7**(2.1)
Renal Tubule Regeneration	0	0	6**(2.3)
Skeletal Muscle	10	10	9
Degeneration	0	0	8**(2.2)
Sarcolemma Nuclear Hyperplasia	0	0	9**(3.1)
Tongue	10	10	9
Degeneration	0	0	7**(2.3)
Sarcolemma Nuclear Hyperplasia	0	0	9**(2.4)
Female			
Brain (Cerebellum/Hippocampus)	10	10	10
Necrosis	0	0	10**(2.9)
Concretions	0	0	1 (4.0)
Kidney	10	10	10
Renal Tubule Degeneration	0	0	8**(1.7)
Renal Tubule Regeneration	0	0	8**(2.0)
Skeletal Muscle	10	10	10
Degeneration	0	0	8**(2.6)
Sarcolemma Nuclear Hyperplasia	0	0	8**(2.7)
Tongue	10	10	10
Degeneration	0	0	6**(2.2)
Sarcolemma Nuclear Hyperplasia	0	0	9**(2.3)

** Significantly different ($P \leq 0.01$) from the control group by Fisher's exact test

[a] Animals examined microscopically and number of animals with lesion; animals in the 3,130, 6,250, and 12,500 ppm groups were not examined microscopically. Average severity grade (in parentheses) for affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked

2-YEAR STUDY

Survival

Estimates of survival probabilities for male and female rats fed diets containing benzyl acetate for 2 years are presented in Table 5 and in the Kaplan-Meier curves in Figure 1. The survival rates among exposed rats were similar to those of the controls.

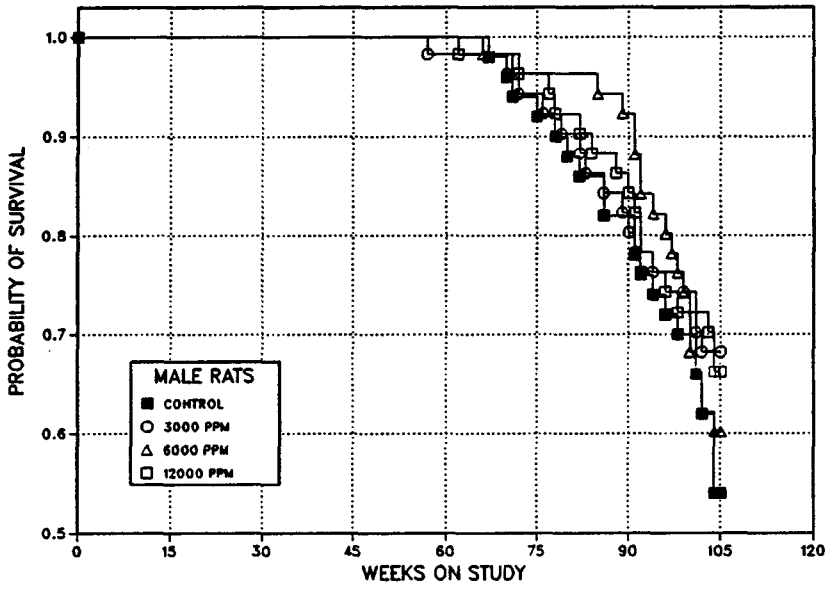
Body Weights, Feed and Compound Consumption, and Clinical Findings

The mean body weights of male rat groups receiving 3,000 and 6,000 ppm were similar to those of the control group throughout the study (Figure 2 and Table 6). The mean body weights of the 12,000 ppm males and exposed females (Table 7) were

TABLE 5
Survival of Rats in the 2-Year Feed Study of Benzyl Acetate

Dose (ppm)	0	3,000	6,000	12,000
Male				
Animals initially in study	60	60	60	60
15-Month interim evaluation[a]	10	10	10	10
Moribund	20	12	16	14
Natural deaths	3	4	4	3
Animals surviving to study termination	27	34	30	33
Percent probability of survival at end of study[b]	54	68	60	66
Mean survival (days)[c]	646	649	658	652
Survival analysis[d]	P=0.455N	P=0.291N	P=0.632N	P=0.346N
Female				
Animals initially in study	60	60	60	60
15-Month interim evaluation[a]	10	10	10	10
Moribund	18	17	13	19
Natural deaths	2	3		3
Animals surviving to study termination	30	30	37	28
Percent probability of survival at end of study	60	60	74	56
Mean survival (days)	654	657	670	663
Survival analysis	P=0.946	P=1.000N	P=0.134N	P=0.924

[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 exposed columns. A negative trend or lower mortality in an exposure group is indicated by N.



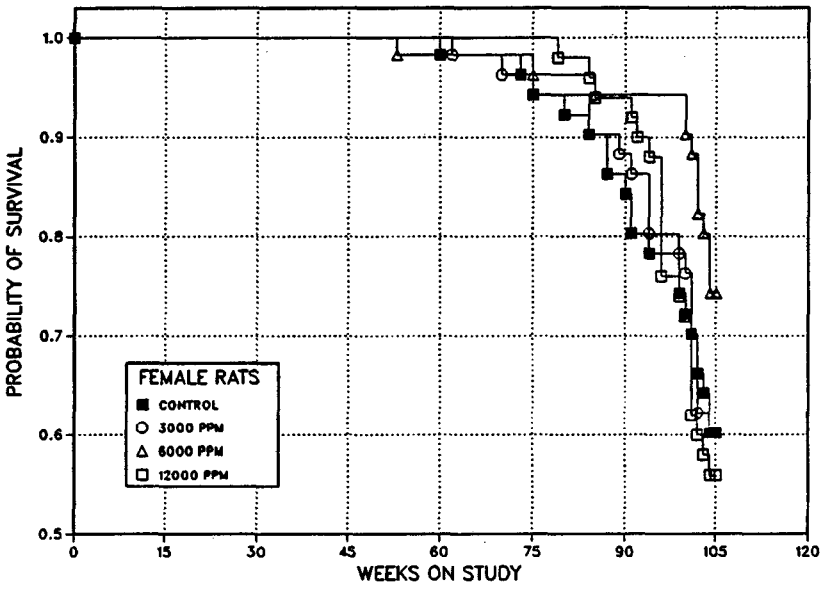


FIGURE 1
Kaplan-Meier Survival Curves for Male and Female F344/N Rats Administered Benzyl Acetate in Feed for 2 Years

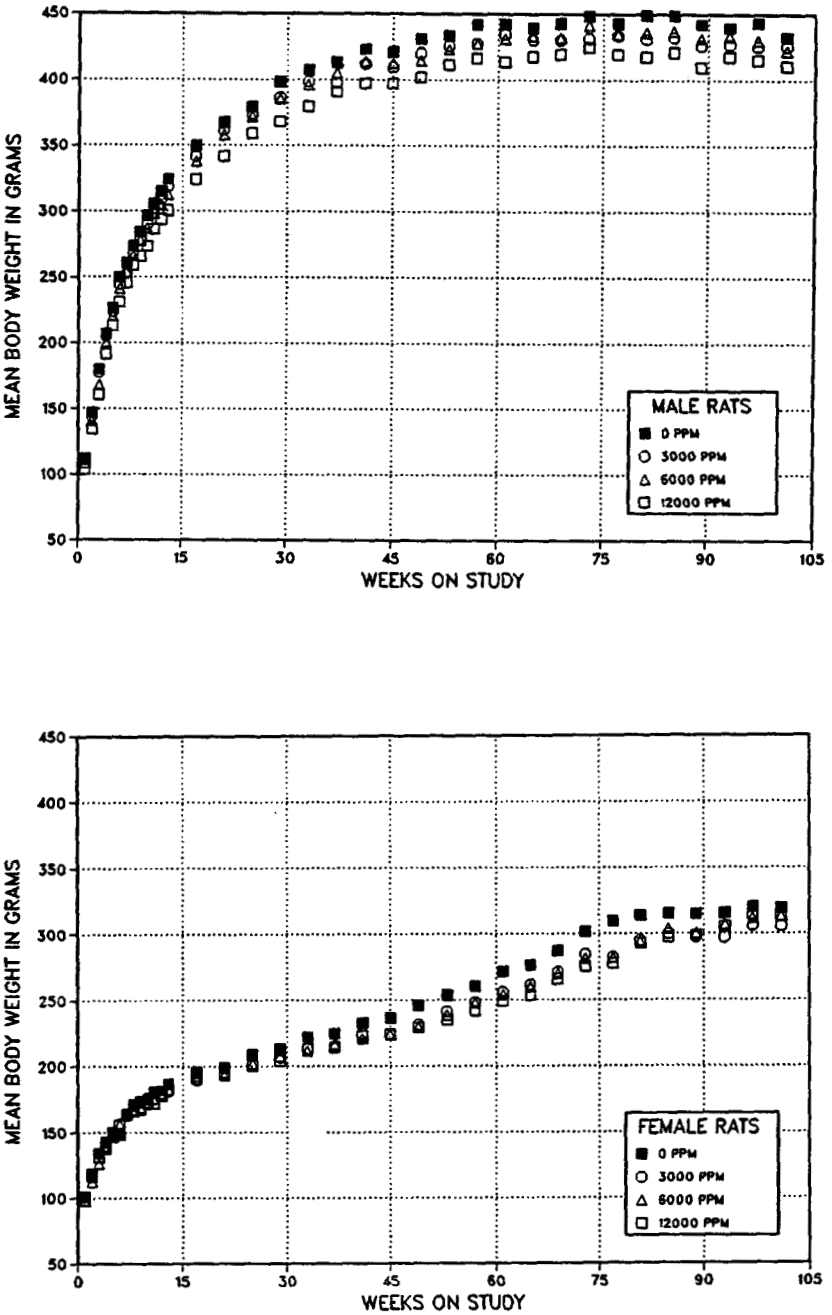


FIGURE 2
Growth Curves for Male and Female F344/N Rats Administered Benzyl Acetate in Feed for 2 Years

TABLE 6
Mean Body Weights and Survival of Male Rats in the 2-Year Feed Study of Benzyl Acetate

Weeks on Study	0 ppm Av. Wt. (g)	0 ppm No. of Survivors	3,000 ppm Av. Wt. (g)	3,000 ppm Wt. (% of controls)	3,000 ppm No. of Survivors	6,000 ppm Av. Wt. (g)	6,000 ppm Wt. (% of controls)	6,000 ppm No. of Survivors	12,000 ppm Av. Wt. (g)	12,000 ppm Wt. (% of controls)	12,000 ppm No. of Survivors
1	107	60	108	101	60	106	99	60	102	95	60
2	147	60	144	98	60	141	96	60	135	92	60
3	180	60	178	99	60	169	94	60	161	89	60
4	207	60	205	99	60	200	97	60	192	93	60
5	227	60	224	99	60	221	98	60	213	94	60
6	250	60	244	98	60	242	97	60	231	93	60
7	261	60	253	97	60	254	97	60	246	94	60
8	274	60	268	98	60	266	97	60	259	95	60
9	284	60	278	98	60	278	98	60	266	94	60
10	297	60	290	98	60	288	97	60	274	92	60
11	306	60	302	99	60	299	98	60	287	94	60
12	315	60	309	98	60	305	97	60	294	93	60
13	324	60	319	98	60	313	97	60	301	93	60
17	350	60	342	98	60	338	97	60	324	93	60
21	367	60	362	99	60	358	98	60	342	93	60
25	379	60	373	98	60	372	98	60	359	95	60
29	398	60	386	97	60	385	97	60	368	92	60
33	407	60	399	98	60	396	97	60	380	93	60
37	413	60	398	96	60	405	98	60	391	95	60
41	423	60	412	97	60	414	98	60	397	94	60
45	421	60	409	97	60	412	98	60	397	94	60
49	431	60	420	97	60	414	96	60	402	93	60
53	434	60	426	98	60	423	98	60	412	95	60
57	442	60	428	97	60	428	97	60	416	94	60
61	442	60	435	98	59	431	97	60	414	94	60
65	439	60	431	98	59	434	99	60	418	95	59
69[a]	443	49	430	97	49	432	98	49	419	95	49
73	448	47	432	96	47	442	99	48	425	95	48
77	443	46	433	98	46	435	98	48	419	95	48
81	449	44	431	96	45	436	97	48	418	93	46
85	449	43	432	96	43	437	97	47	421	94	44
89	443	41	426	96	42	432	98	47	410	93	43
93	440	38	427	97	39	434	99	42	418	95	38
97	443	36	426	96	38	430	97	40	415	94	37
101	432	35	425	98	37	422	98	33	411	95	36
Terminal sacrifice		27			34			30			33
Mean for weeks											
1-13	245		240	98		237	97		228	93	
14-52	399		389	97		388	97		373	93	
53-101	442		429	97		432	98		417	94	

[a] Interim evaluation occurred during week 66.

TABLE 7
Mean Body Weights and Survival of Female Rats in the 2-Year Feed Study of Benzyl Acetate

Weeks on Study	0 ppm		3,000 ppm			6,000 ppm			12,000 ppm		
	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	95	60	97	101	60	95	99	60	95	99	60
2	119	60	117	99	60	113	95	60	117	98	60
3	134	60	131	98	60	127	94	60	131	97	60
4	143	60	140	98	60	138	96	60	139	97	60
5	151	60	149	99	60	147	98	60	149	99	60
6	148	60	157	106	60	156	106	60	156	106	60
7	164	60	163	99	60	164	100	60	164	100	60
8	171	60	168	98	60	168	98	60	167	97	60
9	174	60	169	97	60	168	97	60	170	98	60
10	176	60	172	98	60	173	99	60	173	99	60
11	181	60	176	97	60	177	98	60	173	96	60
12	182	60	180	99	60	178	98	60	178	98	60
13	187	60	181	97	60	182	98	60	183	98	60
17	195	60	190	97	60	191	98	60	193	99	60
21	199	60	195	98	60	194	97	60	196	98	60
25	209	60	202	97	60	202	97	60	200	96	60
29	214	60	207	97	60	208	97	60	205	96	60
33	222	60	214	96	60	212	95	60	213	96	60
37	225	60	216	96	60	217	97	60	214	95	60
41	233	60	225	97	60	221	95	60	223	96	60
45	236	60	225	95	60	224	95	60	224	95	60
49	246	60	231	94	60	230	94	60	229	93	60
53	254	60	241	95	60	239	94	59	235	93	60
57	260	60	249	96	60	248	95	59	242	93	60
61	272	59	256	94	60	254	94	59	250	92	60
65	277	59	262	95	59	260	94	59	254	92	60
69[a]	287	49	271	94	49	270	94	49	266	93	50
73	302	49	285	94	48	282	93	49	275	91	50
77	310	47	282	91	47	282	91	48	278	90	50
81	314	46	295	94	47	294	94	48	293	93	49
85	315	45	300	95	45	304	96	47	298	94	48
89	315	43	298	95	45	301	95	47	299	95	47
93	316	40	297	94	43	307	97	47	306	97	45
97	321	39	306	96	40	312	97	47	314	98	38
101	320	36	306	96	37	313	98	45	313	98	36
Terminal sacrifice		30			30			37			28
Mean for weeks											
1-13	156		154	99		153	98		153	98	
14-52	220		212	96		211	96		211	96	
53-101	297		281	95		282	95		279	94	

[a] Interim evaluation occurred during week 66.

approximately 5% lower than those of the control groups throughout most of the study. The average feed consumption by all exposure groups was similar to that of the control groups, with only the 12,000 ppm males consuming slightly less feed throughout the study (Tables J1 and J2). Dietary levels of 3,000, 6,000, and 12,000 ppm benzyl acetate resulted in average daily consumption of 130, 260, and 510 mg/kg for male rats and 145, 290, and 575 mg/kg for female rats. No clinical findings were associated with the administration of benzyl acetate.

Hematology, Clinical Chemistry, and Pancreatic Enzyme Assays

The hematology profiles of rats at the 15-month interim evaluation showed no chemical-related effects for the parameters measured (Table G2). Alkaline phosphatase activity was slightly higher in 12,000 ppm males than in control males, but the relationship to chemical administration is inconclusive. Pancreatic enzyme activities were measured in male rats only, but no statistically significant differences occurred between any exposure group and the control group for any of the enzymes (Table H2).

Pathology and Statistical Evaluation

No biologically noteworthy changes in the incidences of neoplasms or nonneoplastic lesions occurred in any organ in male or female rats, except for a significant decrease in the incidence of uterine stromal polyps in the 6,000 ppm females (control, 15/60; 3,000 ppm, 18/60; 6,000 ppm, 4/60; and 12,000 ppm, 11/60), which was not considered chemical related. Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, and statistical analyses of primary neoplasms that occurred with an incidence of at least 5% in at least one animal group are presented in Appendix A for male rats and Appendix B for female rats. The incidences of various lesions in all rat groups were within the normal range for F344/N rats in studies of this type.

MICE

13-WEEK STUDY

One 50,000 ppm male mouse died and one 50,000 ppm female mouse was killed moribund before the end of the study. Statistically significant dose-related decreases in final mean body weights occurred in all groups of exposed male and female mice (Table 8). The final mean body weights were 8% to 31% lower in exposed males and 12% to 33% lower in exposed females than in the control groups. The mean feed consumption by all groups of exposed mice was lower than that by the control groups. The significant clinical finding was tremors, which occurred only in females and was predominant in the 50,000 ppm group; however, one 12,500 ppm female and one 25,000 ppm female also exhibited tremors. The tremors occurred first on day 16 of the study in three females receiving 50,000 ppm, day 94 in one female receiving 25,000 ppm, and day 93 in one female receiving 12,500 ppm, and continued until the end of the study. The reduced final mean body weights of all exposed mice made evaluation of absolute and relative organ weights difficult. All significant differences between the exposed and the control groups were attributed to the lower body weights of the exposed groups (Table F3).

TABLE 8
Survival, Mean Body Weights, and Feed Consumption of Mice in the 13-Week Feed Study of Benzyl Acetate

Dose (ppm)	Survival[a]	Mean Body Weights[b] (g) Initial	Final	Change	Final Weight Relative to Controls (%)	Feed Consumption[c]
Male						
0	10/10	21.9 ± 0.4	33.4 ± 0.6	11.5 ± 0.4		5.0
3,130	10/10	22.1 ± 0.4	30.7 ± 0.8**	8.6 ± 0.5**	92	3.6
6,250	10/10	21.9 ± 0.4	28.8 ± 0.8**	6.9 ± 0.7**	86	4.2
12,500	10/10	22.1 ± 0.3	28.1 ± 0.4**	6.0 ± 0.5**	84	4.1
25,000	10/10	21.9 ± 0.4	25.8 ± 0.4**	3.9 ± 0.4**	77	3.6
50,000	9/10[d]	22.3 ± 0.3	22.9 ± 0.2**	0.7 ± 0.2**	69	3.6
Female						
0	10/10	17.2 ± 0.3	28.6 ± 0.6	11.5 ± 0.4		7.3
3,130	10/10	16.6 ± 0.2	25.1 ± 0.8**	8.6 ± 0.7**	88	4.4
6,250	10/10	16.5 ± 0.3	23.5 ± 0.5**	7.0 ± 0.4**	82	4.1
12,500	10/10	17.1 ± 0.2	22.3 ± 0.2**	5.2 ± 0.2**	78	4.7
25,000	10/10	16.9 ± 0.2	21.3 ± 0.3**	4.4 ± 0.4**	74	3.3
50,000	9/10[e]	16.7 ± 0.3	19.3 ± 0.4**	2.5 ± 0.3**	67	3.4

** Significantly different (P≤0.01) 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 studies.
[c] The average feed consumption during weeks 2 through 13 is expressed as grams per animal per day. Feed consumption was not calculated for week 1.
[d] Week of death: 11
[e] Week of death: 3

At the end of the study, no chemical-related effects were observed at necropsy or in the hematology or clinical chemistry (cholesterol and triglycerides) parameters (Table G3). The data collected were relatively consistent among all exposure groups, and none of the variations observed were considered to be exposure related.

In the pancreatic enzyme assays, statistically significant differences occurred in one or more exposure groups for lipase activity in males, and for amylase, carboxypeptidase A, chymotrypsin, and ribonuclease activities in females (Table H3). However, no significant dose-related pattern attributed to chemical administration occurred in any of these data.

In mice, the principal lesions associated with dietary exposure to benzyl acetate occurred in the brain and liver. Brain necrosis occurred in one male and three female mice receiving 50,000 ppm. The brain lesions were similar to those described in the 13-week rat study. The one male mouse with brain lesions died during week 11 of the study. The brain lesions in this male consisted of hippocampal necrosis of moderate severity and cerebellar hemorrhage of mild severity. The three female mice with brain lesions survived to the end of the study. The lesions in these mice consisted of hippocampal necrosis of minimal to mild severity and mild to moderate depletion of the pyramidal layer cells. No brain lesions occurred in 25,000 ppm male or female mice. On reexamination, a similar lesion was observed in the brain of one 1,000 mg/kg female mouse in the previous NTP 13-week gavage study; none were observed in 1,000 mg/kg male mice. The lesion was less severe than that described in the present dosed feed study and consisted of hippocampal necrosis.

Hepatocellular necrosis occurred in the same 50,000 ppm male mouse with brain lesions. The lesion was characterized by necrosis of hepatocytes of moderate severity randomly distributed throughout the hepatic lobules. No chemical-related liver lesions occurred in any 50,000 ppm female mice or in 25,000 ppm male or female mice.

Dose Selection Rationale

Dietary concentrations of benzyl acetate selected for the 2-year study in mice were 0, 330, 1,000, or 3,000 ppm. Dose selection was based on the significant dose-related decreases in body weight and body weight gains for males and females and on poor feed palatability observed at all exposure levels for males and females.

2-YEAR STUDY

Survival

Estimates of survival probabilities for male and female mice fed diets containing benzyl acetate for 2 years are presented in Table 9 and in the Kaplan-Meier curves in Figure 3. Survival of exposed males was similar to that of the control groups. Survival of exposed females increased with exposure level, with survival of 3,000 ppm females significantly higher than that of the control group. Almost all deaths occurred during the last 9 months of the study; only five animals died during the first 15 months.

TABLE 9
Survival of Mice in the 2-Year Feed Study of Benzyl Acetate

Dose (ppm)	0	330	1,000	3,000
Male				
Animals initially in study	60	60	60	60
15-Month interim evaluation[a]	10	10	10	10
Moribund	7	3	6	7
Natural deaths	4	4	3	4
Animals surviving to study termination	39	43	41	39
Percent probability of survival at end of study[b]	78	86	82	78
Mean survival (days)[c]	664	670	673	664
Survival analysis[d]	P=0.718	P=0.444N	P=0.762N	P=0.840
Female				
Animals initially in study	60	60	60	60
15-Month interim evaluation[a]	10	10	10	10
Moribund	12	16	7	3
Natural deaths	9	6	6	3
Animals surviving to study termination	29	28	37	44
Percent probability of survival at end of study	58	56	74	88
Mean survival (days)	644	640	667	663
Survival analysis	P<0.001	P=0.889	P=0.068N	P=0.003N

[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 exposed columns. Lower mortality in an exposure group is indicated by N.

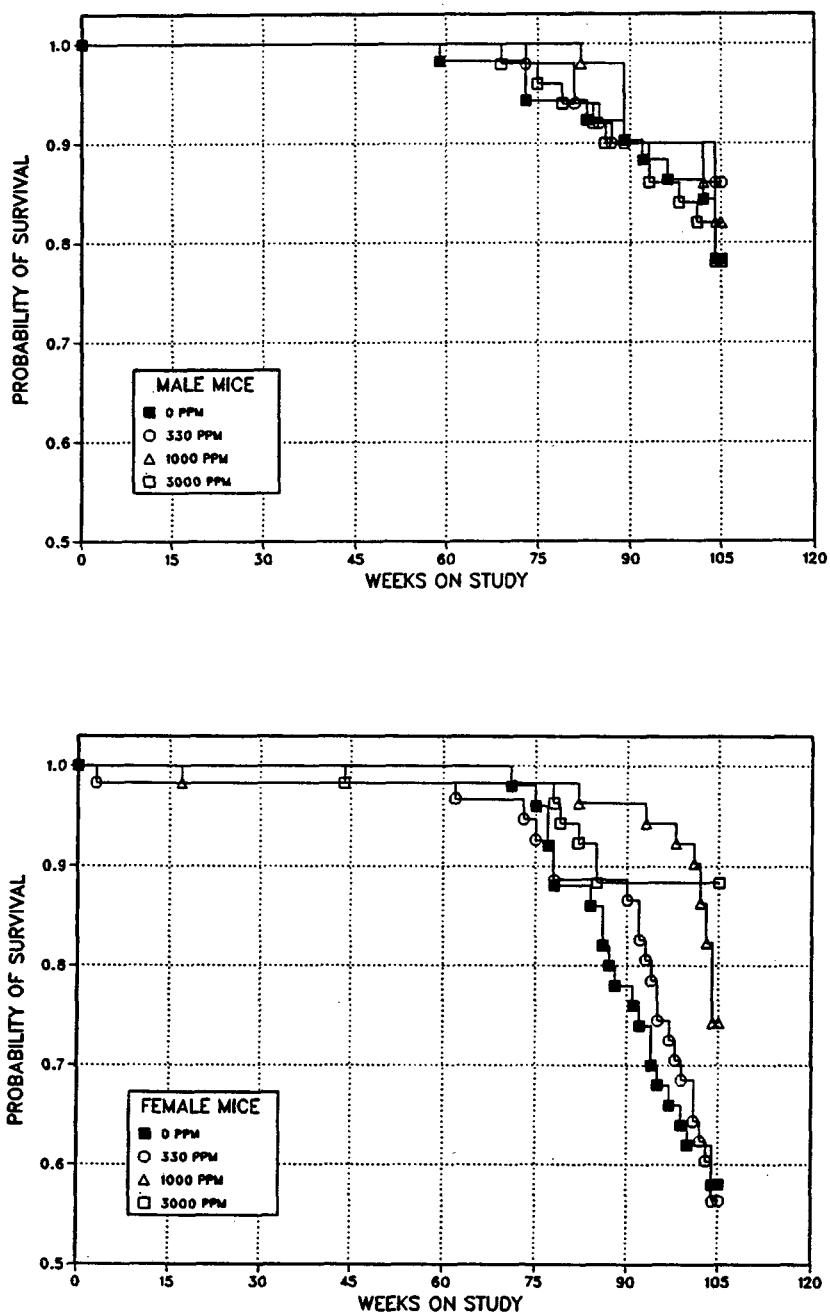


FIGURE 3
Kaplan-Meier Survival Curves for Male and Female B6C3F$_1$ Mice Administered Benzyl Acetate in Feed for 2 Years

Body Weights, Feed and Compound Consumption, and Clinical Findings

Mean body weights of exposed mice were consistently lower than those of the controls, except for the 330 ppm groups (Tables 10 and 11 and Figure 4). Throughout the study, the mean body weight of 1,000 ppm males was as much as 10% lower and that of the 3,000 ppm males was as much as 13% lower than that of the control group. Similarly, the mean body weight of 1,000 ppm females was as much as 12% lower and that of the 3,000 ppm females was as much as 16% lower than that of the control group throughout the study. The lower mean body weights of the 1,000 and 3,000 ppm males and females began after approximately 4 to 8 weeks of exposure and continued throughout the study. A decrease in mean body weight of all control and exposed males and females occurred between weeks 49 and 53 (males) and weeks 50 and 54 (females). The reason for this sudden decrease could not be determined. Recovery of the mean body weights was apparent by week 57 (males) and week 58 (females). The average feed consumption by all exposed mice was similar to that of the control groups (Tables J3 and J4); however, feed consumption by 1,000 and 3,000 ppm males was lower than that by the control group at week 4. Dietary levels of 330, 1,000, and 3,000 ppm benzyl acetate resulted in average daily consumption of 35, 110, and 345 mg/kg body weight for males and 40, 130, and 375 mg/kg for females. No clinical findings were attributed to benzyl acetate administration.

Hematology and Clinical Chemistry

The hematology profiles at the 15-month interim evaluation showed no chemical-related effects. The clinical chemistry results showed some differences in mean values for exposed groups compared to control groups. Triglycerides and cholesterol levels were slightly lower in exposed male and female mice, and the alkaline phosphatase activity was lower in the 1,000 and 3,000 ppm females than in the control group (Table G4).

TABLE 10
Mean Body Weights and Survival of Male Mice in the 2-Year Feed Study of Benzyl Acetate

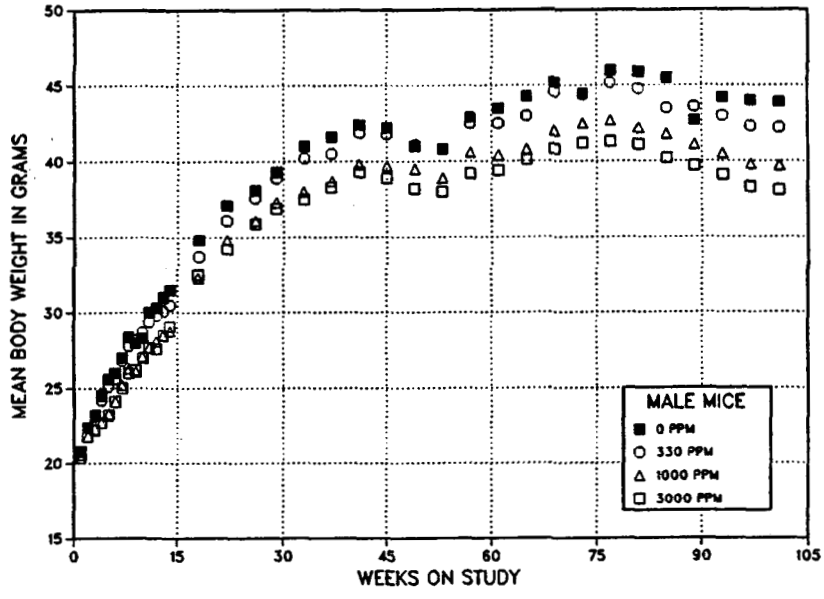
Weeks on Study	0 ppm Av. Wt. (g)	0 ppm No. of Survivors	330 ppm Av. Wt. (g)	330 ppm Wt. (% of controls)	330 ppm No. of Survivors	1,000 ppm Av. Wt. (g)	1,000 ppm Wt. (% of controls)	1,000 ppm No. of Survivors	3,000 ppm Av. Wt. (g)	3,000 ppm Wt. (% of controls)	3,000 ppm No. of Survivors
1	20.8	60	20.6	99	60	20.4	98	60	20.4	98	60
2	22.4	60	22.4	100	60	21.8	97	60	21.8	97	60
3	23.2	60	23.1	100	60	22.3	96	60	22.2	96	60
4	24.5	60	24.2	99	60	22.7	93	60	22.7	93	60
5	25.6	60	25.1	98	60	23.3	91	60	23.2	91	60
6	26.0	60	25.6	99	60	24.1	93	60	24.1	93	60
7	27.0	60	26.8	99	60	25.2	93	60	25.0	93	60
8	28.4	60	27.8	98	60	26.3	93	60	26.0	92	60
9	28.0	60	28.2	101	60	26.1	93	60	26.2	94	60
10	28.3	60	28.7	101	60	27.1	96	60	27.0	95	60
11	30.0	60	29.4	98	60	27.7	92	60	27.7	92	60
12	30.3	60	29.8	98	60	28.1	93	60	27.6	91	60
13	31.0	60	30.1	97	60	28.5	92	60	28.5	92	60
14	31.5	60	30.5	97	60	28.8	91	60	29.1	92	60
18	34.8	60	33.7	97	60	32.3	93	60	32.5	93	60
22	37.1	60	36.1	97	60	34.8	94	60	34.2	92	60
26	38.1	60	37.6	99	60	36.1	95	60	35.9	94	60
29	39.3	60	38.9	99	60	37.3	95	60	36.9	94	60
33	41.0	60	40.2	98	60	38.0	93	60	37.5	92	60
37	41.6	60	40.5	97	60	38.7	93	60	38.3	92	60
41	42.4	60	41.9	99	60	39.8	94	60	39.3	93	60
45	42.2	60	41.8	99	60	39.7	94	60	38.9	92	60
49	41.0	60	41.1	100	60	39.6	97	60	38.2	93	60
53	40.8	60	40.8	100	60	38.9	95	60	38.0	93	60
57	42.9	60	42.5	99	60	40.6	95	60	39.3	92	60
61	43.5	59	42.5	98	60	40.4	93	60	39.4	91	60
65	44.3	59	43.0	97	60	40.8	92	60	40.1	91	60
69[a]	45.2	49	44.6	99	50	42.0	93	50	40.8	90	49
73	44.5	49	44.4	100	50	42.5	96	50	41.2	93	49
77	46.0	47	45.2	98	49	42.7	93	50	41.3	90	48
81	45.9	47	44.8	98	49	42.2	92	50	41.1	90	47
85	45.5	46	43.5	96	46	41.8	92	49	40.2	88	46
89	42.7	46	43.6	102	45	41.1	96	49	39.7	93	45
93	44.2	44	43.0	97	45	40.5	92	45	39.1	89	45
97	44.0	43	42.3	96	45	39.8	91	45	38.3	87	43
101	43.9	43	42.2	96	45	39.7	90	45	38.1	87	41
Terminal sacrifice		39			43			41			39
Mean for weeks											
1-13	26.6		26.3	99		24.9	94		24.8	93	
14-52	38.9		38.2	98		36.5	94		36.1	93	
53-101	44.1		43.3	98		41.0	93		39.7	90	

[a] Interim evaluation occurred during week 66.

TABLE 11
Mean Body Weights and Survival of Female Mice in the 2-Year Feed Study of Benzyl Acetate

Weeks on Study	0 ppm Av. Wt. (g)	0 ppm No. of Survivors	330 ppm Av. Wt. (g)	330 ppm Wt. (% of controls)	330 ppm No. of Survivors	1,000 ppm Av. Wt. (g)	1,000 ppm Wt. (% of controls)	1,000 ppm No. of Survivors	3,000 ppm Av. Wt. (g)	3,000 ppm Wt. (% of controls)	3,000 ppm No. of Survivors
1	17.2	60	17.1	99	60	16.4	95	60	16.1	94	60
2	19.1	60	18.6	97	60	18.0	94	60	17.5	92	60
3	20.5	60	19.6	96	59	18.2	89	60	18.0	88	60
4	21.6	60	20.5	95	59	19.0	88	60	18.3	85	60
5	22.9	60	21.9	96	59	20.3	89	60	19.4	85	60
6	23.5	60	22.7	97	59	21.2	90	60	20.0	85	60
7	24.1	60	23.1	96	59	21.8	91	60	21.1	88	60
8	24.4	60	23.7	97	59	22.4	92	60	21.8	89	60
9	25.1	60	24.5	98	59	23.3	93	60	22.7	90	60
10	26.0	60	25.0	96	59	23.8	92	60	22.5	87	60
11	25.9	60	25.1	97	59	23.7	92	60	23.1	89	60
12	26.5	60	25.7	97	59	24.2	91	60	23.5	89	60
13	26.8	60	26.0	97	59	24.7	92	60	23.9	89	60
17	29.3	60	28.4	97	59	26.7	91	59	26.3	90	60
21	32.0	60	31.5	98	59	29.5	92	59	28.5	89	60
25	33.1	60	32.7	99	59	30.2	91	59	29.9	90	60
29	35.5	60	34.8	98	59	32.5	92	59	32.4	91	60
30	36.0	60	34.9	97	59	32.9	91	59	32.0	89	60
34	37.7	60	36.4	97	59	33.8	90	59	33.0	88	60
38	37.4	60	36.4	97	59	33.4	89	59	32.8	88	60
42	38.3	60	37.8	99	59	34.7	91	59	34.1	89	60
46	38.8	60	38.1	98	59	35.0	90	59	33.9	87	59
50	37.5	60	37.1	99	59	34.1	91	59	33.5	89	59
54	35.8	60	35.6	99	59	33.3	93	59	31.3	87	59
58	39.8	60	38.9	98	59	35.8	90	59	35.1	88	59
62	40.8	60	39.6	97	58	36.5	90	59	35.7	88	59
66[a]	43.0	50	42.6	99	48	38.5	90	49	36.9	86	49
70	44.1	50	43.5	99	48	38.8	88	49	37.2	84	49
74	43.5	49	43.9	101	47	39.5	91	49	37.7	87	49
78	45.1	45	45.1	100	46	40.5	90	49	38.8	86	49
82	44.0	44	44.4	101	44	39.8	91	48	38.6	88	47
86	43.5	42	44.3	102	44	39.6	91	48	39.2	90	44
90	42.3	39	42.0	99	44	37.8	89	48	38.1	90	44
94	41.4	37	42.2	102	40	37.2	90	47	37.5	91	44
98	42.1	33	42.6	101	35	37.0	88	46	37.2	88	44
103	40.3	31	41.7	104	31	36.0	89	43	36.8	91	44
Terminal sacrifice		29			28			37			44
Mean for weeks											
1-13	23.4		22.6	97		21.3	91		20.6	88	
14-52	35.6		34.8	98		32.3	91		31.6	89	
53-103	42.0		42.0	100		37.7	90		36.9	88	

[a] Interim evaluation occurred during week 66.



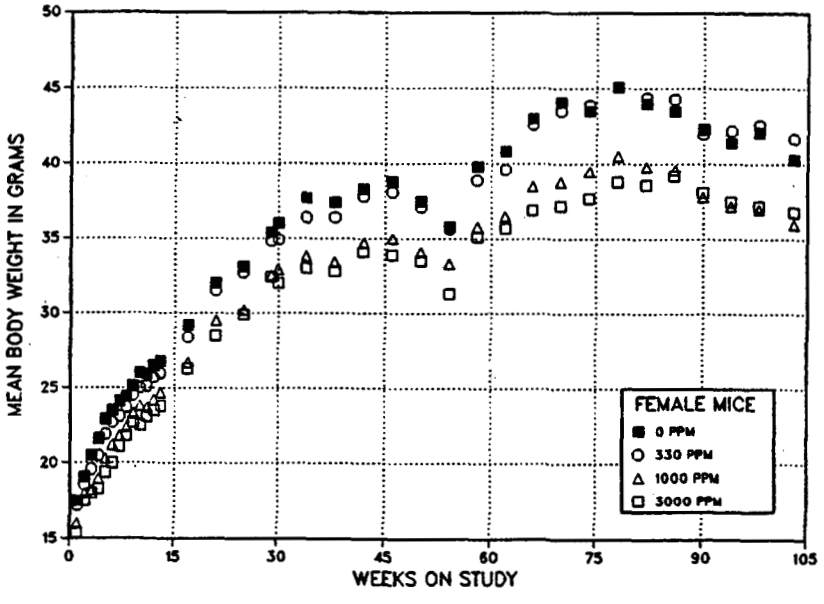


FIGURE 4
Growth Curves for Male and Female B6C3F$_1$ Mice Administered Benzyl Acetate in Feed for 2 Years

Pathology and Statistical Evaluation

This section describes the biologically noteworthy or statistically significant changes in the incidences of neoplasms and nonneoplastic lesions in the liver, uterus, and nose. No increased incidences of neoplasms in male or female mice could be attributed to exposure to benzyl acetate. Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, and statistical analyses of primary neoplasms that occurred with an incidence of at least 5% in at least one animal group are presented in Appendix C for male mice and Appendix D for female mice.

Liver: The incidence of hepatocellular adenoma and of hepatocellular adenoma and carcinoma (combined) occurred with a dose-related negative trend in male mice; the combined incidence in the 3,000 ppm group was significantly lower than that in the control group (control, 22/50; 330 ppm, 22/50; 1,000 ppm, 18/50; and 3,000 ppm, 9/50; Table C3). This effect did not occur in females.

Uterus: A significant decrease in the incidence of uterine stromal polyps occurred in 330 and 1,000 ppm females (control, 8/50; 330 ppm, 2/49; 1,000 ppm, 1/50; and 3,000 ppm, 6/50; Table D3).

Nose: Dose-related increased incidences and severities of nonneoplastic lesions occurred in the nose of male and female mice of all exposure groups (Table 12). The nasal lesions consisted of atrophy and degeneration, primarily of the olfactory epithelium, cystic hyperplasia of the nasal submucosal glands, and exudate and pigmentation of the nasal mucosal epithelium. Atrophy consisted of depletion of bipolar neurons from the sensory cell layer of the olfactory epithelium, whereas degeneration was characterized by disorganization of the remaining sensory and sustentacular cells with enlarged or, occasionally, pyknotic nuclei (Plate 7). The most commonly affected areas of the nose were the dorsal nasal septum, the junctional area (dorsal arch) of the dorsal septum and ethmoid turbinates, and the dorsomedial aspect of the ethmoid turbinates. The lateral portion of the ethmoid turbinates as well as the entire nasal and maxillary turbinates were relatively less involved. The cells were interspersed with amorphous eosinophilic material, clear vacuoles, and occasionally, neutrophils. In some instances, the atrophied and degenerated epithelium contained gland-like structures several microns in diameter similar to hyperplastic Bowman's glands (Plate 8). The submucosal (Bowman's) glands in the affected regions were often hyperplastic and cystic and contained exudate in many mice (Plate 9). The epithelial cells of the hyperplastic glands were enlarged and occasionally extended upward to connect directly with the nasal meatus. Exudate was also present in the nasal meatus of some animals. A significant amount of finely granular, brown pigment was usually present in the affected olfactory epithelial cells and was similar to that in the olfactory epithelium of the control mice; however, the amount of the pigment was increased. The pigment was not identified but was presumed to be an increase in the mucosal pigment normally seen in the olfactory epithelium. Occasionally, hyalinization of the respiratory epithelium and the sustentacular cell layer of the olfactory epithelium was greater in severity than that observed in control mice (Plate 10). The hyalinization was characterized by the presence of abundant eosinophilic material, primarily in the goblet cells of the respiratory epithelium and in the sustentacular and mucus-producing cells of Bowman's glands in the olfactory epithelium. This change is often referred to as hyaline degeneration.

The nasal mucosal changes of atrophy, degeneration, and cystic hyperplasia of the glandular ducts occurred in the majority of male and female control mice and the exposed animals. However, the severity of these lesions was greater and the incidence of the additional lesion of pigmentation was increased in exposed animals in a dose-related manner. The atrophic and degenerative changes were usually minimal in severity, primarily in the anterior portions of the olfactory epithelium, and located dorsomedially in the control and 330 ppm groups and progressed to moderate severity in the 3,000 ppm males and females. The lesions in mice evaluated at the end of the study and those dying after 15 months were similar to those in mice evaluated at the 15-month interim evaluation but were of greater severity. Whether the nasal changes resulted from a systemic effect of the ingested chemical, from a local effect of inhaled chemical vapor, or a combination of the mechanisms is unknown. No neoplasms or preneoplastic treatment-related lesions occurred in the nose.

TABLE 12
Incidences of Nonneoplastic Lesions of the Nose of Mice in the 2-Year Feed Study of Benzyl Acetate[a]

Dose (ppm)	0	330	1,000	3,000
Male				
15-Month Interim Evaluation				
n	10	10	10	10
Mucosa, Atrophy	0	8**(0.8)**	10**(1.8)**	10**(2.6)**
Mucosa, Degeneration	5 (0.5)	5 (0.6)	10*(1.9)**	10*(2.7)**
Glands, Cystic Hyperplasia	2 (0.2)	3 (0.3)	1 (0.1)	10**(1.3)**
Exudate	0	0	1	5*
Mucosa, Pigmentation	0	7**(0.7)**	10**(1.3)**	10**(2.0)**
2-Year Study				
n	50	50	50	50
Mucosa, Atrophy	30 (0.6)	49**(1.0)**	50**(2.0)**	50**(2.9)**
Mucosa, Degeneration	31 (0.6)	50**(1.0)**	50**(2.0)**	50**(2.9)**
Glands, Cystic Hyperplasia	22 (0.7)	43**(1.1)**	47**(1.2)**	50**(1.9)**
Exudate	8	18*	38**	26**
Mucosa, Pigmentation	0	45**(0.9)**	50**(1.2)**	50**(2.0)**
Female				
15-Month Interim Evaluation				
n	10	10	10	10
Mucosa, Atrophy	5 (0.5)	9 (0.9)	10*(2.2)**	10*(3.0)**
Mucosa, Degeneration	10 (1.1)	9 (0.9)	10 (2.2)**	10 (3.0)**
Glands, Cystic Hyperplasia	8 (0.8)	9 (0.9)	10 (1.1)	10 (2.1)**
Exudate	0	0	0	2
Mucosa, Pigmentation	0	7**(0.7)**	10**(1.4)**	10**(1.8)**
2-Year Study				
n	50	50	50	50
Mucosa, Atrophy	41 (0.8)	48*(1.2)**	49**(2.4)**	50**(2.8)**
Mucosa, Degeneration	48 (1.0)	48 (1.2)*	0 (2.3)**	50 (2.8)**
Glands, Cystic Hyperplasia	39 (1.3)	45 (1.1)	49**(1.4)**	50**(1.9)**
Exudate	15	26*	36**	43**
Mucosa, Pigmentation	0	46**(0.9)**	48**(1.3)**	48**(1.5)**

* Significantly different ($P \leq 0.05$) from the control group by Fisher's exact test (15-month interim) or logistic regression (2-year)
** $P \leq 0.01$
[a] Animals examined microscopically and number of animals with lesion; average severity grade (in parentheses) for all animals: 0=none, 1=minimal, 2=mild, 3=moderate, 4=marked

GENETIC TOXICOLOGY

Benzyl acetate was tested for mutagenicity in a variety of systems, both *in vitro* and *in vivo*, and, with one exception, all results were negative (Appendix E). Benzyl acetate (33 to 10,000 μg/plate) did not induce mutations in *Salmonella typhimurium* strains TA98, TA100, TA1535, or TA1537 when tested in a pre-incubation protocol, with or without induced hamster or rat liver exogenous metabolic activation (S9) (Table E1; Mortelmans *et al.*, 1986). Benzyl acetate was tested in two laboratories for induction of trifluorothymidine resistance in L5178Y mouse lymphoma cells (Table E2; McGregor *et al.*, 1988). In one laboratory, a positive response was observed only in the presence of Aroclor 1254-induced male Fischer 344 rat liver S9; in the second laboratory, a positive response was observed in two of three trials without S9, and no tests were conducted with S9. Benzyl acetate did not induce significant increases in sister chromatid exchanges or chromosomal aberrations in cultured Chinese hamster ovary cells *in vitro*, with or without induced S9 (Tables E3 and E4; Galloway *et al.*, 1987). No induction of sex-linked recessive lethal mutations was observed in germ cells of male *Drosophila melanogaster* administered benzyl acetate by feeding or by injection (Table E5).

In vivo mouse bone marrow chromosome damage tests conducted with benzyl acetate yielded uniformly negative results. No induction of sister chromatid exchanges (Table E6) or chromosomal aberrations (Table E7) was observed in bone marrow cells of male mice treated by intraperitoneal injection with benzyl acetate, where both standard and extended harvest times were employed. The highest dose tested was 1,700 mg/kg for the standard harvest protocol and 1,300 mg/kg for the extended harvest time experiments. No increase in micronucleated polychromatic erythrocytes was observed in bone marrow smears of male mice treated with benzyl acetate (312.5 to 1,250 mg/kg) by intraperitoneal injection three times at 24-hour intervals (Table E8). No increases in the frequencies of micronucleated polychromatic erythrocytes or normochromatic erythrocytes were observed in peripheral blood smears prepared from male and female mice at the end of the 13-week toxicity study, where benzyl acetate was administered in feed (3,130 to 50,000 ppm benzyl acetate) (Table E9).

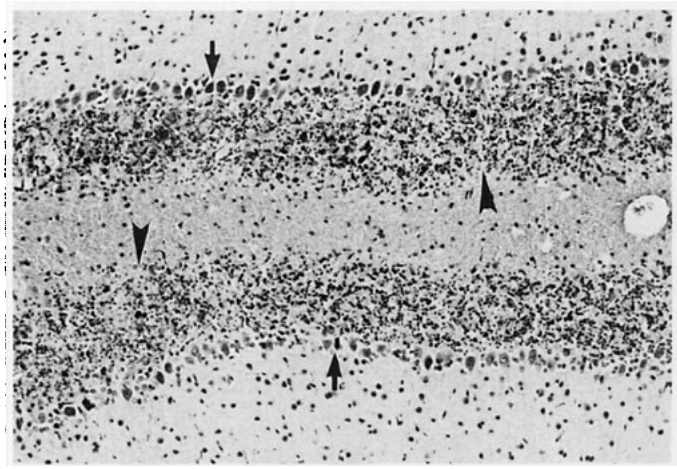


PLATE 1
Necrosis of cells in the internal or external granular layer of the cerebellum (arrowheads) in a male F344/N rat receiving 50,000 ppm benzyl acetate in the 13-week feed study. Note the sparing of the Purkinje's cells (arrows). Magnification 39×

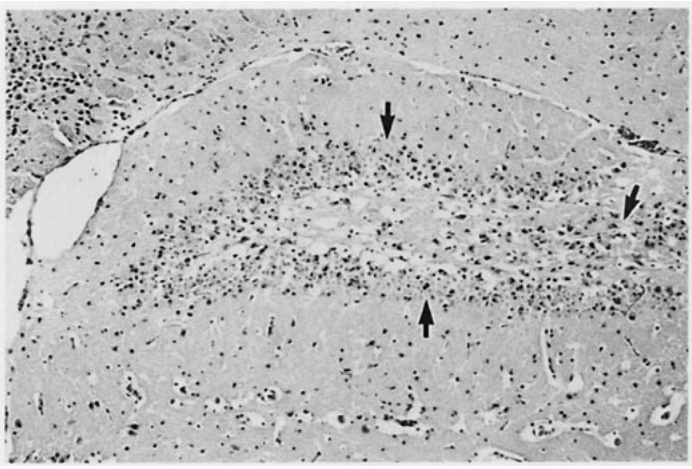


PLATE 2
Necrosis of glial cells and neurons (arrows) of the hippocampus in a male F344/N rat receiving 50,000 ppm benzyl acetate in the 13-week feed study. Magnification 39×

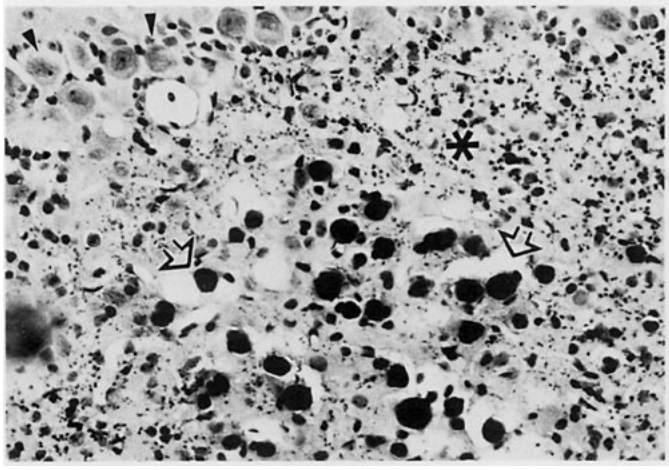


PLATE 3
Concretions of mineral (open arrows) within areas of marked necrosis (asterisk) in the granular layer of the cerebellum in a male F344/N rat receiving 50,000 ppm benzyl acetate in the 13-week feed study. Note the sparing of the Purkinje's cells (arrowheads). Magnification 72×

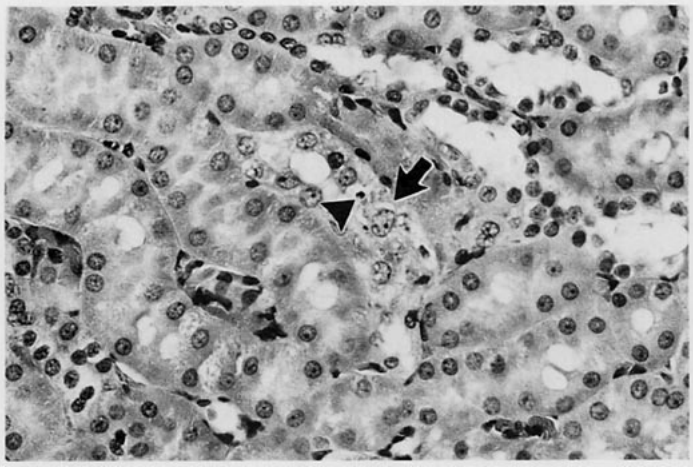


PLATE 4
Renal tubule degeneration and necrosis of lining epithelial cells in a male F344/N rat receiving 50,000 ppm benzyl acetate in the 13-week feed study. Note the degenerative cells with enlarged nuclei and vacuolated cytoplasm (arrow) and a necrotic cell with a karyorrhectic nucleus (arrowhead). Magnification 75×

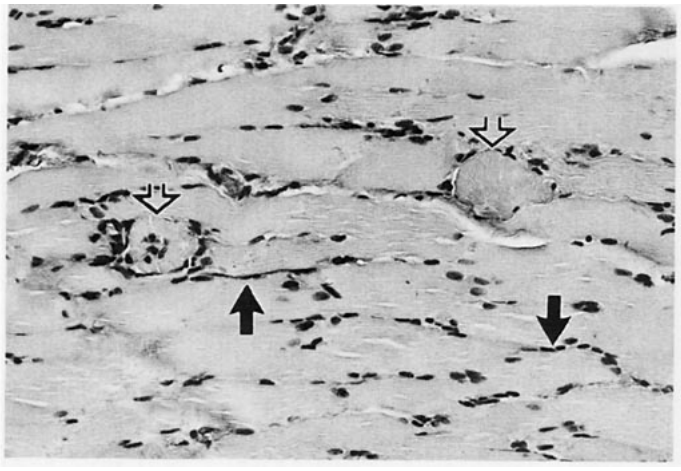


PLATE 5
Mild degeneration and moderate sarcolemma nuclear hyperplasia in a male F344/N rat receiving 50,000 ppm benzyl acetate in the 13-week feed study. Note the increased numbers of sarcolemmal nuclei (arrows) and the degenerative myocytes (open arrows). Magnification 69×

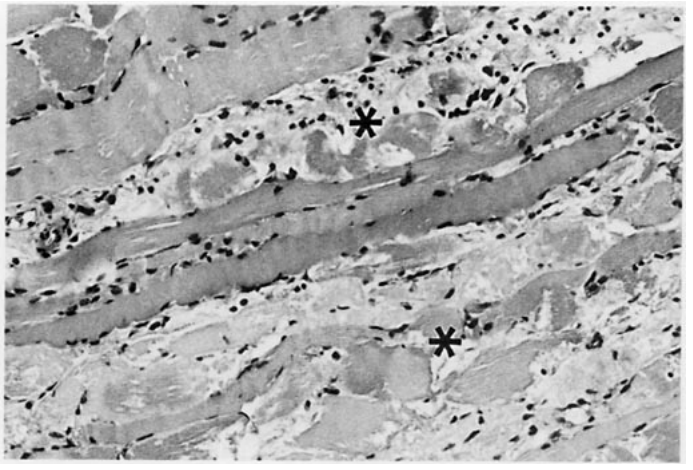


PLATE 6
Marked degeneration, necrosis, and sarcolemma nuclear hyperplasia in a male F344/N rat receiving 50,000 ppm benzyl acetate in the 13-week feed study. Note the discrete areas of degeneration and necrosis of myocytes (asterisks) interspersed among relatively normal myocytes. Magnification 75×

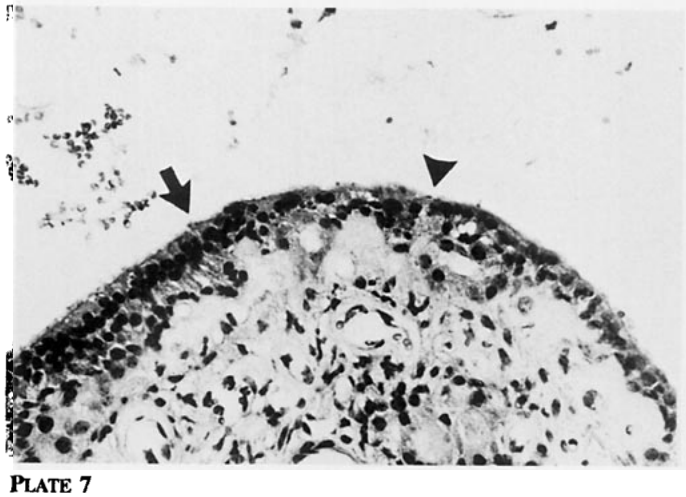


PLATE 7
Atrophy and degeneration of the olfactory epithelium in a male $B6C3F_1$ mouse receiving 3,000 ppm benzyl acetate in the 2-year feed study. Note the disorganization (arrow) and thinning (arrowhead) of the olfactory epithelium. Magnification 75×

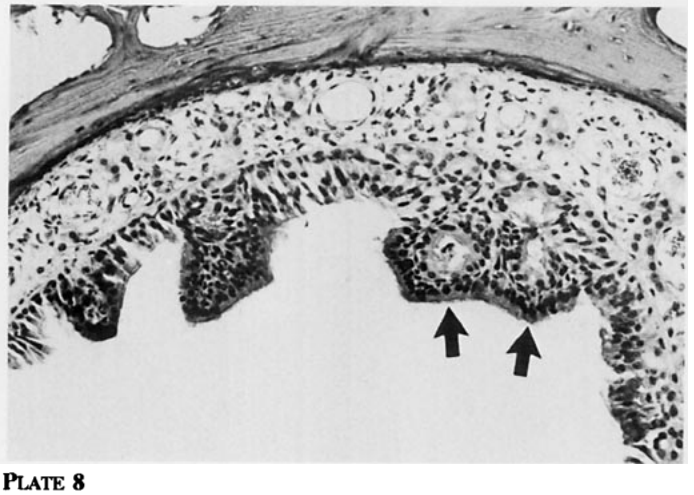


PLATE 8
Atrophy and degeneration of the olfactory epithelium of the nose in a male $B6C3F_1$ mouse receiving 3,000 ppm benzyl acetate in the 2-year feed study. Note the gland-like structures (arrows). Magnification 69×

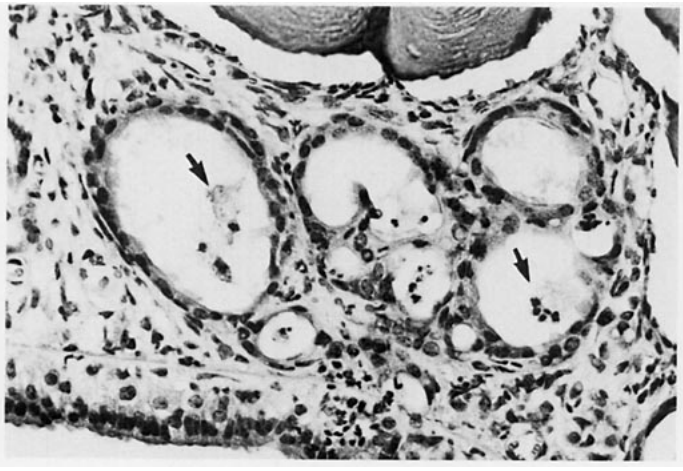


PLATE 9
Hyperplastic and cystic submucosal glands of the nose in a male $B6C3F_1$ mouse receiving 3,000 ppm benzyl acetate in the 2-year feed study. Note the luminal exudate containing low numbers of inflammatory cells (arrows). Magnification 75×

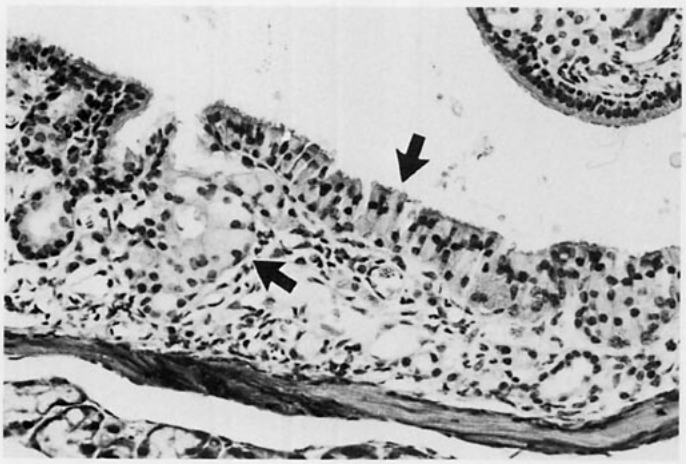


PLATE 10
Hyaline degeneration of the respiratory epithelium of the nose of a male $B6C3F_1$ mouse receiving 3,000 ppm benzyl acetate in the 2-year feed study. Note the distended cells along the surface and in the glands (arrows). Magnification 72×

DISCUSSION AND CONCLUSIONS

The toxicology and carcinogenicity of benzyl acetate administered in corn oil by gavage to F344/N rats and B6C3F$_1$ mice was investigated in 14-day, 13-week, and 2-year studies (NTP, 1986). However, because of the confounding effect of corn oil on the incidence of pancreatic acinar cell adenomas in rats and because of questions about the use of the gavage route of administration, the NTP decided to reexamine the toxicology and carcinogenicity of benzyl acetate in these two rodent species using dosed feed.

In 13-week studies, based on body weight, the amount of benzyl acetate consumed by male and female mice was two to three times that consumed by male and female rats receiving equal concentrations in feed. Rats in the 50,000 ppm groups consumed approximately equivalent amounts of benzyl acetate as did mice in the 25,000 ppm groups. Only one male rat and one female rat in the 50,000 ppm groups survived to the end of the study; all 25,000 ppm mice survived. The final mean body weights of rats receiving 50,000 ppm were half those of the controls; mice receiving 25,000 ppm had final mean body weights 23% to 26% lower than the controls. Chemical-related nonneoplastic lesions in 50,000 ppm male and female rats were necrosis of the brain, renal tubule degeneration and regeneration, and degeneration and sarcolemma nuclear hyperplasia in the tongue and the skeletal muscles of the thigh; no chemical-related nonneoplastic lesions occurred in 25,000 ppm mice. Because survival was lower, body weight gains were lower, and chemical-related lesions were more frequent and more severe in rats than in mice, rats were considered more sensitive than mice to benzyl acetate toxicity. Males and females within a species showed no difference in sensitivity. The difference in sensitivity between the two species may be related to the difference in the rate of elimination of the chemical. F344/N rats given a single dose of 5 or 500 mg/kg eliminated approximately 83% of the dose in the urine and feces in 4 days, whereas C57BL/6N mice given a single dose of 10 mg/kg eliminated more than 98% of the dose in 2 hours (McMahon *et al.*, 1989).

The major clinical findings in the 13-week studies were tremors and ataxia in male rats fed diets containing 50,000 ppm of benzyl acetate and tremors in female mice fed diets containing 12,500, 25,000, or 50,000 ppm. These findings occurred in similar studies with F344/N rats and B6C3F$_1$ mice given benzyl acetate or benzyl alcohol by gavage (NTP, 1986, 1989). Neurological effects such as central nervous system depression occurred in mice and cats exposed by inhalation to benzyl acetate (mice, 1.3 mg/L; cats, 1.5 mg/L) for as long as 13 hours (von Oettingen, 1960).

The brain was the organ most affected by benzyl acetate toxicity in both rats and mice in the 13-week studies. Necrosis of the cerebellum and hippocampus occurred in rats and necrosis of the hippocampus in mice. These lesions occurred in animals receiving 50,000 ppm benzyl acetate, the highest exposure level, and were considered the cause of death in these animals. In addition to the brain lesions, degeneration and regeneration of renal tubules, degenerative myopathy, and sarcolemma nuclear hyperplasia of the tongue and skeletal muscle of the thigh occurred. None of these lesions were reported in the benzyl acetate gavage study (NTP, 1986). The lesions apparently were not diagnosed by the study and quality assurance pathologists. Microscopic reexamination of the brain, kidney, and skeletal muscle of rats and the brain of female mice in the 1,000 mg/kg group in the 13-week benzyl acetate gavage study revealed the presence of the same lesions, although less severe than those described in the present dosed feed study. Some of these lesions were also noted in gavage studies conducted in rats and mice with benzyl acetate metabolites, namely benzyl alcohol (NTP, 1989) and benzaldehyde (Kluwe *et al.*, 1983; NTP, 1990). In rats given 800 mg/kg of benzyl alcohol for 13 weeks, necrosis of the hippocampus in males and females and skeletal muscle necrosis in males occurred; none of these lesions occurred in mice. In the 13-week study of benzaldehyde, male and female rats receiving 800 mg/kg had focal degeneration and necrosis of the cerebellum,

necrosis of the neurons and degeneration in the hippocampus, necrosis of hepatocytes and proximal tubule epithelial cells of the kidney, and hyperkeratosis of the stratified squamous epithelium of the forestomach. The only chemical-related lesion in mice in the benzaldehyde study was renal tubule degeneration, which occurred in males at the highest dose of 1,200 mg/kg.

In the current 13-week studies, significant chemical-related findings included decreases in cholesterol levels and an increase in volume, surface, and numerical densities of hepatic peroxisomes in female rats. Triglycerides and cholesterol levels and peroxisomal proliferation were examined in the current benzyl acetate feed studies because of the carcinogenic effect that occurred in rats and mice in the 2-year gavage study of benzyl acetate and because of a structural similarity between benzyl acetate and known peroxisomal proliferators such as the hypolipidemic agents (colifibrate and nafinopin) and industrial plasticizers such as di(2-ethylhexyl)phthalate and di(2-ethylhexyl) adipate, which were also identified as hepatocarcinogens in rats and/or mice (Reddy and Rao, 1977; Kluwe *et al.*, 1982; Reddy and Lalwani, 1983; Conway *et al.*, 1989). The presence of a carboxylate functional group is the major feature common to these agents. Benzyl acetate is hydrolyzed in the body to benzyl alcohol and then oxidized to benzoic acid (Clapp and Young, 1970). Because the hypothesis suggests an association between lipid and cholesterol lowering effect and peroxisomal proliferation, only animals showing hypolipidemic effects were studied for peroxisomal proliferation. In the current feed studies, peroxisomal proliferation was studied in female rats only, because hypolipidemia and/or hypocholesterolemia occurred only in female rats. The underlying cause for this sex and species difference is not known.

Because rats receiving benzyl acetate in corn oil by gavage showed an increased incidence of acinar cell hyperplasia (NTP, 1986), it was hypothesized that this lesion could lead to an increase in the level of enzymes produced by these cells. For this reason, amylase, lipase, carboxypeptidase, chymotrypsin, and ribonuclease activities were measured in homogenates of pancreata obtained from rats and mice at the end of the 13-week studies and at 15 months from male rats in the 2-year study. The apparently dose-related differences in enzyme activities were limited to male rats in the 13-week studies. These differences included increases in amylase and carboxypeptidase A activities with increasing dose and decreases in chymotrypsin activities with increasing dose of benzyl acetate. Because these differences were not observed at 15 months and because no increase in the incidence of acinar cell hyperplasia of the pancreas occurred in male rats receiving benzyl acetate, the differences observed were not considered to be related to chemical administration.

Doses used in the 2-year feed studies were 0, 3,000, 6,000, or 12,000 ppm (0, 130, 260, or 510 mg/kg body weight for males and 0, 145, 290, or 575 mg/kg for females) for rats, and 0, 330, 1,000, or 3,000 ppm (0, 35, 110, or 345 mg/kg for males and 0, 40, 130, or 375 mg/kg for females) for mice. Dose selection for rats was based on the lower final mean body weights and survival and the increased incidences of chemical-related lesions of 50,000 ppm rats in the 13-week study. For mice, dose selection was based on decreased final mean body weights of all exposed groups in the 13-week study.

Although the dose selection rationale for rats in the 2-year studies was appropriate, the similarity in survival and minimal body weight differences between control and exposed groups and the absence of chemical-related lesions suggest that rats could have tolerated higher doses. In contrast, doses selected for mice in the 2-year studies were high enough to evaluate the carcinogenic potential of benzyl acetate, as evidenced by the dose-related decrease in mean body weights and the occurrence of chemical-related nasal lesions in male and female mice receiving benzyl acetate.

The differences in survival among the exposed groups and the controls were limited to a dose-related increase in the survival of female mice and the significantly greater survival of females receiving 3,000 ppm. These increases may be due to the lower incidence of inflammation of the urogenital tract. Suppurative inflammation of the kidney occurred in 4 of 50 control females but not in females receiving benzyl acetate. The incidences of ovarian suppurative inflammation were: control, 12/49; 330 ppm, 6/48; 1,000 ppm, 10/49; 3,000 ppm, 4/49. The incidences of uterine suppurative inflammation were 13/50, 6/49, 10/50, 6/50. Although the contribution of benzyl acetate to the decreased incidences of suppurative inflammation in the urogenital tract is not clear, this effect may be due to the bacteriostatic effect of benzyl acetate metabolites (benzyl alcohol and benzoic acid).

The doses selected for the 2-year feed studies of benzyl acetate were intended to be as close as possible to those used in the previous 2-year gavage studies. This goal was achieved for the rats but not for the mice. The estimated highest dose received by mice in the feed studies was about three times lower than that received by mice in the gavage studies (360 mg/kg versus 1,000 mg/kg). A higher exposure level was not selected for mice because of poor feed palatability and lower mean body weight gains and final mean body weights observed at higher doses in the 13-week study.

In the feed study, no increased incidences of neoplasms or nonneoplastic lesions could be associated with benzyl acetate administration in male or female rats. By comparison, male rats administered benzyl acetate in corn oil by gavage at doses of 250 or 500 mg/kg had significantly increased incidences of pancreatic acinar cell adenoma and hyperplasia. This effect did not occur in females. These contrasting results were probably due to the use of corn oil as a vehicle in the latter study. The administration of high levels of fat to experimental animals has been shown to enhance the development of spontaneous and chemical-induced neoplasms. The incidence of 7,12-dimethylbenz(a)anthracene-induced mammary gland neoplasms in rats consuming diets containing 20% corn oil was increased by 30% over controls consuming the basal diet (Kritchevsky *et al.*, 1986). Administration of corn oil, safflower oil, and tricaprylin by gavage at doses of 2.5, 5, or 10 mL/kg body weight for as long as 2 years to male F344/N rats was associated with increased incidences of proliferative lesions of the exocrine pancreas. The incidences of male rats with these lesions were almost doubled when corn oil (5 or 10 mL/kg) was administered with dichloromethane (500 mg/kg) for as long as 2 years (NTP, 1993). Longnecker *et al.* (1986) found a linear relationship between the amount of corn oil and the number and volume of pancreatic acinar cell foci in Lewis rats pretreated with azaserine (a pancreatic carcinogen) in a 4-month study. However, this effect was not seen in azaserine-treated Lewis rats administered benzyl acetate in corn oil by gavage at a dose of 500 mg/kg body weight or 9,000 ppm of the chemical in the diet. Longnecker *et al.* (1990) also observed a low but significantly increased incidence of pancreatic acinar cell carcinoma in azaserine-treated male F344 rats fed diets containing 8,000 ppm benzyl acetate for 2 years. Together, the results of these studies suggest that benzyl acetate is a weak promoter of carcinogen-induced pancreatic neoplasms and possibly spontaneous preneoplastic lesions.

Administration of benzyl acetate in feed for 2 years did not increase the incidence of neoplasms in male or female mice. By comparison, administration of benzyl acetate (1,000 mg/kg) in corn oil by gavage for 2 years significantly increased the incidences of hepatocellular adenomas and marginally increased the incidences of squamous cell neoplasms of the forestomach in male and female mice. This effect did not occur at the lowest dose (500 mg/kg) used in the gavage study.

These contrasting results might be due in part simply to differences in the size of the administered dose. McMahon *et al.* (1989) observed that plasma levels of benzyl acetate increased with dose. In the NTP studies, the high dose administered by gavage was 2.7 times higher than the high dose used in the feed study. Also, rats and mice in the gavage studies were temporarily exposed to large concentrations of benzyl acetate, whereas animals in the feed studies received their daily dose over 24 hours.

However, more likely the differences in response were due to the different methods of administration and the resulting metabolites. In a subsequent toxicokinetic study conducted at NIEHS by Yuan *et al.* (1993), groups of 6 rats and 12 mice were administered benzyl acetate in corn oil by gavage at 500 mg/kg (rats) and 1,000 mg/kg (mice) for 7 days and groups of 10 F344/N male rats and 10 B6C3F$_1$ male mice were exposed to 10,800 ppm (rats) and 2,700 ppm (mice) benzyl acetate in feed for 7 days. High benzoic acid plasma concentrations were observed in the gavage study. In contrast, much lower concentrations were found after dosed feed administration. Although the daily doses of benzyl acetate are comparable, bolus gavage administration effectively saturated the benzoic acid elimination pathway while dosed feed administration did not. In contrast, hippuric acid plasma concentrations were similar after both gavage and dosed feed administration due to the depletion of the glycine supply pool. Compared to the dosed feed method of administration, the gavage method of administration is likely to result in higher blood levels of benzyl acetate and its metabolites.

Benzyl acetate administration in the feed study was also associated with increased incidences of nasal lesions in male and female mice. The lesions included atrophy and degeneration of the nasal epithelium and luminal exudate and pigmentation of the nasal mucosal epithelium. By comparison, benzyl acetate given in corn oil by gavage was associated with an increased incidence of forestomach hyperplasia (Abdo *et al.*, 1985; NTP, 1986). In humans, benzyl acetate is a known respiratory tract irritant when inhaled (Opdyke, 1973) and causes generalized intestinal irritation when ingested (Clayton and Clayton, 1981). Thus, the nonneoplastic lesions observed in both the dosed feed and the gavage mouse studies could be caused by a direct exposure of the respective tissue to a high concentration of the chemical. The forestomach is the deposition site for chemicals administered by gavage. Although in the feed study, the nose was not the deposition site for benzyl acetate, nasal tissue could have been exposed directly to high concentrations of the chemical or its degradation products. The results of chemical recovery studies showed that approximately 10% of the benzyl acetate in the feed was lost during storage in the animal room in open feeders for 24 hours. This loss could be due to the volatility of benzyl acetate, since this chemical has a relatively high vapor pressure (5 mmHg at 73° C). Since the mice were housed in polycarbonate cages with polyester cage filters, a buildup in benzyl acetate concentration is likely to have occurred in the cage air.

Nasal lesions did not occur in any of the previous studies with benzyl acetate or other structurally related chemicals (von Oettingen, 1960; Jenner *et al.*, 1964; NTP, 1986, 1989, and 1990). This difference could be related to the method of chemical administration. In all previous studies (except for von Oettingen, 1960), the chemical studied was administered by gavage and thus direct exposure of nasal tissue to benzyl acetate vapor was minimal. However, the von Oettingen study was an inhalation study and nasal tissue was exposed directly to benzyl acetate once for 7 hours. The cause of the nasal lesions that occurred in mice and not in rats is unclear. Because of lack of competition for feed for the individually housed mice compared to the group housed rats, mice could have spent more time at the feed troughs, leading to longer exposure to lower concentrations of benzyl acetate. The absence of nasal lesions in rats and mice in the 13-week study could be due to the possibility that a longer exposure period may be required for the development of these lesions.

CONCLUSIONS

Under the conditions of these 2-year feed studies, there was *no evidence of carcinogenic activity** of benzyl acetate in male or female F344/N rats receiving 3,000, 6,000, or 12,000 ppm; however, rats may have tolerated higher doses. There was *no evidence of carcinogenic activity* of benzyl acetate in male or female B6C3F$_1$ mice receiving 330, 1,000, or 3,000 ppm.

Nasal lesions associated with benzyl acetate exposure in male and female mice included nasal mucosa atrophy and degeneration (primarily of the olfactory epithelium), cystic hyperplasia of the nasal submucosal gland, and luminal exudate and pigmentation of the nasal mucosal epithelium.

In previous 2-year gavage studies, benzyl acetate increased the incidence of acinar cell adenomas of the exocrine pancreas in male F344/N rats; the gavage vehicle may have been a contributing factor. There was no evidence of carcinogenic activity in female F344/N rats receiving 250 or 500 mg/kg a day. There was some evidence of carcinogenic activity in male and female B6C3F$_1$ mice, indicated by the increased incidences of hepatocellular adenomas and squamous cell neoplasms of the forestomach.

* Explanation of Levels of Evidence of Carcinogenic Activity is on page 9. A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on page 11.

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APPENDIX A
SUMMARY OF LESIONS IN MALE RATS IN THE 2-YEAR FEED STUDY OF BENZYL ACETATE

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Feed Study of Benzyl Acetate[a]

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	10	10
Early deaths				
Moribund	20	12	16	14
Natural deaths	3	4	4	3
Survivors				
Terminal sacrifice	27	34	30	33
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Liver	(10)	(10)	(10)	(10)
Hepatocellular adenoma	1 (10%)			
Cardiovascular System				
None				
Endocrine System				
Adrenal gland, medulla	(10)	(10)	(10)	(10)
Pheochromocytoma benign		1 (10%)		
Pituitary gland	(10)	(10)	(9)	(10)
Pars distalis, adenoma	3 (30%)		1 (11%)	
Thyroid gland	(10)	(10)	(10)	(10)
C-cell, adenoma	1 (10%)			
General Body System				
None				
Genital System				
Preputial gland	(10)	(10)	(10)	(10)
Adenoma	1 (10%)	1 (10%)		
Testes	(10)	(10)	(10)	(10)
Bilateral, interstitial cell, adenoma	10 (100%)	8 (80%)	10 (100%)	10 (100%)
Interstitial cell, adenoma		1 (10%)		
Hematopoietic System				
None				
Integumentary System				
None				

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
15-Month Interim Evaluation (continued)				
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
Lung	(10)	(10)	(10)	(10)
Alveolar/bronchiolar adenoma	1 (10%)		1 (10%)	1 (10%)
Special Senses System				
Zymbal's gland			(1)	(1)
Carcinoma			1 (100%)	
Urinary System				
Urinary bladder	(10)	(10)	(10)	(10)
Squamous cell papilloma		1 (10%)		
2-Year Study				
Alimentary System				
Intestine large, cecum	(50)	(50)	(50)	(49)
Intestine large, colon	(50)	(50)	(49)	(49)
Adenocarcinoma		1 (2%)		
Intestine small, ileum	(49)	(50)	(50)	(49)
Intestine small, jejunum	(49)	(50)	(50)	(48)
Liver	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, intestine large		1 (2%)		
Hepatocellular carcinoma	1 (2%)			
Hepatocellular adenoma	4 (8%)	4 (8%)	3 (6%)	3 (6%)
Hepatocellular adenoma, two, multiple	1 (2%)			
Hepatocellular adenoma, three, multiple		1 (2%)		
Hepatocellular adenoma, four, multiple		1 (2%)		
Sarcoma, metastatic, uncertain primary site			1 (2%)	
Mesentery	(16)	(15)	(13)	(10)
Adenocarcinoma, metastatic, intestine large		1 (7%)		
Lipoma				1 (10%)
Sarcoma, metastatic, uncertain primary site			1 (8%)	
Pancreas	(50)	(50)	(50)	(49)
Adenocarcinoma, metastatic, intestine large		1 (2%)		
Acinar cell, adenoma	1 (2%)		3 (6%)	1 (2%)
Acinar cell, adenoma, multiple		2 (4%)		
Pharynx			(2)	(1)
Palate, squamous cell carcinoma			2 (100%)	
Palate, squamous cell papilloma				1 (100%)

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Alimentary System (continued)				
Salivary glands	(50)	(50)	(50)	(49)
Adenoma		1 (2%)		
Sarcoma, metastatic, uncertain primary site				1 (2%)
Stomach, forestomach	(50)	(50)	(50)	(50)
Basal cell adenoma				1 (2%)
Squamous cell papilloma				1 (2%)
Stomach, glandular	(50)	(50)	(50)	(50)
Tongue	(50)	(50)	(49)	(50)
Squamous cell carcinoma				1 (2%)
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic		1 (2%)		
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(50)
Adenoma	1 (2%)		2 (4%)	
Adrenal gland, medulla	(50)	(50)	(50)	(50)
Pheochromocytoma malignant	1 (2%)	2 (4%)	2 (4%)	2 (4%)
Pheochromocytoma complex	1 (2%)	2 (4%)		
Pheochromocytoma benign	16 (32%)	7 (14%)	15 (30%)	13 (26%)
Bilateral, pheochromocytoma benign	1 (2%)	4 (8%)	1 (2%)	1 (2%)
Islets, pancreatic	(50)	(50)	(50)	(50)
Adenoma	2 (4%)		1 (2%)	1 (2%)
Carcinoma				1 (2%)
Pituitary gland	(49)	(50)	(50)	(48)
Pars distalis, adenoma	8 (16%)	9 (18%)	9 (18%)	6 (13%)
Thyroid gland	(50)	(49)	(50)	(48)
C-cell, adenoma	8 (16%)	4 (8%)	7 (14%)	7 (15%)
C-cell, carcinoma	1 (2%)	1 (2%)	5 (10%)	1 (2%)
General Body System				
Tissue NOS	(1)	(1)	(2)	(1)
Cranial, sarcoma, metastatic, uncertain primary site				1 (100%)
Pelvic, sarcoma, metastatic, uncertain primary site			1 (50%)	
Genital System				
Epididymis	(50)	(50)	(50)	(50)
Preputial gland	(50)	(50)	(50)	(50)
Adenoma	2 (4%)	1 (2%)	3 (6%)	2 (4%)
Carcinoma		1 (2%)	1 (2%)	
Prostate	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, intestine large		1 (2%)		
Seminal vesicle	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, intestine large		1 (2%)		

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Genital System (continued)				
Testes	(50)	(50)	(50)	(50)
Bilateral, interstitial cell, adenoma	44 (88%)	48 (96%)	45 (90%)	44 (88%)
Interstitial cell, adenoma	3 (6%)	1 (2%)	5 (10%)	5 (10%)
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(49)
Lymph node	(50)	(50)	(50)	(49)
Deep cervical, carcinoma, metastatic, Zymbal's gland				1 (2%)
Mediastinal, adenocarcinoma, metastatic, intestine large		1 (2%)		
Renal, adenocarcinoma, metastatic, intestine large		1 (2%)		
Lymph node, mandibular	(50)	(49)	(50)	(48)
Carcinoma, metastatic, Zymbal's gland				1 (2%)
Sarcoma, metastatic, uncertain primary site				1 (2%)
Lymph node, mesenteric	(50)	(50)	(48)	(49)
Adenocarcinoma, metastatic, intestine large		1 (2%)		
Spleen	(50)	(50)	(50)	(50)
Fibroma		1 (2%)		
Osteosarcoma, metastatic, bone		1 (2%)		
Thymus	(48)	(48)	(48)	(46)
Adenocarcinoma, metastatic		1 (2%)		
Epithelial cell, thymoma benign	1 (2%)	1 (2%)		
Integumentary System				
Mammary gland	(48)	(48)	(50)	(50)
Fibroadenoma	4 (8%)	2 (4%)		1 (2%)
Skin	(50)	(50)	(50)	(50)
Basal cell carcinoma		1 (2%)		
Histiocytic sarcoma	1 (2%)			
Keratoacanthoma	5 (10%)		1 (2%)	
Schwannoma malignant, metastatic, skeletal muscle	1 (2%)			
Squamous cell papilloma				1 (2%)
Subcutaneous tissue, fibroma	4 (8%)	2 (4%)	3 (6%)	3 (6%)
Subcutaneous tissue, fibrosarcoma		1 (2%)		2 (4%)
Subcutaneous tissue, leiomyoma			1 (2%)	
Subcutaneous tissue, lipoma		1 (2%)		
Subcutaneous tissue, sarcoma	1 (2%)			
Subcutaneous tissue, sarcoma, metastatic, uncertain primary site				1 (2%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma		1 (2%)		

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Musculoskeletal System (continued)				
Skeletal muscle	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, intestine large		1 (2%)		
Sarcoma, metastatic, uncertain primary site				1 (2%)
Schwannoma malignant	1 (2%)			
Nervous System				
Brain	(50)	(50)	(50)	(50)
Glioma malignant		1 (2%)		
Glioma NOS		1 (2%)		
Oligodendroglioma malignant				1 (2%)
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, intestine large		1 (2%)		
Alveolar/bronchiolar adenoma	1 (2%)		1 (2%)	
Alveolar/bronchiolar adenoma, four, multiple				1 (2%)
Osteosarcoma, metastatic, bone		1 (2%)		
Squamous cell carcinoma, metastatic, uncertain primary site				1 (2%)
Mediastinum, adenocarcinoma, metastatic, intestine large		1 (2%)		
Nose	(50)	(50)	(50)	(50)
Mucosa, squamous cell carcinoma		1 (2%)	1 (2%)	1 (2%)
Vomeronasal organ, carcinoma		1 (2%)		
Special Senses System				
Zymbal's gland	(1)			(1)
Carcinoma	1 (100%)			1 (100%)
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, intestine large		1 (2%)		
Lipoma		1 (2%)		
Squamous cell carcinoma, metastatic, uncertain primary site				1 (2%)
Renal tubule, adenoma		1 (2%)		
Urinary bladder	(50)	(50)	(50)	(50)
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Histiocytic sarcoma	1 (2%)			
Leukemia mononuclear	16 (32%)	19 (38%)	18 (36%)	15 (30%)
Mesothelioma benign	1 (2%)	2 (4%)	1 (2%)	
Mesothelioma malignant		1 (2%)	1 (2%)	

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Neoplasm Summary				
Total animals with primary neoplasms[c]				
15-Month interim evaluation	10	9	10	10
2-Year study	50	50	50	50
Total primary neoplasms				
15-Month interim evaluation	17	12	13	11
2-Year study	131	128	131	118
Total animals with benign neoplasms				
15-Month interim evaluation	10	9	10	10
2-Year study	50	50	50	50
Total benign neoplasms				
15-Month interim evaluation	17	12	12	11
2-Year study	107	94	101	93
Total animals with malignant neoplasms				
15-Month interim evaluation			1	
2-Year study	20	29	27	22
Total malignant neoplasms				
15-Month interim evaluation			1	
2-Year study	24	33	30	25
Total animals with metastatic neoplasms				
2-Year study	1	2	1	3
Total metastatic neoplasms				
2-Year study	1	16	3	9
Total animals with malignant neoplasms of uncertain primary site				
2-Year study			1	2
Total animals with uncertain neoplasms 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] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 0 ppm

Number of Days on Study	4 6 7	4 8 7	4 9 5	5 2 5	5 4 2	5 6 0	5 7 4	6 0 0	6 0 0	6 3 1	6 3 3	6 4 3	6 5 4	6 6 8	6 8 2	7 0 5	7 0 5	7 1 0	7 1 4	7 2 4	7 2 5	7 2 5	7 2 5	7 2 9	7 2 9
Carcass ID Number	0 4 4	0 1 2	0 4 8	0 3 7	0 5 2	0 1 5	0 5 9	0 0 6	0 1 4	0 2 8	0 2 1	0 1 8	0 0 5	0 2 4	0 5 0	0 2 2	0 3 2	0 0 4	0 0 8	0 3 9	0 0 9	0 1 1	0 2 6	0 0 1	0 0 2
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																									
Hepatocellular adenoma																									X
Hepatocellular adenoma, two, multiple											X														
Mesentery				+	+		+				+				+	+	+			+			+		
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell, adenoma																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth															+								+		
Cardiovascular System																									
Blood vessel																							+		
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma													X												
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant															X										
Pheochromocytoma complex									X																
Pheochromocytoma benign								X					X				X	X	X						
Bilateral, pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma											X	X			X		X			X					
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma											X			X			X								
C-cell, carcinoma																									

+: 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 Feed Study of Benzyl Acetate: 0 ppm (continued)

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	00003	00007	00013	00116	00117	00120	00225	00330	00331	00333	00334	00336	00338	00340	00341	00442	00445	00447	00449	00551	00553	00555	00557	00558	00560	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma																X										1
Hepatocellular adenoma			X													X	X									4
Hepatocellular adenoma, two, multiple																										1
Mesentery					+		+		+			+							+					+	+	16
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Acinar cell, adenoma																					X					1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth																										2
Cardiovascular System																										
Blood vessel		+											+													3
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																										1
Pheochromocytoma complex																										1
Pheochromocytoma benign	X	X					X		X							X	X	X		X	X	X		X		16
Bilateral, pheochromocytoma benign																			X							1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																	X	X								2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma														X		X								X		8
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma		X	X									X										X	X			8
C-cell, carcinoma																								X		1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 0 ppm (continued)

Number of Days on Study	4 6 7	4 8 7	4 9 5	5 2 5	5 4 2	5 6 0	5 7 4	6 0 0	6 0 0	6 3 1	6 3 3	6 4 3	6 5 4	6 6 8	6 8 2	7 0 5	7 0 5	7 1 0	7 1 4	7 2 4	7 2 5	7 2 5	7 2 5	7 2 9	7 2 9
Carcass ID Number	0 4 4	0 1 2	0 4 8	0 3 7	0 5 2	0 1 5	0 5 9	0 0 6	0 1 4	0 2 8	0 2 1	0 1 8	0 0 5	0 2 4	0 5 0	0 2 2	0 3 2	0 0 4	0 0 8	0 3 9	0 0 9	0 1 1	0 2 6	0 0 1	0 0 2
General Body System																									
Tissue NOS																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma	X	X		X	X	X	X	X	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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Epithelial cell, thymoma benign																									
Integumentary System																									
Mammary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Fibroadenoma										X		X													
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																			X						
Keratoacanthoma																	X	X			X		X		
Schwannoma malignant, metastatic, skeletal muscle																									
Subcutaneous tissue, fibroma																X					X	X	X		
Subcutaneous tissue, sarcoma													X												
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Schwannoma malignant																									
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve									+																
Spinal cord							+		+																

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 0 ppm *(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 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	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	0 0 3	0 0 7	0 1 3	0 1 6	0 1 7	0 2 0	0 2 5	0 3 0	0 3 1	0 3 3	0 3 4	0 3 6	0 3 8	0 4 0	0 4 1	0 4 2	0 4 5	0 4 7	0 4 9	0 5 1	0 5 3	0 5 5	0 5 7	0 5 8	0 6 0	Total Tissues/ Tumors
General Body System																										
Tissue NOS							+																			1
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma			X			X																				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	X	X	44
Interstitial cell, adenoma																										3
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	48
Epithelial cell, thymoma benign				X																						1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Fibroadenoma								X														X				4
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Keratoacanthoma												X														5
Schwannoma malignant, metastatic, skeletal muscle																X										1
Subcutaneous tissue, fibroma																										4
Subcutaneous tissue, sarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Schwannoma malignant																X										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																										1
Spinal cord																										2

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 0 ppm (continued)

Number of Days on Study	4 6 7	4 8 7	4 9 5	5 2 5	5 4 2	5 6 0	5 7 4	6 0 0	6 0 0	6 3 1	6 3 3	6 4 3	6 5 4	6 6 8	6 8 2	7 0 5	7 0 5	7 1 0	7 1 4	7 2 4	7 2 5	7 2 5	7 2 9	7 2 9
Carcass ID Number	0 4 4	0 1 2	0 4 8	0 3 7	0 5 2	0 1 5	0 5 9	0 0 6	0 1 4	0 2 8	0 2 1	0 1 8	0 0 5	0 2 4	0 5 0	0 2 2	0 3 2	0 0 4	0 0 8	0 3 9	0 0 9	0 1 1	0 2 6	0 0 1	0 0 2
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																									
Eye							+		+																
Zymbal's gland																									
Carcinoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																			X						
Leukemia mononuclear					X	X		X		X	X		X		X			X	X		X			X
Mesothelioma benign																									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 0 ppm (continued)

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	00033	00077	00133	00166	00177	00220	00225	00330	00331	00333	00334	00336	00338	00340	00411	00422	00445	00447	00449	00451	00453	00455	00457	00458	00460	Total Tissues/ Tumors
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma														X												1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																+										1
Eye								+																		3
Zymbal's gland																	+									1
Carcinoma																	X									1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Leukemia mononuclear							X								X	X				X			X			16
Mesothelioma benign																								X		1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm

Number of Days on Study	3 9 6	4 8 8	5 0 4	5 2 8	5 5 3	5 7 0	5 8 1	6 0 0	6 1 8	6 3 0	6 3 3	6 5 5	6 9 3	7 0 4	7 0 5	7 1 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
Carcass ID Number	0 8 2	0 9 1	1 0 6	0 6 1	0 6 6	0 7 5	0 9 4	1 0 4	1 1 4	1 0 8	0 7 0	1 1 3	0 1 6	1 3 5	1 0 5	1 0 8	1 6 3	1 6 4	1 6 5	1 6 9	1 7 1	1 7 2	1 7 4	1 7 6	1 7 7
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma													X												
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, intestine large													X												
Hepatocellular adenoma																X									
Hepatocellular adenoma, three, multiple																									
Hepatocellular adenoma, four, multiple																									
Mesentery		+				+	+	+			+		+	+	+										
Adenocarcinoma, metastatic, intestine large													X												
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, intestine large													X												
Acinar cell, adenoma, multiple																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma												X													
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel																					+	+			
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic													X												
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant			X																			X			
Pheochromocytoma complex									X							X									
Pheochromocytoma benign																		X	X						
Bilateral, pheochromocytoma benign							X																		X
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																X	X								
Thyroid gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma									X							X		X		X					
C-cell, carcinoma																									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm (continued)

Number of Days on Study	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	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	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 7 9	0 8 1	0 8 3	0 8 4	0 8 6	0 8 7	0 8 8	0 8 9	0 9 0	0 9 2	0 9 5	0 9 6	0 9 8	0 9 9	1 0 0	1 0 1	1 0 3	1 0 7	1 0 9	1 1 1	1 1 2	1 1 6	1 1 7	1 1 8	1 2 0	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																										1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, intestine large																										1
Hepatocellular adenoma									X									X					X			4
Hepatocellular adenoma, three, multiple			X																							1
Hepatocellular adenoma, four, multiple								X																		1
Mesentery		+		+								+				+	+		+			+				15
Adenocarcinoma, metastatic, intestine large																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, intestine large																										1
Acinar cell, adenoma, multiple							X		X																	2
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Blood vessel																									+	3
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic																										1
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																										2
Pheochromocytoma complex																										2
Pheochromocytoma benign		X	X			X										X						X				7
Bilateral, pheochromocytoma benign																		X			X					4
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	46
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma					X	X											X	X	X	X				X		9
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
C-cell, adenoma																										4
C-cell, carcinoma																				X						1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm (continued)

Number of Days on Study	3 9 6	4 8 8	5 0 4	5 2 8	5 5 3	5 7 0	5 8 1	6 0 1	6 1 0	6 3 8	6 3 0	6 5 3	6 9 5	7 0 3	7 0 4	7 1 5	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
Carcass ID Number	0 8 2	0 9 1	1 0 6	0 6 1	0 6 6	0 7 5	0 9 4	1 0 4	1 1 4	1 0 8	0 7 0	1 1 3	0 6 8	1 0 5	1 0 5	1 7 8	0 6 3	0 6 4	0 6 5	0 6 9	0 7 1	0 7 2	0 7 4	0 7 6	0 7 7
General Body System																									
Tissue NOS													+												
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma												X													
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, intestine large													X												
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, intestine large													X												
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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	X	X
Interstitial cell, adenoma																					X				
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, adenocarcinoma, metastatic, intestine large													X												
Renal, adenocarcinoma, metastatic, intestine large													X												
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, intestine large													X												
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																		X							
Osteosarcoma, metastatic, bone																									X
Thymus	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic													X												
Epithelial cell, thymoma benign																									
Integumentary System																									
Mammary gland	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma																									
Subcutaneous tissue, fibroma								X																	
Subcutaneous tissue, fibrosarcoma																									
Subcutaneous tissue, lipoma																		X							

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm (continued)

Number of Days on Study	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	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	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 7 9	0 8 1	0 8 3	0 8 4	0 8 6	0 8 7	0 8 8	0 8 9	0 9 0	0 9 2	0 9 5	0 9 6	0 9 8	0 9 9	0 9 0	1 0 1	1 0 3	1 0 7	1 0 9	1 1 1	1 1 2	1 1 6	1 1 7	1 1 8	1 2 0	Total Tissues/ Tumors
General Body System																										
Tissue NOS																										1
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma							X																			1
Carcinoma																										1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, intestine large																										1
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, intestine large																										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		X	X	X	48
Interstitial cell, adenoma																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mediastinal, adenocarcinoma, metastatic, intestine large																										1
Renal, adenocarcinoma, metastatic, intestine large																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, intestine large																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroma																										1
Osteosarcoma, metastatic, bone																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenocarcinoma, metastatic																										1
Epithelial cell, thymoma benign																	X									1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Fibroadenoma									X			X														2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Basal cell carcinoma																		X								1
Subcutaneous tissue, fibroma								X																		2
Subcutaneous tissue, fibrosarcoma													X													1
Subcutaneous tissue, lipoma																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm (continued)

Number of Days on Study	3 9 6	4 8 8	5 0 4	5 2 8	5 5 3	5 7 0	5 8 1	6 0 0	6 1 8	6 3 0	6 3 3	6 5 5	6 9 3	7 0 4	7 0 5	7 1 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
Carcass ID Number	0 8 2	0 9 1	1 0 6	0 6 1	0 6 6	0 7 5	0 9 4	1 0 4	1 1 4	1 0 8	0 7 0	1 1 3	0 6 8	1 0 5	1 0 5	0 7 8	0 6 3	0 6 4	0 6 5	0 7 9	0 7 1	0 7 2	0 7 4	0 7 6	0 7 7
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma																									X
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, intestine large													X												
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glioma malignant																									
Glioma NOS								X																	
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, intestine large													X												
Osteosarcoma, metastatic, bone																									X
Mediastinum, adenocarcinoma, metastatic, intestine large													X												
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucosa, squamous cell carcinoma														X											
Vomeronasal organ, carcinoma	X																								
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																								+	
Eye																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, intestine large													X												
Lipoma																						X			
Renal tubule, adenoma																							X		
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X	X		X		X	X		X	X	X					X			X						
Mesothelioma benign								X																	
Mesothelioma malignant															X										

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm (continued)

Number of Days on Study	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	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	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 7 9	0 8 1	0 8 3	0 8 4	0 8 6	0 8 7	0 8 8	0 8 9	0 9 0	0 9 2	0 9 5	0 9 6	0 9 8	0 9 9	0 9 0	1 0 1	1 0 3	1 0 7	1 0 9	1 1 1	1 1 2	1 1 6	1 1 7	1 1 8	1 2 0	Total Tissues/ Tumors
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, intestine large																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Glioma malignant								X																		1
Glioma NOS																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, intestine large																										1
Osteosarcoma, metastatic, bone																										1
Mediastinum, adenocarcinoma, metastatic, intestine large																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mucosa, squamous cell carcinoma																										1
Vomeronasal organ, carcinoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																										1
Eye						+											+									2
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, intestine large																										1
Lipoma																										1
Renal tubule, adenoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X	X			X	X	X			X	X											X			19
Mesothelioma benign																X										2
Mesothelioma malignant																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 6,000 ppm

Number of Days on Study	4 5 7	4 9 1	5 8 9	6 2 2	6 3 3	6 3 4	6 4 1	6 4 4	6 5 8	6 6 8	6 7 4	6 8 3	6 9 3	6 9 6	6 9 7	6 9 9	7 0 1	7 1 0	7 1 0	7 2 4	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0
Carcass ID Number	1 7 3	1 6 8	1 2 5	1 3 4	1 5 3	1 2 1	1 2 4	1 7 9	1 5 7	1 5 9	1 3 5	1 4 3	1 2 7	1 7 6	1 4 4	1 3 0	1 2 3	1 5 1	1 6 5	1 2 6	1 2 8	1 2 9	1 3 1	1 3 2	1 3 6
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma							X										X		X						
Sarcoma, metastatic, uncertain primary site																X									
Mesentery	+				+						+	+		+		+	+					+			
Sarcoma, metastatic, uncertain primary site																X									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell, adenoma																									
Pharynx				+																					
Palate, squamous cell carcinoma				X																					
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																	X								
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																									
Pheochromocytoma benign					X						X							X	X	X	X				X
Bilateral, pheochromocytoma benign																								X	
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma					X																				
Parathyroid gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma								X		X													X		
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																					X			X	
C-cell, carcinoma										X												X			
General Body System																									
Tissue NOS																+									
Pelvic, sarcoma, metastatic, uncertain primary site																X									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 6,000 ppm (continued)

Number of Days on Study	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 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 0	7 3 0	7 3 0	7 3 0	
Carcass ID Number	1 3 7	1 3 9	1 4 0	1 4 2	1 4 6	1 4 7	1 4 8	1 4 9	1 5 0	1 5 2	1 5 4	1 5 5	1 5 6	1 6 0	1 6 1	1 6 3	1 6 4	1 6 6	1 6 9	1 7 1	1 7 2	1 7 5	1 7 7	1 7 8	1 8 0	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma																										3
Sarcoma, metastatic, uncertain primary site																										1
Mesentery									+	+					+	+	+									13
Sarcoma, metastatic, uncertain primary site																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Acinar cell, adenoma										X							X								X	3
Pharynx								+																		2
Palate, squamous cell carcinoma								X																		2
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cardiovascular System																										
Blood vessel																									+	1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma	X																									2
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																					X			X		2
Pheochromocytoma benign	X	X	X						X			X		X		X	X									15
Bilateral, pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma	X										X			X					X			X	X			9
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma									X										X		X	X	X			7
C-cell, carcinoma				X											X										X	5
General Body System																										
Tissue NOS																	+									2
Pelvic, sarcoma, metastatic, uncertain primary site																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 6,000 ppm (continued)

Number of Days on Study	4 5 7	4 9 1	5 8 9	6 2 2	6 3 3	6 3 4	6 4 1	6 4 4	6 5 8	6 6 8	6 7 4	6 8 3	6 9 3	6 9 6	6 9 7	6 9 9	7 0 1	7 1 0	7 1 0	7 2 4	7 3 0	7 3 0	7 3 0	7 3 0
Carcass ID Number	1 7 3	1 6 8	1 2 5	1 3 4	1 5 3	1 2 1	1 2 4	1 7 9	1 5 7	1 5 9	1 3 5	1 4 3	1 2 7	1 7 6	1 4 4	1 3 0	1 2 3	1 5 1	1 6 5	1 2 6	1 2 8	1 2 9	1 3 1	1 3 2	1 3 6
Genital System																								
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma																				X					
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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
Interstitial cell, adenoma	X															X								X	
Hematopoietic System																									
Blood																		+							
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																	X								
Subcutaneous tissue, fibroma							X						X				X								
Subcutaneous tissue, leiomyoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																	X								
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucosa, squamous cell carcinoma			X																						
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																									
Eye																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X				X	X	X	X	X			X		X	X			X	X	X				X	
Mesothelioma benign																									
Mesothelioma malignant											X														

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 6,000 ppm (continued)

Number of Days on Study	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 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 0	7 3 0	7 3 0	
Carcass ID Number	1 3 7	1 3 9	1 4 0	1 4 2	1 4 6	1 4 7	1 4 8	1 4 9	1 5 0	1 5 2	1 5 4	1 5 5	1 5 6	1 6 0	1 6 1	1 6 3	1 6 4	1 6 6	1 6 9	1 7 1	1 7 2	1 7 5	1 7 7	1 7 8	1 8 0	Total Tissues/ Tumors
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma					X						X	X														3
Carcinoma																										1
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	X	45
Interstitial cell, adenoma																X							X			5
Hematopoietic System																										
Blood																										1
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Keratoacanthoma																										1
Subcutaneous tissue, fibroma																										3
Subcutaneous tissue, leiomyoma		X																								1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mucosa, squamous cell carcinoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear			+																							1
Eye													+													1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear		X		X											X							X	X			18
Mesothelioma benign																	X									1
Mesothelioma malignant																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 12,000 ppm

Number of Days on Study	4 3 1	5 0 1	5 3 9	5 4 6	5 7 3	5 8 4	6 1 3	6 3 0	6 3 1	6 3 8	6 4 3	6 4 4	6 4 8	6 6 6	7 1 5	7 2 4	7 2 4	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 0 4	2 3 3	2 1 0	2 3 7	2 2 6	2 0 9	2 2 5	2 0 1	2 2 9	2 0 6	2 1 0	1 4 8	2 1 3	1 8 2	2 2 4	1 8 4	2 2 2	1 8 3	1 8 5	1 8 6	1 8 7	1 9 8	1 9 0	1 9 1	1 9 2	1 9 3
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																										
Mesentery	+					+					+												+		+	
Lipoma																										
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell, adenoma																										
Pharynx																										
Palate, squamous cell papilloma																										
Salivary glands	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uncertain primary site						X																				
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell adenoma																										
Squamous cell papilloma																										
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma	X																									
Tooth																										
Cardiovascular System																										
Blood vessel																					+					
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																										
Pheochromocytoma benign																X	X	X	X					X	X	
Bilateral, pheochromocytoma benign																										
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																								X		
Carcinoma							X																			
Parathyroid gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	M	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma												X	X			X										
Thyroid gland	+	+	+	+	+	+	+	M	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma															X			X								
C-cell, carcinoma																										

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 12,000 ppm (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 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 0	
Carcass ID Number	1 9 5	1 9 6	1 9 7	1 9 9	2 0 0	2 0 3	2 0 5	2 0 8	2 1 1	2 1 3	2 1 5	2 1 6	2 1 7	2 1 8	2 1 9	2 2 1	2 2 2	2 2 3	2 2 7	2 2 8	2 3 0	2 3 4	2 3 5	2 3 8	2 3 9	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma		X	X							X																3
Mesentery			+	+	+																		+		+	10
Lipoma				X																						1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Acinar cell, adenoma											X															1
Pharynx		+																								1
Palate, squamous cell papilloma		X																								1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sarcoma, metastatic, uncertain primary site																										1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Basal cell adenoma										X																1
Squamous cell papilloma																				X						1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma																										1
Tooth							+																			1
Cardiovascular System																										
Blood vessel				+			+																+	+		5
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																			X	X						2
Pheochromocytoma benign		X			X				X						X				X	X		X				13
Bilateral, pheochromocytoma benign			X																							1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Carcinoma																										1
Parathyroid gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma					X									X		X										6
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
C-cell, adenoma				X				X			X	X		X												7
C-cell, carcinoma																								X		1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 12,000 ppm (continued)

Number of Days on Study	4 3 1	5 0 1	5 3 9	5 4 6	5 7 3	5 8 4	6 1 3	6 3 0	6 3 1	6 3 8	6 4 3	6 4 4	6 6 8	6 8 6	7 1 5	7 2 4	7 2 4	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 0 4	2 3 3	2 1 0	2 3 7	2 2 6	2 0 9	2 2 5	2 0 1	2 2 9	2 0 6	2 4 0	1 8 3	2 1 2	1 8 4	2 8 4	1 3 2	2 8 2	3 3 2	1 8 5	1 8 6	1 8 7	1 8 8	1 9 0	1 9 1	1 9 2	1 9 3
General Body System																										
Tissue NOS						+																				
Cranial, sarcoma, metastatic, uncertain primary site						X																				
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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	X
Interstitial cell, adenoma							X						X													
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Deep cervical, carcinoma, metastatic, Zymbal's gland									X																	
Lymph node, mandibular	+	+	+	+	+	+	+	M	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, Zymbal's gland									X																	
Sarcoma, metastatic, uncertain primary site						X																				
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	M	M	+	+	+	+	+	+
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma														X												
Subcutaneous tissue, fibroma															X				X							
Subcutaneous tissue, fibrosarcoma			X																							
Subcutaneous tissue, sarcoma, metastatic, uncertain primary site						X																				
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uncertain primary site						X																				

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 12,000 ppm (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 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 0	
Carcass ID Number	1 9 5	1 9 6	1 9 7	1 9 9	2 0 0	2 0 3	2 0 5	2 0 8	2 1 1	2 1 3	2 1 5	2 1 6	2 1 7	2 1 8	2 1 9	2 2 1	2 2 2	2 2 3	2 2 7	2 2 8	2 3 0	2 3 4	2 3 5	2 3 8	2 3 9	Total Tissues/ Tumors
General Body System																										
Tissue NOS																										1
Cranial, sarcoma, metastatic, uncertain primary site																										1
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma	X																				X					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	44
Interstitial cell, adenoma	X	X																			X					5
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Deep cervical, carcinoma, metastatic, Zymbal's gland																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, metastatic, Zymbal's gland																										1
Sarcoma, metastatic, uncertain primary site																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroadenoma									X																	1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																										1
Subcutaneous tissue, fibroma										X																3
Subcutaneous tissue, fibrosarcoma									X																	2
Subcutaneous tissue, sarcoma, metastatic, uncertain primary site																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, uncertain primary site																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 12,000 ppm (continued)

Number of Days on Study	4 3 1	5 0 1	5 3 9	5 4 6	5 7 3	5 8 4	6 1 3	6 3 0	6 3 1	6 3 8	6 4 3	6 4 4	6 6 8	6 8 6	7 1 5	7 2 4	7 2 4	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 0 4	2 3 3	2 1 0	2 3 7	2 2 6	2 0 9	2 2 5	2 0 1	2 2 9	2 0 6	2 4 0	1 8 3	2 1 2	1 8 4	2 2 4	1 8 4	2 8 2	1 3 2	1 8 2	1 8 5	1 8 6	1 8 7	1 9 8	1 9 0	1 9 1	1 9 2	1 9 3
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Oligodendroglioma malignant					X																						
Spinal cord							+																				
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma, four, multiple																											
Squamous cell carcinoma, metastatic, uncertain primary site										X																	
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucosa, squamous cell carcinoma									X																		
Trachea	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																											
Eye		+				+																					
Zymbal's gland									+																		
Carcinoma									X																		
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, uncertain primary site										X																	
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X	X		X			X				X			X	X	X	X										

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Feed Study of Benzyl Acetate: 12,000 ppm (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 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 0	
Carcass ID Number	1 9 5	1 9 6	1 9 7	1 9 9	2 0 0	2 0 3	2 0 5	2 0 8	2 1 1	2 1 3	2 1 5	2 1 6	2 1 7	2 1 8	2 1 9	2 2 1	2 2 2	2 2 3	2 2 7	2 2 8	2 3 0	2 3 4	2 3 5	2 3 8	2 3 9	Total Tissues/ Tumors
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Oligodendroglioma malignant																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma, four, multiple			X																							1
Squamous cell carcinoma, metastatic, uncertain primary site																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mucosa, squamous cell carcinoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Special Senses System																										
Eye									I																	2
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, metastatic, uncertain primary site																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X										X			X		X					X				15

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Feed Study of Benzyl Acetate

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Adrenal Medulla: Benign Pheochromocytoma				
Overall rate[a]	17/60 (28%)	12/60 (20%)	16/60 (27%)	14/60 (23%)
Adjusted rate[b]	51.8%	32.2%	45.1%	40.0%
Interim evaluation	0/10 (0%)	1/10 (10%)	0/10 (0%)	0/10 (0%)
Terminal rate[c]	12/27 (44%)	10/34 (29%)	11/30 (37%)	12/33 (36%)
First incidence (days)	600	457 (I)	633	724
Life table test[d]	P=0.270N	P=0.075N	P=0.389N	P=0.158N
Logistic regression test[d]	P=0.351N	P=0.163N	P=0.402N	P=0.261N
Cochran-Armitage test[d]	P=0.410N			
Fisher exact test[d]		P=0.197N	P=0.500N	P=0.339N
Adrenal Medulla: Pheochromocytoma (Benign, Complex, or Malignant)				
Overall rate	19/60 (32%)	16/60 (27%)	18/60 (30%)	15/60 (25%)
Adjusted rate	54.2%	39.6%	50.9%	42.9%
Interim evaluation	0/10 (0%)	1/10 (10%)	0/10 (0%)	0/10 (0%)
Terminal rate	12/27 (44%)	11/34 (32%)	13/30 (43%)	13/33 (39%)
First incidence (days)	600	457 (I)	633	724
Life table test	P=0.165N	P=0.175N	P=0.379N	P=0.117N
Logistic regression test	P=0.225N	P=0.314N	P=0.395N	P=0.202N
Cochran-Armitage test	P=0.281N			
Fisher exact test		P=0.344N	P=0.500N	P=0.272N
Liver: Hepatocellular Adenoma				
Overall rate	6/60 (10%)	6/60 (10%)	3/60 (5%)	3/60 (5%)
Adjusted rate	18.5%	17.1%	8.0%	9.1%
Interim evaluation	1/10 (10%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	4/27 (15%)	5/34 (15%)	0/30 (0%)	3/33 (9%)
First incidence (days)	458 (I)	710	641	729 (T)
Life table test	P=0.109N	P=0.492N	P=0.216N	P=0.172N
Logistic regression test	P=0.127N	P=0.606N	P=0.232N	P=0.231N
Cochran-Armitage test	P=0.141N			
Fisher exact test		P=0.619N	P=0.245N	P=0.245N
Mammary Gland: Fibroadenoma				
Overall rate	4/60 (7%)	2/60 (3%)	0/60 (0%)	1/60 (2%)
Adjusted rate	12.0%	5.9%	0.0%	3.0%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	2/27 (7%)	2/34 (6%)	0/30 (0%)	1/33 (3%)
First incidence (days)	631	729 (T)	–[e]	729 (T)
Life table test	P=0.071N	P=0.273N	P=0.053N	P=0.146N
Logistic regression test	P=0.080N	P=0.326N	P=0.059N	P=0.172N
Cochran-Armitage test	P=0.087N			
Fisher exact test		P=0.340N	P=0.059N	P=0.182N
Pancreas: Adenoma				
Overall rate	1/60 (2%)	2/60 (3%)	3/60 (5%)	1/59 (2%)
Adjusted rate	3.7%	5.9%	10.0%	3.0%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	1/27 (4%)	2/34 (6%)	3/30 (10%)	1/33 (3%)
First incidence (days)	729 (T)	729 (T)	729 (T)	729 (T)
Life table test	P=0.525N	P=0.581	P=0.342	P=0.717N
Logistic regression test	P=0.525N	P=0.581	P=0.342	P=0.717N
Cochran-Armitage test	P=0.584N			
Fisher exact test		P=0.500	P=0.309	P=0.748

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	11/59 (19%)	9/60 (15%)	10/60 (17%)	6/58 (10%)
Adjusted rate	26.8%	25.7%	28.3%	16.2%
Interim evaluation	3/10 (30%)	0/10 (0%)	1/10 (10%)	0/10 (0%)
Terminal rate	3/27 (11%)	8/34 (24%)	7/30 (23%)	3/33 (9%)
First incidence (days)	456 (I)	710	458 (I)	644
Life table test	P=0.099N	P=0.286N	P=0.430N	P=0.116N
Logistic regression test	P=0.133N	P=0.383N	P=0.479N	P=0.154N
Cochran-Armitage test	P=0.145N			
Fisher exact test		P=0.387N	P=0.483N	P=0.156N
Preputial Gland: Adenoma				
Overall rate	3/60 (5%)	2/60 (3%)	3/60 (5%)	2/60 (3%)
Adjusted rate	9.1%	4.6%	10.0%	6.1%
Interim evaluation	1/10 (10%)	1/10 (10%)	0/10 (0%)	0/10 (0%)
Terminal rate	2/27 (7%)	1/34 (3%)	3/30 (10%)	2/33 (6%)
First incidence (days)	458 (I)	456 (I)	729 (T)	729 (T)
Life table test	P=0.406N	P=0.437N	P=0.622N	P=0.427N
Logistic regression test	P=0.450N	P=0.502N	P=0.647N	P=0.493N
Cochran-Armitage test	P=0.457N			
Fisher exact test		P=0.500N	P=0.660N	P=0.500N
Preputial Gland: Adenoma or Carcinoma				
Overall rate	3/60 (5%)	3/60 (5%)	4/60 (7%)	2/60 (3%)
Adjusted rate	9.1%	7.0%	12.9%	6.1%
Interim evaluation	1/10 (10%)	1/10 (10%)	0/10 (0%)	0/10 (0%)
Terminal rate	2/27 (7%)	1/34 (3%)	3/30 (10%)	2/33 (6%)
First incidence (days)	458 (I)	456 (I)	724	729 (T)
Life table test	P=0.371N	P=0.603N	P=0.541	P=0.427N
Logistic regression test	P=0.412N	P=0.661	P=0.522	P=0.493N
Cochran-Armitage test	P=0.421N			
Fisher exact test		P=0.660N	P=0.500	P=0.500N
Skin: Keratoacanthoma				
Overall rate	5/60 (8%)	0/60 (0%)	1/60 (2%)	0/60 (0%)
Adjusted rate	15.3%	0.0%	2.9%	0.0%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	1/27 (4%)	0/34 (0%)	0/30 (0%)	0/33 (0%)
First incidence (days)	705	–	701	–
Life table test	P=0.017N	P=0.027N	P=0.109N	P=0.028N
Logistic regression test	P=0.016N	P=0.028N	P=0.088N	P=0.028N
Cochran-Armitage test	P=0.018N			
Fisher exact test		P=0.029N	P=0.103N	P=0.029N
Skin: Squamous Cell Papilloma, Keratoacanthoma, or Basal Cell Carcinoma				
Overall rate	5/60 (8%)	1/60 (2%)	1/60 (2%)	1/60 (2%)
Adjusted rate	15.3%	2.9%	2.9%	2.7%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	1/27 (4%)	1/34 (3%)	0/30 (0%)	0/33 (0%)
First incidence (days)	705	729 (T)	701	686
Life table test	P=0.067N	P=0.081N	P=0.109N	P=0.089N
Logistic regression test	P=0.065N	P=0.090N	P=0.088N	P=0.092N
Cochran-Armitage test	P=0.072N			
Fisher exact test		P=0.103N	P=0.103N	P=0.103N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Skin (Subcutaneous Tissue): Fibroma				
Overall rate	4/60 (7%)	2/60 (3%)	3/60 (5%)	3/60 (5%)
Adjusted rate	12.6%	5.2%	7.6%	8.7%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	0/27 (0%)	1/34 (3%)	0/30 (0%)	2/33 (6%)
First incidence (days)	705	600	641	715
Life table test	P=0.466N	P=0.294N	P=0.491N	P=0.434N
Logistic regression test	P=0.483N	P=0.325N	P=0.470N	P=0.467N
Cochran-Armitage test	P=0.500N			
Fisher exact test		P=0.340N	P=0.500N	P=0.500N
Skin (Subcutaneous Tissue): Fibroma, Fibrosarcoma, or Sarcoma				
Overall rate	5/60 (8%)	3/60 (5%)	3/60 (5%)	5/60 (8%)
Adjusted rate	14.9%	8.1%	7.6%	13.5%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	0/27 (0%)	2/34 (6%)	0/30 (0%)	3/33 (9%)
First incidence (days)	654	600	641	539
Life table test	P=0.541	P=0.303N	P=0.347N	P=0.557N
Logistic regression test	P=0.515	P=0.343N	P=0.330N	P=0.611N
Cochran-Armitage test	P=0.500			
Fisher exact test		P=0.359N	P=0.359N	P=0.628N
Testes: Adenoma				
Overall rate	57/60 (95%)	58/60 (97%)	60/60 (100%)	59/60 (98%)
Adjusted rate	98.2%	98.3%	100.0%	100.0%
Interim evaluation	10/10 (100%)	9/10 (90%)	10/10 (100%)	10/10 (100%)
Terminal rate	26/27 (96%)	33/34 (97%)	30/30 (100%)	33/33 (100%)
First incidence (days)	456 (I)	396	456 (I)	431
Life table test	P=0.352N	P=0.199N	P=0.497N	P=0.271N
Logistic regression test	P=0.162	P=0.499	P=0.113	P=0.293
Cochran-Armitage test	P=0.164			
Fisher exact test		P=0.500	P=0.122	P=0.309
Thyroid Gland (C-cell): Adenoma				
Overall rate	9/60 (15%)	4/59 (7%)	7/60 (12%)	7/58 (12%)
Adjusted rate	26.2%	10.7%	23.3%	20.5%
Interim evaluation	1/10 (10%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	5/27 (19%)	2/34 (6%)	7/30 (23%)	6/33 (18%)
First incidence (days)	457 (I)	618	729 (T)	715
Life table test	P=0.397N	P=0.082N	P=0.320N	P=0.277N
Logistic regression test	P=0.479N	P=0.117N	P=0.348N	P=0.391N
Cochran-Armitage test	P=0.510N			
Fisher exact test		P=0.126N	P=0.395N	P=0.423N
Thyroid Gland (C-cell): Carcinoma				
Overall rate	1/60 (2%)	1/59 (2%)	5/60 (8%)	1/58 (2%)
Adjusted rate	3.7%	2.9%	15.4%	3.0%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	1/27 (4%)	1/34 (3%)	4/30 (13%)	1/33 (3%)
First incidence (days)	729 (T)	729 (T)	668	729 (T)
Life table test	P=0.551	P=0.710N	P=0.129	P=0.717N
Logistic regression test	P=0.513	P=0.710N	P=0.116	P=0.717N
Cochran-Armitage test	P=0.488			
Fisher exact test		P=0.748	P=0.103	P=0.744

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Thyroid Gland (C-cell): Adenoma or Carcinoma				
Overall rate	10/60 (17%)	5/59 (8%)	12/60 (20%)	8/58 (14%)
Adjusted rate	29.6%	13.5%	38.2%	23.4%
Interim evaluation	1/10 (10%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	6/27 (22%)	3/34 (9%)	11/30 (37%)	7/33 (21%)
First incidence (days)	457 (I)	618	668	715
Life table test	P=0.430N	P=0.084N	P=0.504	P=0.268N
Logistic regression test	P=0.528N	P=0.129N	P=0.466	P=0.393N
Cochran-Armitage test	P=0.534			
Fisher exact test		P=0.142N	P=0.407	P=0.430N
All Organs: Mononuclear Cell Leukemia				
Overall rate	16/60 (27%)	19/60 (32%)	18/60 (30%)	15/60 (25%)
Adjusted rate	40.4%	42.6%	41.3%	34.4%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	6/27 (22%)	10/34 (29%)	6/30 (20%)	6/33 (18%)
First incidence (days)	542	396	457	431
Life table test	P=0.303N	P=0.503	P=0.525	P=0.375N
Logistic regression test	P=0.371N	P=0.350	P=0.459	P=0.485N
Cochran-Armitage test	P=0.386N			
Fisher exact test		P=0.344	P=0.420	P=0.500N
All Organs: Benign or Malignant Mesothelioma				
Overall rate	1/60 (2%)	3/60 (5%)	2/60 (3%)	0/60 (0%)
Adjusted rate	3.7%	7.8%	5.8%	0.0%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	1/27 (4%)	1/34 (3%)	1/30 (3%)	0/33 (0%)
First incidence (days)	729 (T)	600	674	–
Life table test	P=0.222N	P=0.352	P=0.537	P=0.460N
Logistic regression test	P=0.234N	P=0.311	P=0.521	P=0.460N
Cochran-Armitage test	P=0.242N			
Fisher exact test		P=0.309	P=0.500	P=0.500N
All Organs: Benign Neoplasms				
Overall rate	60/60 (100%)	59/60 (98%)	60/60 (100%)	60/60 (100%)
Adjusted rate	100.0%	100.0%	100.0%	100.0%
Interim evaluation	10/10 (100%)	9/10 (90%)	10/10 (100%)	10/10 (100%)
Terminal rate	27/27 (100%)	34/34 (100%)	30/30 (100%)	33/33 (100%)
First incidence (days)	456 (I)	396	456 (I)	431
Life table test	P=0.247N	P=0.115N	P=0.316N	P=0.173N
Logistic regression test	P=0.577	P=0.542N	–[f]	–
Cochran-Armitage test	P=0.567			
Fisher exact test		P=0.500N	P=1.000N	P=1.000N
All Organs: Malignant Neoplasms				
Overall rate	20/60 (33%)	29/60 (48%)	29/60 (48%)	24/60 (40%)
Adjusted rate	49.0%	60.1%	59.5%	50.2%
Interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	0/10 (0%)
Terminal rate	8/27 (30%)	15/34 (44%)	11/30 (37%)	10/33 (30%)
First incidence (days)	542	396	456 (I)	431
Life table test	P=0.529	P=0.215	P=0.178	P=0.466
Logistic regression test	P=0.399	P=0.069	P=0.082	P=0.299
Cochran-Armitage test	P=0.379			
Fisher exact test		P=0.068	P=0.068	P=0.285

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
All Organs: Benign or Malignant Neoplasms				
Overall rate	60/60 (100%)	59/60 (98%)	60/60 (100%)	60/60 (100%)
Adjusted rate	100.0%	100.0%	100.0%	100.0%
Interim evaluation	10/10 (100%)	9/10 (90%)	10/10 (100%)	10/10 (100%)
Terminal rate	27/27 (100%)	34/34 (100%)	30/30 (100%)	33/33 (100%)
First incidence (days)	456 (I)	396	456 (I)	431
Life table test	P=0.247N	P=0.115N	P=0.316N	P=0.173N
Logistic regression test	P=0.577	P=0.542N	–	–
Cochran-Armitage test	P=0.567			
Fisher exact test		P=0.500N	P=1.000N	P=1.000N

(T)Terminal sacrifice
(I)Interim evaluation
[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 exposure group incidence are the P values corresponding to pairwise comparisons between the controls and that exposure 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 test regards 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 an exposure group is indicated by N.
[e] Not applicable; no neoplasms in animal group
[f] Value of statistic cannot be computed.

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Feed Study of Benzyl Acetate[a]

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	10	10
Early deaths				
Moribund	20	12	16	14
Natural deaths	3	4	4	3
Survivors				
Terminal sacrifice	27	34	30	33
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Intestine large, cecum	(10)	(10)	(10)	(10)
Parasite metazoan		1 (10%)		
Intestine large, colon	(10)	(10)	(10)	(10)
Parasite metazoan		1 (10%)		
Intestine large, rectum	(10)	(10)	(10)	(10)
Parasite metazoan	1 (10%)			2 (20%)
Intestine small, ileum	(10)	(10)	(10)	(10)
Congestion		1 (10%)		
Liver	(10)	(10)	(10)	(10)
Fatty change	7 (70%)	8 (80%)	9 (90%)	7 (70%)
Focal cellular change	2 (20%)	1 (10%)		
Hepatodiaphragmatic nodule	1 (10%)	1 (10%)		
Infiltration cellular, mixed cell	1 (10%)			
Inflammation, focal	10 (100%)	10 (100%)	10 (100%)	9 (90%)
Bile duct, hyperplasia	9 (90%)	10 (100%)	10 (100%)	10 (100%)
Biliary tract, fibrosis	7 (70%)	8 (80%)	10 (100%)	9 (90%)
Mesentery	(1)	(1)		(1)
Fat, necrosis	1 (100%)	1 (100%)		1 (100%)
Pancreas	(10)	(10)	(10)	(10)
Atrophy, focal	3 (30%)	5 (50%)	5 (50%)	3 (30%)
Acinar cell, hyperplasia	2 (20%)		3 (30%)	
Salivary glands	(10)	(10)	(10)	(10)
Atrophy, focal			1 (10%)	
Stomach, forestomach	(10)	(10)	(10)	(10)
Inflammation, chronic				1 (10%)
Cardiovascular System				
Blood vessel				(1)
Mesenteric artery, inflammation, chronic				1 (100%)
Endocrine System				
Adrenal gland, cortex	(10)	(10)	(10)	(10)
Focal cellular change	3 (30%)	1 (10%)		
Adrenal gland, medulla	(10)	(10)	(10)	(10)
Angiectasis	1 (10%)			
Hyperplasia	1 (10%)			

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
15-Month Interim Evaluation (continued)				
Endocrine System (continued)				
Pituitary gland	(10)	(10)	(9)	(10)
Angiectasis	1 (10%)			
Cyst				1 (10%)
Pars distalis, focal cellular change		1 (10%)	1 (11%)	3 (30%)
Thyroid gland	(10)	(10)	(10)	(10)
C-cell, hyperplasia			1 (10%)	1 (10%)
Follicle, cyst	1 (10%)			
General Body System				
None				
Genital System				
Preputial gland	(10)	(10)	(10)	(10)
Degeneration, cystic	9 (90%)	10 (100%)	10 (100%)	10 (100%)
Inflammation, chronic	1 (10%)	1 (10%)		
Prostate	(10)	(10)	(10)	(10)
Dilatation	1 (10%)	1 (10%)		
Hyperplasia		1 (10%)		
Inflammation, suppurative	5 (50%)	4 (40%)	3 (30%)	6 (60%)
Testes	(10)	(10)	(10)	(10)
Germinal epithelium, degeneration	1 (10%)			
Hematopoietic System				
Lymph node	(10)	(10)	(10)	(10)
Mediastinal, angiectasis	1 (10%)		2 (20%)	
Spleen	(10)	(10)	(10)	(10)
Fibrosis				1 (10%)
Integumentary System				
Skin	(10)	(10)	(10)	(10)
Inflammation, chronic		1 (10%)		
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
Lung	(10)	(10)	(10)	(10)
Hemorrhage	1 (10%)			1 (10%)
Alveolar epithelium, hyperplasia				1 (10%)

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
15-Month Interim Evaluation (continued)				
Respiratory System (continued)				
Nose	(10)	(10)	(10)	(10)
Foreign body				1 (10%)
Fungus	1 (10%)	2 (20%)	1 (10%)	1 (10%)
Inflammation, suppurative	2 (20%)	2 (20%)	3 (30%)	2 (20%)
Special Senses System				
Ear				(1)
Inflammation, suppurative				1 (100%)
Zymbal's gland			(1)	(1)
Dilatation				1 (100%)
Urinary System				
Kidney	(10)	(10)	(10)	(10)
Nephropathy	10 (100%)	10 (100%)	10 (100%)	10 (100%)
Urethra	(1)		(1)	
Bulbourethral gland, dilatation	1 (100%)		1 (100%)	
2-Year Study				
Alimentary System				
Intestine large, cecum	(50)	(50)	(50)	(49)
Parasite metazoan				1 (2%)
Intestine large, colon	(50)	(50)	(49)	(49)
Cyst				1 (2%)
Parasite metazoan	4 (8%)	7 (14%)	2 (4%)	3 (6%)
Intestine large, rectum	(49)	(50)	(49)	(48)
Parasite metazoan	4 (8%)	2 (4%)	3 (6%)	5 (10%)
Intestine small, ileum	(49)	(50)	(50)	(49)
Inflammation, chronic		1 (2%)		
Intestine small, jejunum	(49)	(50)	(50)	(48)
Diverticulum				1 (2%)
Inflammation, chronic				1 (2%)
Metaplasia, osseous				1 (2%)
Mucosa, dysplasia				1 (2%)
Liver	(50)	(50)	(50)	(50)
Angiectasis	4 (8%)	2 (4%)		
Congestion		1 (2%)	1 (2%)	
Degeneration, cystic	17 (34%)	20 (40%)	14 (28%)	14 (28%)
Fatty change	29 (58%)	29 (58%)	24 (48%)	28 (56%)
Fibrosis, focal		1 (2%)	1 (2%)	
Focal cellular change	25 (50%)	28 (56%)	28 (56%)	29 (58%)
Hematopoietic cell proliferation		3 (6%)		
Hemorrhage	1 (2%)	1 (2%)		
Hepatodiaphragmatic nodule	8 (16%)	5 (10%)	4 (8%)	4 (8%)
Hyperplasia, multifocal	16 (32%)	17 (34%)	11 (22%)	18 (36%)
Infiltration cellular, mixed cell	6 (12%)	5 (10%)	5 (10%)	7 (14%)
Inflammation, focal	34 (68%)	26 (52%)	27 (54%)	29 (58%)
Necrosis, focal	1 (2%)	1 (2%)	3 (6%)	2 (4%)

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Alimentary System (continued)				
Liver (continued)	(50)	(50)	(50)	(50)
Pigmentation		1 (2%)		
Thrombosis	1 (2%)			
Bile duct, dilatation				1 (2%)
Bile duct, hyperplasia	47 (94%)	50 (100%)	49 (98%)	50 (100%)
Biliary tract, fibrosis	47 (94%)	47 (94%)	47 (94%)	49 (98%)
Centrilobular, atrophy	13 (26%)	14 (28%)	15 (30%)	10 (20%)
Centrilobular, necrosis	1 (2%)	3 (6%)		1 (2%)
Mesentery	(16)	(15)	(13)	(10)
Inflammation, chronic	1 (6%)	2 (13%)		1 (10%)
Fat, necrosis	11 (69%)	8 (53%)	10 (77%)	8 (80%)
Pancreas	(50)	(50)	(50)	(49)
Atrophy, focal	29 (58%)	27 (54%)	25 (50%)	27 (55%)
Focal cellular change	6 (12%)			4 (8%)
Acinar cell, hyperplasia	1 (2%)	1 (2%)	4 (8%)	3 (6%)
Salivary glands	(50)	(50)	(50)	(49)
Dilatation				1 (2%)
Focal cellular change		1 (2%)		
Hyperplasia		1 (2%)		
Stomach, forestomach	(50)	(50)	(50)	(50)
Edema		1 (2%)	1 (2%)	1 (2%)
Erosion		1 (2%)	1 (2%)	1 (2%)
Inflammation, chronic	1 (2%)	5 (10%)	2 (4%)	
Ulcer	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Mucosa, hyperplasia	3 (6%)	5 (10%)	3 (6%)	3 (6%)
Stomach, glandular	(50)	(50)	(50)	(50)
Edema	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Erosion	3 (6%)	1 (2%)	3 (6%)	3 (6%)
Hyperplasia, lymphoid	3 (6%)		1 (2%)	
Inflammation, chronic	1 (2%)	1 (2%)	1 (2%)	
Pigmentation	1 (2%)			2 (4%)
Ulcer			1 (2%)	
Mucosa, pigmentation			1 (2%)	
Tongue	(50)	(50)	(49)	(50)
Ectopic tissue		1 (2%)		
Mucosa, hyperplasia			1 (2%)	
Tooth	(2)			(1)
Incisor, dysplasia	1 (50%)			1 (100%)
Incisor, inflammation, suppurative	2 (100%)			1 (100%)
Cardiovascular System				
Blood vessel	(3)	(3)	(1)	(5)
Mesenteric artery, inflammation, chronic	3 (100%)	3 (100%)	1 (100%)	4 (80%)
Thoracic, artery, inflammation, chronic				1 (20%)
Heart	(50)	(50)	(50)	(50)
Dilatation				1 (2%)
Thrombosis		2 (4%)	2 (4%)	2 (4%)
Artery, inflammation, chronic		1 (2%)		
Epicardium, inflammation, chronic			1 (2%)	

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(50)
Accessory adrenal cortical nodule		2 (4%)		1 (2%)
Angiectasis			1 (2%)	
Congestion	1 (2%)		1 (2%)	
Focal cellular change	6 (12%)	5 (10%)	7 (14%)	6 (12%)
Hematopoietic cell proliferation		1 (2%)		
Vacuolization cytoplasmic			2 (4%)	
Adrenal gland, medulla	(50)	(50)	(50)	(50)
Fibrosis			1 (2%)	
Hyperplasia	11 (22%)	12 (24%)	16 (32%)	13 (26%)
Mineralization			1 (2%)	
Parathyroid gland	(50)	(46)	(48)	(48)
Hyperplasia			2 (4%)	1 (2%)
Pituitary gland	(49)	(50)	(50)	(48)
Angiectasis	1 (2%)	1 (2%)		1 (2%)
Cyst	3 (6%)	3 (6%)	4 (8%)	
Hemorrhage		2 (4%)		
Pars distalis, focal cellular change	5 (10%)	3 (6%)	6 (12%)	3 (6%)
Pars distalis, hyperplasia, focal	1 (2%)	2 (4%)	2 (4%)	3 (6%)
Pars distalis, vacuolization cytoplasmic			1 (2%)	
Pars nervosa, focal cellular change				1 (2%)
Rathke's cleft, hyperplasia, cystic			1 (2%)	
Thyroid gland	(50)	(49)	(50)	(48)
Degeneration, cystic	1 (2%)			
Fibrosis, focal			1 (2%)	
Pigmentation	1 (2%)			1 (2%)
Ultimobranchial cyst		1 (2%)		
C-cell, hyperplasia	4 (8%)	5 (10%)	5 (10%)	6 (13%)
Follicle, cyst	2 (4%)	2 (4%)		2 (4%)
Follicular cell, hyperplasia	2 (4%)		2 (4%)	3 (6%)
General Body System				
Tissue NOS	(1)	(1)	(2)	(1)
Thoracic, metaplasia, osseous			1 (50%)	
Genital System				
Epididymis	(50)	(50)	(50)	(50)
Atrophy		1 (2%)		
Preputial gland	(50)	(50)	(50)	(50)
Degeneration, cystic	45 (90%)	50 (100%)	49 (98%)	50 (100%)
Hyperplasia	1 (2%)	3 (6%)		
Inflammation, chronic			4 (8%)	3 (6%)
Prostate	(50)	(50)	(50)	(50)
Dilatation	1 (2%)			1 (2%)
Hyperplasia	1 (2%)	5 (10%)	2 (4%)	1 (2%)
Inflammation, suppurative	32 (64%)	23 (46%)	23 (46%)	22 (44%)
Vacuolization cytoplasmic				1 (2%)
Seminal vesicle	(50)	(50)	(50)	(50)
Dilatation	3 (6%)			1 (2%)

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Genital System (continued)				
Testes	(50)	(50)	(50)	(50)
Germinal epithelium, degeneration	9 (18%)	7 (14%)	8 (16%)	11 (22%)
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(49)
Hypercellularity		3 (6%)		
Hypocellularity	1 (2%)			1 (2%)
Myelofibrosis		1 (2%)		1 (2%)
Lymph node	(50)	(50)	(50)	(49)
Cyst	1 (2%)			
Mediastinal, angiectasis	3 (6%)	2 (4%)	3 (6%)	1 (2%)
Mediastinal, hemorrhage		1 (2%)		
Mediastinal, hyperplasia				1 (2%)
Mediastinal, pigmentation		1 (2%)		
Pancreatic, angiectasis	1 (2%)			
Pancreatic, cyst	1 (2%)			
Lymph node, mandibular	(50)	(49)	(50)	(48)
Angiectasis	2 (4%)	1 (2%)	2 (4%)	1 (2%)
Cyst	1 (2%)	3 (6%)	2 (4%)	
Edema	1 (2%)			
Hyperplasia	3 (6%)	2 (4%)		
Lymph node, mesenteric	(50)	(50)	(48)	(49)
Angiectasis			1 (2%)	2 (4%)
Cyst	1 (2%)	2 (4%)		3 (6%)
Hyperplasia	1 (2%)			1 (2%)
Spleen	(50)	(50)	(50)	(50)
Congestion		1 (2%)		
Developmental malformation			1 (2%)	
Fibrosis	10 (20%)	12 (24%)	10 (20%)	7 (14%)
Hematopoietic cell proliferation	3 (6%)	6 (12%)	2 (4%)	3 (6%)
Hemorrhage	1 (2%)			
Hyperplasia, histiocytic	1 (2%)			2 (4%)
Necrosis, focal	2 (4%)	1 (2%)	2 (4%)	
Thymus	(48)	(48)	(48)	(46)
Cyst	3 (6%)	1 (2%)	1 (2%)	
Depletion cellular			1 (2%)	
Hyperplasia, lymphoid	1 (2%)			
Integumentary System				
Mammary gland	(48)	(48)	(50)	(50)
Dilatation	7 (15%)	8 (17%)	8 (16%)	8 (16%)
Fibrosis			1 (2%)	1 (2%)
Hemorrhage	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Hyperplasia	2 (4%)	1 (2%)	1 (2%)	3 (6%)
Skin	(50)	(50)	(50)	(50)
Cyst epithelial inclusion		1 (2%)		
Edema	1 (2%)			
Exudate		1 (2%)		
Hemorrhage	1 (2%)			

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Integumentary System (continued)				
Skin (continued)	(50)	(50)	(50)	(50)
Hyperkeratosis, focal	1 (2%)			
Infiltration cellular, lymphocyte	1 (2%)			
Inflammation, chronic	2 (4%)			
Ulcer	2 (4%)			
Epidermis, hyperplasia	1 (2%)		1 (2%)	
Subcutaneous tissue, fat, necrosis	1 (2%)			
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Hyperostosis		1 (2%)	1 (2%)	
Trabecula, proliferation				1 (2%)
Skeletal muscle	(50)	(50)	(50)	(50)
Hemorrhage	1 (2%)			
Inflammation, chronic	1 (2%)			
Nervous System				
Brain	(50)	(50)	(50)	(50)
Compression	3 (6%)	2 (4%)	1 (2%)	2 (4%)
Hemorrhage	2 (4%)	2 (4%)	1 (2%)	1 (2%)
Hydrocephalus	2 (4%)			
Meninges, angiectasis		1 (2%)		
Meninges, hemorrhage		1 (2%)		1 (2%)
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Congestion	1 (2%)			
Exudate		1 (2%)		
Fibrosis, focal		1 (2%)		
Fungus		1 (2%)		
Granuloma			1 (2%)	
Hemorrhage	5 (10%)	4 (8%)	3 (6%)	3 (6%)
Hyperplasia, lymphoid	1 (2%)	1 (2%)		1 (2%)
Hyperplasia, macrophage		2 (4%)	2 (4%)	3 (6%)
Infiltration cellular, mixed cell	2 (4%)	3 (6%)		
Inflammation, chronic		4 (8%)		2 (4%)
Alveolar epithelium, hyperplasia	8 (16%)	10 (20%)	3 (6%)	2 (4%)
Mediastinum, cyst				1 (2%)
Mediastinum, ectopic tissue		1 (2%)		
Nose	(50)	(50)	(50)	(50)
Fungus	10 (20%)	14 (28%)	14 (28%)	13 (26%)
Inflammation, suppurative	14 (28%)	16 (32%)	20 (40%)	16 (32%)
Mucosa, hyperkeratosis	1 (2%)			
Mucosa, metaplasia, squamous	2 (4%)			1 (2%)
Nasolacrimal duct, cyst			1 (2%)	

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Special Senses System				
Eye	(3)	(2)	(1)	(2)
Atrophy		1 (50%)		
Cataract	1 (33%)	2 (100%)	1 (100%)	
Inflammation, chronic	1 (33%)			1 (50%)
Cornea, necrosis	1 (33%)			1 (50%)
Retina, degeneration	1 (33%)	2 (100%)	1 (100%)	
Retrobulbar, inflammation, suppurative				1 (50%)
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Cyst		2 (4%)		2 (4%)
Necrosis, focal	1 (2%)			
Nephropathy	49 (98%)	49 (98%)	49 (98%)	50 (100%)
Pigmentation	1 (2%)	2 (4%)		
Artery, inflammation, chronic		1 (2%)		
Pelvis, dilatation		1 (2%)		
Urinary bladder	(50)	(50)	(50)	(50)
Inflammation, chronic	1 (2%)			

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

APPENDIX B
SUMMARY OF LESIONS IN FEMALE RATS IN THE 2-YEAR FEED STUDY OF BENZYL ACETATE

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Feed Study of Benzyl Acetate[a]

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	10	10
Early deaths				
Moribund	18	17	13	19
Natural deaths	2	3		3
Survivors				
Terminal sacrifice	30	30	37	28
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Liver	(10)	(10)	(10)	(10)
Hepatocellular adenoma	1 (10%)			
Cardiovascular System				
None				
Endocrine System				
Pituitary gland	(10)	(10)	(10)	(10)
Pars distalis, adenoma	2 (20%)			
Thyroid gland	(10)	(10)	(10)	(9)
C-cell, adenoma		1 (10%)		
General Body System				
None				
Genital System				
Uterus	(10)	(10)	(10)	(10)
Endometrium, polyp stromal	2 (20%)	3 (30%)		1 (10%)
Hematopoietic System				
None				
Integumentary System				
Mammary gland	(10)	(10)	(10)	(10)
Fibroadenoma				2 (20%)
Musculoskeletal System				
None				

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
15-Month Interim Evaluation (continued)				
Nervous System				
Brain	(10)	(10)	(10)	(10)
Glioma malignant	1 (10%)			
Respiratory System				
None				
Special Senses System				
None				
Urinary System				
None				
2-Year Study				
Alimentary System				
Intestine large, cecum	(50)	(50)	(50)	(50)
Intestine small, ileum	(50)	(50)	(50)	(50)
Intestine small, jejunum	(49)	(50)	(50)	(50)
Leiomyosarcoma				1 (2%)
Liver	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, uncertain primary site		1 (2%)		
Cholangiocarcinoma			1 (2%)	
Hepatocellular carcinoma				1 (2%)
Hepatocellular adenoma	1 (2%)	1 (2%)	1 (2%)	3 (6%)
Mesentery	(9)	(4)	(7)	(10)
Adenocarcinoma, metastatic, uncertain primary site		1 (25%)		
Adenocarcinoma, metastatic, uterus	1 (11%)			
Liposarcoma, metastatic, kidney				1 (10%)
Pancreas	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, uncertain primary site		1 (2%)		
Salivary glands	(50)	(50)	(50)	(50)
Adenoma				1 (2%)
Stomach, forestomach	(50)	(50)	(50)	(50)
Stomach, glandular	(50)	(50)	(50)	(50)
Tongue	(50)	(50)	(50)	(50)
Squamous cell carcinoma			1 (2%)	
Squamous cell papilloma	1 (2%)			
Tooth	(1)	(3)	(1)	
Peridontal tissue, adenocarcinoma, metastatic, uncertain primary site		1 (33%)		

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Pheochromocytoma malignant, metastatic, adrenal gland	1 (2%)			
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, uncertain primary site		1 (2%)		
Adenoma	3 (6%)	2 (4%)	1 (2%)	1 (2%)
Adrenal gland, medulla	(50)	(50)	(50)	(50)
Ganglioneuroma			1 (2%)	
Pheochromocytoma malignant	1 (2%)	1 (2%)	1 (2%)	
Pheochromocytoma benign	1 (2%)	5 (10%)	1 (2%)	
Islets, pancreatic	(50)	(50)	(50)	(50)
Adenoma	3 (6%)	1 (2%)		
Parathyroid gland	(48)	(50)	(49)	(49)
Adenoma				1 (2%)
Pituitary gland	(50)	(50)	(50)	(50)
Pars distalis, adenoma	36 (72%)	33 (66%)	31 (62%)	33 (66%)
Pars distalis, adenoma, two, multiple		1 (2%)		
Pars distalis, carcinoma	1 (2%)	1 (2%)		
Pars intermedia, adenoma	1 (2%)		1 (2%)	
Pars intermedia, carcinoma			1 (2%)	
Thyroid gland	(50)	(50)	(50)	(50)
C-cell, adenoma	4 (8%)	3 (6%)	9 (18%)	5 (10%)
C-cell, carcinoma				2 (4%)
Follicular cell, adenoma			1 (2%)	1 (2%)
Follicular cell, carcinoma	1 (2%)		1 (2%)	
General Body System				
None				
Genital System				
Clitoral gland	(50)	(50)	(50)	(49)
Adenoma		1 (2%)	1 (2%)	1 (2%)
Carcinoma	1 (2%)	1 (2%)		
Sarcoma			1 (2%)	
Squamous cell papilloma		1 (2%)		
Ovary	(50)	(50)	(50)	(49)
Adenocarcinoma, metastatic, uncertain primary site		1 (2%)		
Adenocarcinoma, metastatic, uterus	1 (2%)			
Uterus	(50)	(50)	(50)	(50)
Adenocarcinoma	1 (2%)			1 (2%)
Adenoma	2 (4%)			
Sarcoma				1 (2%)
Schwannoma malignant		1 (2%)		
Endometrium, polyp stromal	13 (26%)	13 (26%)	4 (8%)	9 (18%)
Endometrium, polyp stromal, multiple		2 (4%)		

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Genital System (continued)				
Uterus (continued)	(50)	(50)	(50)	(50)
Endometrium, sarcoma stromal			1 (2%)	2 (4%)
Endothelium, polyp stromal				1 (2%)
Vagina	(2)	(1)	(2)	(2)
Basal cell adenoma			1 (50%)	
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, uncertain primary site		1 (2%)		
Lymph node	(50)	(50)	(50)	(50)
Lymph node, mandibular	(50)	(50)	(50)	(49)
Lymph node, mesenteric	(50)	(50)	(50)	(49)
Spleen	(50)	(50)	(50)	(50)
Thymus	(49)	(44)	(49)	(50)
Leiomyoma			1 (2%)	
Epithelial cell, thymoma benign		1 (2%)		
Integumentary System				
Mammary gland	(50)	(50)	(50)	(50)
Adenocarcinoma		1 (2%)	1 (2%)	
Adenoma				1 (2%)
Fibroadenoma	10 (20%)	13 (26%)	10 (20%)	14 (28%)
Fibroadenoma, two, multiple	2 (4%)	4 (8%)	2 (4%)	1 (2%)
Fibroadenoma, three, multiple				1 (2%)
Fibroma				1 (2%)
Skin	(50)	(50)	(50)	(50)
Subcutaneous tissue, fibroma	1 (2%)		2 (4%)	
Musculoskeletal System				
Skeletal muscle	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, uncertain primary site		1 (2%)		
Adenocarcinoma, metastatic, uterus	1 (2%)			
Nervous System				
Brain	(50)	(50)	(50)	(50)
Astrocytoma malignant			1 (2%)	
Glioma malignant		1 (2%)		
Peripheral nerve		(1)		(1)
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Adenocarcinoma	1 (2%)			
Adenocarcinoma, metastatic, uncertain primary site		1 (2%)		

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Respiratory System (continued)				
Lung (continued)	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, uterus	1 (2%)			
Carcinoma, metastatic, Zymbal's gland		1 (2%)		
Pheochromocytoma malignant, metastatic, adrenal gland	1 (2%)			
Mediastinum, adenocarcinoma, metastatic, uncertain primary site		1 (2%)		
Nose	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, uncertain primary site		1 (2%)		
Special Senses System				
Harderian gland	(1)			(1)
Zymbal's gland	(1)	(3)		
Carcinoma	1 (100%)	2 (67%)		
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, uncertain primary site		1 (2%)		
Adenocarcinoma, metastatic, uterus	1 (2%)			
Liposarcoma				1 (2%)
Urinary bladder	(50)	(50)	(50)	(50)
Adenocarcinoma, metastatic, uterus	1 (2%)			
Transitional epithelium, papilloma		1 (2%)		
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Leukemia mononuclear	9 (18%)	6 (12%)	12 (24%)	12 (24%)
Mesothelioma benign	1 (2%)			
Neoplasm Summary				
Total animals with primary neoplasms[c]				
15-Month interim evaluation	5	4		3
2-Year study	48	46	45	49
Total primary neoplasms				
15-Month interim evaluation	6	4		3
2-Year study	95	96	88	95
Total animals with benign neoplasms				
15-Month interim evaluation	4	4		3
2-Year study	43	41	39	44
Total benign neoplasms				
15-Month interim evaluation	5	4		3
2-Year study	79	82	67	74

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Neoplasm Summary (continued)				
Total animals with malignant neoplasms				
2-Year study	14	13	18	18
Total malignant neoplasms				
2-Year study	16	14	21	21
Total animals with metastatic neoplasms				
2-Year study	2	2		1
Total metastatic neoplasms				
2-Year study	8	13		1
Total animals with malignant neoplasms of uncertain primary site				
2-Year study			1	

[a] Number of animals examined microscopically at site and number of animals with lesion
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 0 ppm

Number of Days on Study	4 2 0	5 0 8	5 2 5	5 6 0	5 8 4	6 0 3	6 0 6	6 2 7	6 3 1	6 3 4	6 5 8	6 9 3	6 9 3	6 9 6	7 0 4	7 0 8	7 1 0	7 2 1	7 2 4	7 2 7	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1
Carcass ID Number	2 4 3	2 4 1	2 8 8	2 4 4	2 7 7	2 9 8	3 0 0	2 9 0	2 6 9	2 4 5	2 8 9	2 8 4	2 9 5	2 6 3	2 8 5	2 5 8	2 7 1	2 8 1	2 7 9	2 8 2	2 8 7	2 4 8	2 4 9	2 5 0	2 5 2
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Mesentery				+				+				+	+		+									+	
Adenocarcinoma, metastatic, uterus																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Tooth			+																						
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant, metastatic, adrenal gland																									
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma						X																X			
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																									
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma					X	X	X	X	X	X	X		X		X	X	X	X	X	X	X	X	X	X	
Pars distalis, carcinoma																									
Pars intermedia, adenoma																									
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-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 B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 0 ppm
(continued)

Number of Days on Study	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	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	2 5 3	2 5 4	2 5 5	2 5 6	2 5 7	2 6 0	2 6 1	2 6 2	2 6 5	2 6 6	2 6 7	2 6 8	2 7 0	2 7 2	2 7 4	2 7 5	2 7 8	2 8 0	2 8 6	2 9 1	2 9 2	2 9 4	2 9 6	2 9 7	2 9 9	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma		X																								1
Mesentery											+	+											+			9
Adenocarcinoma, metastatic, uterus												X														1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																					X					1
Tooth																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant, metastatic, adrenal gland					X																					1
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																	X									3
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant					X																					1
Pheochromocytoma benign																			X							1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma	X			X		X																				3
Parathyroid gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma		X		X		X	X	X	X	X		X	X	X	X	X	X	X	X		X		X	X		36
Pars distalis, carcinoma			X																							1
Pars intermedia, adenoma														X												1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma															X								X			4
Follicular cell, carcinoma																										1
General Body System																										
None																										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 0 ppm
(continued)

Number of Days on Study	4 2 0	5 0 8	5 2 5	5 6 0	5 8 4	6 0 3	6 0 6	6 2 7	6 3 1	6 3 4	6 5 8	6 9 3	6 9 3	6 9 6	7 0 4	7 0 8	7 1 0	7 2 1	7 2 4	7 2 7	7 3 1	7 3 1	7 3 1	7 3 1
Carcass ID Number	2 4 3	2 4 1	2 8 8	2 4 4	2 7 7	2 9 8	3 0 0	2 0 0	2 6 9	2 4 5	2 8 9	2 8 4	2 9 5	2 6 3	2 8 5	2 5 8	2 7 1	2 8 1	2 7 9	2 8 2	2 4 7	2 4 8	2 4 9	2 5 0	2 5 2
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Adenoma																	X								
Endometrium, polyp stromal															X	X		X					X		
Vagina							+																		
Hematopoietic System																									
Blood																		+							
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma					X					X	X		X	X		X				X					X
Fibroadenoma, two, multiple																		X							
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibroma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus																									
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																		X							
Adenocarcinoma, metastatic, uterus																									
Pheochromocytoma malignant, metastatic, adrenal gland																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye			+																						
Harderian gland																									
Zymbal's gland			+																						
Carcinoma			X																						

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 0 ppm
(continued)

Number of Days on Study	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	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	2 5 3	2 5 4	2 5 5	2 5 6	2 5 7	2 6 0	2 6 1	2 6 2	2 6 5	2 6 6	2 6 7	2 6 8	2 7 0	2 7 2	2 7 4	2 7 5	2 7 8	2 8 0	2 8 6	2 9 1	2 9 2	2 9 4	2 9 6	2 9 7	2 9 9	Total Tissues/ Tumors
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma															X											1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, uterus												X														1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma												X														1
Adenoma											X															2
Endometrium, polyp stromal		X					X		X							X	X	X	X		X				X	13
Vagina												+														2
Hematopoietic System																										
Blood																										1
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroadenoma						X							X													10
Fibroadenoma, two, multiple											X															2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibroma						X																				1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, uterus												X														1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																										1
Adenocarcinoma, metastatic, uterus												X														1
Pheochromocytoma malignant, metastatic, adrenal gland					X																					1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye						+																				2
Harderian gland											+															1
Zymbal's gland																										1
Carcinoma																										1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 0 ppm
(continued)

Number of Days on Study	4 2 0	5 0 8	5 2 5	5 6 0	5 8 4	6 0 3	6 0 6	6 2 7	6 3 1	6 3 4	6 5 8	6 9 3	6 9 3	6 9 6	7 0 4	7 0 8	7 1 0	7 2 1	7 2 4	7 2 7	7 3 1	7 3 1	7 3 1	7 3 2
Carcass ID Number	2 4 3	2 4 1	2 8 8	2 4 4	2 7 7	2 9 8	3 0 0	2 9 0	2 6 9	2 4 5	2 8 9	2 8 4	2 9 5	2 6 3	2 8 5	2 5 8	2 7 1	2 8 1	2 7 9	2 8 2	2 4 7	2 4 8	2 4 9	2 5 0	2 5 2
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus																									
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X										X	X			X									X	
Mesothelioma benign				X																					

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 0 ppm
(continued)

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

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm

Number of Days on Study	4 3 0	4 8 7	5 2 0	5 8 4	5 8 4	6 2 1	6 3 3	6 5 4	6 5 4	6 5 5	6 9 3	6 9 6	7 0 1	7 0 4	7 0 7	7 1 0	7 1 0	7 1 0	7 1 0	7 2 6	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5
Carcass ID Number	3 3 8	3 2 0	3 2 4	3 1 4	3 3 4	3 1 1	3 0 5	3 1 7	3 1 8	3 0 3	3 4 3	3 0 4	3 1 5	3 2 8	3 0 9	3 2 7	3 3 2	3 4 7	3 4 8	3 5 4	3 0 1	3 0 6	3 0 7	3 0 8	3 1 0
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uncertain primary site											X														
Hepatocellular adenoma							X																		
Mesentery							+				+			+											
Adenocarcinoma, metastatic, uncertain primary site											X														
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uncertain primary site											X														
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth		+									+	+													
Peridontal tissue, adenocarcinoma, metastatic, uncertain primary site											X														
Cardiovascular System																									
Blood vessel		+																							
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uncertain primary site											X														
Adenoma																									X
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																									
Pheochromocytoma benign																				X					
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma	X			X			X	X	X			X	X	X	X		X	X	X	X	X	X		X	X
Pars distalis, adenoma, two, multiple																									
Pars distalis, carcinoma																									
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																	X								

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm
(continued)

Number of Days on Study	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	
Carcass ID Number	3 1 2	3 1 6	3 2 1	3 2 2	3 2 5	3 2 9	3 3 0	3 3 1	3 3 3	3 3 5	3 3 7	3 4 0	3 4 1	3 4 2	3 4 5	3 4 6	3 4 9	3 5 1	3 5 2	3 5 3	3 5 5	3 5 6	3 5 8	3 5 9	3 6 0	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, uncertain primary site																										1
Hepatocellular adenoma																										1
Mesentery				+																						4
Adenocarcinoma, metastatic, uncertain primary site																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, uncertain primary site																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth																										3
Peridontal tissue, adenocarcinoma, metastatic, uncertain primary site																										1
Cardiovascular System																										
Blood vessel																										1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, uncertain primary site																										1
Adenoma							X																			2
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant		X																								1
Pheochromocytoma benign								X	X										X		X					5
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																						X				1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma	X		X				X		X	X	X	X		X	X	X	X		X	X		X	X	X		33
Pars distalis, adenoma, two, multiple						X																				1
Pars distalis, carcinoma					X																					1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma					X																X					3

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm
(continued)

Number of Days on Study	4 3 0	4 8 7	5 2 0	5 8 4	5 8 4	6 2 1	6 3 3	6 5 4	6 5 4	6 5 5	6 9 3	6 9 6	7 0 1	7 0 4	7 0 7	7 1 0	7 1 0	7 1 0	7 1 0	7 2 6	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5
Carcass ID Number	3 3 8	3 2 0	3 2 4	3 1 4	3 3 4	3 1 1	3 0 5	3 1 7	3 1 8	3 0 3	3 4 3	3 0 4	3 1 5	3 2 8	3 0 9	3 2 7	3 3 2	3 4 7	3 4 8	3 5 4	3 0 1	3 0 6	3 0 7	3 0 8	3 1 0
General Body System																									
None																									
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																				X					
Carcinoma																			X						
Squamous cell papilloma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uncertain primary site											X														
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Schwannoma malignant			X																						
Endometrium, polyp stromal							X			X					X		X						X		X
Endometrium, polyp stromal, multiple														X											
Vagina																									
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uncertain primary site											X														
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	M	+	I	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Epithelial cell, thymoma benign																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma												X													
Fibroadenoma	X								X			X	X							X				X	
Fibroadenoma, two, multiple																X		X							
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uncertain primary site											X														
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glioma malignant																		X							
Peripheral nerve									+																
Spinal cord									+																

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm
(continued)

Number of Days on Study	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	
Carcass ID Number	3 1 2	3 1 6	3 2 1	3 2 2	3 2 5	3 2 9	3 3 0	3 3 1	3 3 3	3 3 5	3 3 7	3 4 0	3 4 1	3 4 2	3 4 5	3 4 6	3 4 9	3 5 1	3 5 2	3 5 3	3 5 5	3 5 6	3 5 8	3 5 9	3 6 0	Total Tissues/ Tumors
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Carcinoma																										1
Squamous cell papilloma																							X			1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, uncertain primary site																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Schwannoma malignant																										1
Endometrium, polyp stromal					X				X		X						X	X		X			X			13
Endometrium, polyp stromal, multiple	X																									2
Vagina					+																					1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, uncertain primary site																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	44
Epithelial cell, thymoma benign	X																									1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																										1
Fibroadenoma	X					X									X		X					X	X	X		13
Fibroadenoma, two, multiple							X												X							4
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, uncertain primary site																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Glioma malignant																										1
Peripheral nerve																										1
Spinal cord																										1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm
(continued)

Number of Days on Study	4 3 0	4 8 7	5 2 0	5 8 4	5 8 4	6 2 1	6 3 3	6 5 4	6 5 4	6 5 5	6 9 3	6 9 6	7 0 1	7 0 4	7 0 7	7 1 0	7 1 0	7 1 0	7 2 6	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5
Carcass ID Number	3 3 8	3 2 0	3 2 4	3 1 4	3 3 4	3 1 1	3 0 5	3 1 7	3 1 8	3 0 3	3 4 3	3 0 4	3 1 5	3 2 8	3 0 9	3 2 7	3 3 2	3 4 7	3 4 8	3 5 4	3 0 1	3 0 6	3 0 7	3 0 8	3 1 0
Respiratory System																								
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uncertain primary site											X													
Carcinoma, metastatic, Zymbal's gland		X																						
Mediastinum, adenocarcinoma, metastatic, uncertain primary site											X													
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uncertain primary site											X													
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																								
Eye																								
Zymbal's gland		+			+																			
Carcinoma		X			X																			
Urinary System																								
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uncertain primary site											X													
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Transitional epithelium, papilloma																			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 Feed Study of Benzyl Acetate: 3,000 ppm
(continued)

Number of Days on Study	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	
Carcass ID Number	3 1 2	3 1 6	3 2 1	3 2 2	3 2 5	3 2 9	3 3 0	3 3 1	3 3 3	3 3 5	3 3 7	3 4 0	3 4 1	3 4 2	3 4 5	3 4 6	3 4 9	3 5 1	3 5 2	3 5 3	3 5 5	3 5 6	3 5 8	3 5 9	3 6 0	Total Tissues/ Tumors
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, uncertain primary site																										1
Carcinoma, metastatic, Zymbal's gland																										1
Mediastinum, adenocarcinoma, metastatic, uncertain primary site																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, uncertain primary site																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye							+											+		+		+				4
Zymbal's gland												+														3
Carcinoma																										2
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, uncertain primary site																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Transitional epithelium, papilloma																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear																										6

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 6,000 ppm

Number of Days on Study	3 6 7	5 2 1	5 9 2	6 9 6	7 0 0	7 0 7	7 1 0	7 1 1	7 1 1	7 1 5	7 2 5	7 2 5	7 2 7	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2
Carcass ID Number	3 6 8	3 8 3	4 0 6	3 7 5	3 6 5	3 7 4	3 7 6	3 7 9	4 0 0	4 0 7	3 6 3	3 8 1	4 1 3	3 6 1	3 6 2	3 6 6	3 6 7	3 6 9	3 7 0	3 7 1	3 7 3	3 7 7	3 7 8	3 7 9	3 8 0
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cholangiocarcinoma																							X		
Hepatocellular adenoma					X																				
Mesentery		+	+	+		+							+												
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																							X		
Tooth		+																							
Cardiovascular System																									
Blood vessel			+																						
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma											X														
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ganglioneuroma																					X				
Pheochromocytoma malignant																			X						
Pheochromocytoma benign					X																				
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma			X		X	X	X	X			X	X	X		X	X	X				X	X			
Pars intermedia, adenoma																									
Pars intermedia, carcinoma									X																
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma					X	X						X									X		X	X	
Follicular cell, adenoma																									
Follicular cell, carcinoma																									
General Body System																									
None																									

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 6,000 ppm
(continued)

Number of Days on Study	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	
Carcass ID Number	3 8 2	3 8 4	3 8 6	3 8 7	3 8 9	3 9 0	3 9 1	3 9 2	3 9 3	3 9 4	3 9 5	3 9 7	4 0 1	4 0 2	4 0 3	4 0 5	4 0 8	4 1 0	4 1 1	4 1 2	4 1 4	4 1 6	4 1 7	4 1 8	4 1 9	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
Cholangiocarcinoma																										1
Hepatocellular adenoma																										1
Mesentery										+													+			7
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma																										1
Tooth																										1
Cardiovascular System																										
Blood vessel																										1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Ganglioneuroma																										1
Pheochromocytoma malignant																										1
Pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma	X		X	X	X	X	X	X	X		X	X		X	X				X	X	X	X		X	X		31
Pars intermedia, adenoma												X														1
Pars intermedia, carcinoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma							X					X									X					9
Follicular cell, adenoma								X																		1
Follicular cell, carcinoma																					X					1
General Body System																										
None																										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 6,000 ppm
(continued)

Number of Days on Study	3 6 7	5 2 1	5 9 2	6 9 6	7 0 0	7 0 7	7 1 0	7 1 1	7 1 1	7 1 5	7 2 5	7 2 5	7 2 7	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2
Carcass ID Number	3 6 8	3 8 3	4 0 6	3 7 5	3 6 5	3 7 4	3 7 6	3 9 9	4 0 0	4 0 7	3 6 3	3 8 1	4 1 3	3 6 1	3 6 2	3 6 6	3 6 7	3 6 9	3 7 0	3 7 1	3 7 3	3 7 7	3 7 8	3 7 9	3 8 0
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Sarcoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrium, polyp stromal								X									X								
Endometrium, sarcoma stromal	X																								
Vagina																									
Basal cell adenoma																									
Hematopoietic System																									
Blood															+										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyoma																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Fibroadenoma										X	X	X	X									X	X		X
Fibroadenoma, two, multiple																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibroma																		X							
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma malignant																									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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 Feed Study of Benzyl Acetate: 6,000 ppm
(continued)

Number of Days on Study	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	
Carcass ID Number	3 8 2	3 8 4	3 8 6	3 8 7	3 8 9	3 9 0	3 9 1	3 9 2	3 9 3	3 9 4	3 9 5	3 9 7	4 0 1	4 0 2	4 0 3	4 0 5	4 0 8	4 1 0	4 1 1	4 1 2	4 1 4	4 1 6	4 1 7	4 1 8	4 1 9	Total Tissues/ Tumors
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma							X																			1
Sarcoma																					X					1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endometrium, polyp stromal	X								X																	4
Endometrium, sarcoma stromal																										1
Vagina	+			+																						2
Basal cell adenoma				X																						1
Hematopoietic System																										
Blood								+																		2
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leiomyoma														X												1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																									X	1
Fibroadenoma													X	X							X					10
Fibroadenoma, two, multiple										X												X				2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibroma																X										2
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Astrocytoma malignant								X																		1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye										+						+										2
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear										X		X	X													12

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 12,000 ppm

Number of Days on Study	5 5 3	5 8 2	5 9 3	6 3 1	6 4 1	6 5 8	6 6 7	6 6 8	6 6 8	6 6 8	6 6 9	6 7 2	6 9 3	7 0 0	7 0 4	7 0 7	7 0 7	7 0 7	7 0 7	7 0 8	7 1 5	7 2 6	7 3 2	7 3 2	7 3 2
Carcass ID Number	4 5 3	4 4 1	4 4 7	4 4 8	4 8 0	4 2 4	4 7 2	4 4 6	4 5 4	4 7 3	4 3 3	4 6 5	4 7 0	4 5 6	4 2 9	4 2 7	4 2 8	4 3 0	4 3 4	4 7 1	4 5 1	4 2 2	4 2 1	4 2 3	4 2 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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																		X							
Hepatocellular adenoma						X										X									X
Mesentery						+		+			+	+		+				+			+				+
Liposarcoma, metastatic, kidney											X														
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																	X								
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																		X							
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma		X			X	X	X	X	X	X			X	X	X	X	X		X	X	X	X	X	X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma															X									X	
C-cell, carcinoma																									
Follicular cell, adenoma																									
General Body System																									
None																									

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 12,000 ppm
(continued)

Number of Days on Study	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	4 3 1	4 3 2	4 3 5	4 3 7	4 3 8	4 4 0	4 4 2	4 4 3	4 4 5	4 4 9	4 5 0	4 5 5	4 5 8	4 5 9	4 6 0	4 6 1	4 6 3	4 6 4	4 6 7	4 6 8	4 6 9	4 7 5	4 7 6	4 7 7	4 7 8	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyosarcoma								X																		1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma																										1
Hepatocellular adenoma																										3
Mesentery															+		+									10
Liposarcoma, metastatic, kidney																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma	X																									1
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma			X			X	X	X		X			X		X	X	X	X	X	X	X		X	X		33
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma				X		X									X											5
C-cell, carcinoma	X								X																	2
Follicular cell, adenoma																								X		1
General Body System																										
None																										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 12,000 ppm
(continued)

Number of Days on Study	555	589	563	611	641	658	667	668	668	668	669	677	679	700	704	707	717	720	730	730	751	762	732	732
Carcass ID Number	445	444	447	448	480	424	427	426	455	437	433	435	436	707	505	229	267	208	304	371	755	211	252	225
Genital System																								
Clitoral gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																								
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																								
Sarcoma									X															
Endometrium, polyp stromal	X										X		X						X			X		
Endometrium, sarcoma stromal				X																				
Endothelium, polyp stromal						X																		
Vagina																	+				+			
Hematopoietic System																								
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																								
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma					X																			
Fibroadenoma					X	X	X					X	X		X			X		X	X			X
Fibroadenoma, two, multiple																								
Fibroadenoma, three, multiple																								
Fibroma																								
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																								
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve																				+				
Respiratory System																								
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																								
Harderian gland																		+						
Urinary System																								
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liposarcoma											X													
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																								
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear			X	X				X	X	X		X			X						X			

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Feed Study of Benzyl Acetate: 12,000 ppm
(continued)

Number of Days on Study	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	4 3 1	4 3 2	4 3 5	4 3 7	4 3 8	4 4 0	4 4 2	4 4 3	4 4 5	4 4 9	4 5 0	4 5 5	4 5 8	4 5 9	4 6 0	4 6 1	4 6 3	4 6 4	4 6 7	4 6 8	4 6 9	4 7 5	4 7 6	4 7 7	4 7 8	Total Tissues/ Tumors
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma				X																						1
Ovary	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																X										1
Sarcoma																										1
Endometrium, polyp stromal								X		X				X								X				9
Endometrium, sarcoma stromal										X																2
Endothelium, polyp stromal																										1
Vagina																										2
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Fibroadenoma			X				X		X	X																14
Fibroadenoma, two, multiple												X														1
Fibroadenoma, three, multiple					X																					1
Fibroma					X																					1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Harderian gland																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liposarcoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear											X					X							X		X	12

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Feed Study of Benzyl Acetate

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Adrenal Cortex: Adenoma				
Overall rate[a]	3/60 (5%)	2/60 (3%)	1/60 (2%)	1/60 (2%)
Adjusted rate[b]	8.7%	6.7%	2.5%	2.9%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate[c]	2/30 (7%)	2/30 (7%)	0/37 (0%)	0/28 (0%)
First incidence (days)	603	731 (T)	725	707
Life table test[d]	P=0.198N	P=0.500N	P=0.247N	P=0.316N
Logistic regression test[d]	P=0.187N	P=0.494N	P=0.282N	P=0.297N
Cochran-Armitage test[d]	P=0.200N			
Fisher exact test[d]		P=0.500N	P=0.309N	P=0.309N
Adrenal Medulla: Benign Pheochromocytoma				
Overall rate	1/60 (2%)	5/60 (8%)	1/60 (2%)	0/60 (0%)
Adjusted rate	3.3%	16.1%	2.2%	0.0%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	1/30 (3%)	4/30 (13%)	0/37 (0%)	0/28 (0%)
First incidence (days)	731 (T)	726	700	–[e]
Life table test	P=0.133N	P=0.104	P=0.709N	P=0.514N
Logistic regression test	P=0.125N	P=0.096	P=0.737N	P=0.514N
Cochran-Armitage test	P=0.135N			
Fisher exact test		P=0.103	P=0.752N	P=0.500N
Adrenal Medulla: Benign or Malignant Pheochromocytoma				
Overall rate	2/60 (3%)	6/60 (10%)	2/60 (3%)	0/60 (0%)
Adjusted rate	6.7%	19.4%	4.8%	0.0%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	2/30 (7%)	5/30 (17%)	1/37 (3%)	0/28 (0%)
First incidence (days)	731 (T)	726	700	–
Life table test	P=0.075N	P=0.133	P=0.613N	P=0.253N
Logistic regression test	P=0.070N	P=0.123	P=0.639N	P=0.253N
Cochran-Armitage test	P=0.078N			
Fisher exact test		P=0.136	P=0.691N	P=0.248N
Liver: Hepatocellular Adenoma				
Overall rate	2/60 (3%)	1/60 (2%)	1/60 (2%)	3/60 (5%)
Adjusted rate	5.0%	2.3%	2.2%	8.4%
Interim evaluation	1/10 (10%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	1/30 (3%)	0/30 (0%)	0/37 (0%)	1/28 (4%)
First incidence (days)	457 (I)	633	700	658
Life table test	P=0.335	P=0.492N	P=0.448N	P=0.498
Logistic regression test	P=0.324	P=0.503N	P=0.513N	P=0.499
Cochran-Armitage test	P=0.325			
Fisher exact test		P=0.500N	P=0.500N	P=0.500
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	2/60 (3%)	1/60 (2%)	1/60 (2%)	4/60 (7%)
Adjusted rate	5.0%	2.3%	2.2%	11.1%
Interim evaluation	1/10 (10%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	1/30 (3%)	0/30 (0%)	0/37 (0%)	1/28 (4%)
First incidence (days)	457 (I)	633	700	658
Life table test	P=0.172	P=0.492N	P=0.448N	P=0.339
Logistic regression test	P=0.166	P=0.503N	P=0.513N	P=0.340
Cochran-Armitage test	P=0.165			
Fisher exact test		P=0.500N	P=0.500N	P=0.340

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Mammary Gland: Fibroadenoma				
Overall rate	12/60 (20%)	17/60 (28%)	12/60 (20%)	18/60 (30%)
Adjusted rate	30.3%	44.6%	29.3%	43.5%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	2/10 (20%)
Terminal rate	4/30 (13%)	10/30 (33%)	8/37 (22%)	7/28 (25%)
First incidence (days)	584	430	715	456 (I)
Life table test	P=0.185	P=0.225	P=0.381N	P=0.157
Logistic regression test	P=0.212	P=0.200	P=0.482N	P=0.159
Cochran-Armitage test	P=0.188			
Fisher exact test		P=0.197	P=0.590N	P=0.146
Mammary Gland: Fibroadenoma or Carcinoma				
Overall rate	12/60 (20%)	17/60 (28%)	13/60 (22%)	18/60 (30%)
Adjusted rate	30.3%	44.6%	31.7%	43.5%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	2/10 (20%)
Terminal rate	4/30 (13%)	10/30 (33%)	9/37 (24%)	7/28 (25%)
First incidence (days)	584	430	715	456 (I)
Life table test	P=0.179	P=0.225	P=0.457N	P=0.157
Logistic regression test	P=0.206	P=0.200	P=0.567N	P=0.159
Cochran-Armitage test	P=0.182			
Fisher exact test		P=0.197	P=0.500	P=0.146
Pancreatic Islets: Adenoma				
Overall rate	3/60 (5%)	1/60 (2%)	0/60 (0%)	0/60 (0%)
Adjusted rate	10.0%	3.3%	0.0%	0.0%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	3/30 (10%)	1/30 (3%)	0/37 (0%)	0/28 (0%)
First incidence (days)	731 (T)	731 (T)	–	–
Life table test	P=0.040N	P=0.304N	P=0.086N	P=0.132N
Logistic regression test	P=0.040N	P=0.304N	P=0.086N	P=0.132N
Cochran-Armitage test	P=0.044N			
Fisher exact test		P=0.309N	P=0.122N	P=0.122N
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	38/60 (63%)	34/60 (57%)	31/60 (52%)	33/60 (55%)
Adjusted rate	82.3%	78.6%	68.7%	76.2%
Interim evaluation	2/10 (20%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	22/30 (73%)	21/30 (70%)	23/37 (62%)	18/28 (64%)
First incidence (days)	458 (I)	430	592	582
Life table test	P=0.273N	P=0.303N	P=0.020N	P=0.332N
Logistic regression test	P=0.111N	P=0.234N	P=0.039N	P=0.130N
Cochran-Armitage test	P=0.214N			
Fisher exact test		P=0.288N	P=0.134N	P=0.229N
Pituitary Gland (Pars Distalis): Adenoma or Carcinoma				
Overall rate	39/60 (65%)	35/60 (58%)	31/60 (52%)	33/60 (55%)
Adjusted rate	84.5%	81.0%	68.7%	76.2%
Interim evaluation	2/10 (20%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	23/30 (77%)	22/30 (73%)	23/37 (62%)	18/28 (64%)
First incidence (days)	458 (I)	430	592	582
Life table test	P=0.212N	P=0.301N	P=0.013N	P=0.280N
Logistic regression test	P=0.067N	P=0.226N	P=0.023N	P=0.087N
Cochran-Armitage test	P=0.155N			
Fisher exact test		P=0.287N	P=0.097N	P=0.176N

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Thyroid Gland (C-cell): Adenoma				
Overall rate	4/60 (7%)	4/60 (7%)	9/60 (15%)	5/60 (8%)
Adjusted rate	11.1%	11.0%	21.9%	16.7%
Interim evaluation	0/10 (0%)	1/10 (10%)	0/10 (0%)	0/10 (0%)
Terminal rate	2/30 (7%)	2/30 (7%)	6/37 (16%)	4/28 (14%)
First incidence (days)	606	458 (I)	700	704
Life table test	P=0.332	P=0.635N	P=0.221	P=0.474
Logistic regression test	P=0.374	P=0.641N	P=0.162	P=0.517
Cochran-Armitage test	P=0.353			
Fisher exact test		P=0.641N	P=0.120	P=0.500
Thyroid Gland (C-cell): Adenoma or Carcinoma				
Overall rate	4/60 (7%)	4/60 (7%)	9/60 (15%)	7/60 (12%)
Adjusted rate	11.1%	11.0%	21.9%	23.6%
Interim evaluation	0/10 (0%)	1/10 (10%)	0/10 (0%)	0/10 (0%)
Terminal rate	2/30 (7%)	2/30 (7%)	6/37 (16%)	6/28 (21%)
First incidence (days)	606	458 (I)	700	704
Life table test	P=0.137	P=0.635N	P=0.221	P=0.238
Logistic regression test	P=0.166	P=0.641N	P=0.162	P=0.275
Cochran-Armitage test	P=0.154			
Fisher exact test		P=0.641N	P=0.120	P=0.264
Uterus: Stromal Polyp				
Overall rate	15/60 (25%)	18/60 (30%)	4/60 (7%)	11/60 (18%)
Adjusted rate	41.1%	44.7%	10.2%	28.1%
Interim evaluation	2/10 (20%)	3/10 (30%)	0/10 (0%)	1/10 (10%)
Terminal rate	10/30 (33%)	10/30 (33%)	3/37 (8%)	4/28 (14%)
First incidence (days)	457 (I)	456 (I)	711	456 (I)
Life table test	P=0.088N	P=0.351	P=0.002N	P=0.303N
Logistic regression test	P=0.069N	P=0.347	P=0.004N	P=0.235N
Cochran-Armitage test	P=0.078N			
Fisher exact test		P=0.342	P=0.005N	P=0.253N
Uterus: Stromal Polyp or Stromal Sarcoma				
Overall rate	15/60 (25%)	18/60 (30%)	5/60 (8%)	12/60 (20%)
Adjusted rate	41.1%	44.7%	11.7%	29.6%
Interim evaluation	2/10 (20%)	3/10 (30%)	0/10 (0%)	1/10 (10%)
Terminal rate	10/30 (33%)	10/30 (33%)	3 ' (8%)	4/28 (14%)
First incidence (days)	457 (I)	456 (I)	3..	456 (I)
Life table test	P=0.144N	P=0.351	P=0.005N	P=0.378N
Logistic regression test	P=0.121N	P=0.347	P=0.011N	P=0.311N
Cochran-Armitage test	P=0.130N			
Fisher exact test		P=0.342	P=0.013N	P=0.331N
All Organs: Mononuclear Cell Leukemia				
Overall rate	9/60 (15%)	6/60 (10%)	12/60 (20%)	12/60 (20%)
Adjusted rate	24.3%	14.8%	27.1%	30.0%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	5/30 (17%)	1/30 (3%)	6/37 (16%)	4/28 (14%)
First incidence (days)	420	584	521	593
Life table test	P=0.159	P=0.288N	P=0.502	P=0.319
Logistic regression test	P=0.162	P=0.286N	P=0.364	P=0.332
Cochran-Armitage test	P=0.150			
Fisher exact test		P=0.291N	P=0.316	P=0.316

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
All Organs: Benign Neoplasms				
Overall rate	47/60 (78%)	45/60 (75%)	39/60 (65%)	47/60 (78%)
Adjusted rate	92.1%	91.7%	84.7%	93.9%
Interim evaluation	4/10 (40%)	4/10 (40%)	0/10 (0%)	3/10 (30%)
Terminal rate	26/30 (87%)	26/30 (87%)	30/37 (81%)	25/28 (89%)
First incidence (days)	457 (I)	430	592	456 (I)
Life table test	P=0.493	P=0.418N	P=0.007N	P=0.471
Logistic regression test	P=0.371N	P=0.378N	P=0.012N	P=0.466N
Cochran-Armitage test	P=0.520N			
Fisher exact test		P=0.415N	P=0.078N	P=0.588N
All Organs: Malignant Neoplasms				
Overall rate	15/60 (25%)	14/60 (23%)	18/60 (30%)	18/60 (30%)
Adjusted rate	37.9%	31.4%	39.0%	44.8%
Interim evaluation	1/10 (10%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	8/30 (27%)	3/30 (10%)	10/37 (27%)	8/28 (29%)
First incidence (days)	420	487	367	593
Life table test	P=0.247	P=0.489N	P=0.573	P=0.330
Logistic regression test	P=0.255	P=0.498N	P=0.377	P=0.365
Cochran-Armitage test	P=0.238			
Fisher exact test		P=0.500N	P=0.342	P=0.342
All Organs: Benign or Malignant Neoplasms				
Overall rate	53/60 (88%)	51/60 (85%)	45/60 (75%)	52/60 (87%)
Adjusted rate	98.1%	94.4%	90.0%	98.1%
Interim evaluation	5/10 (50%)	4/10 (40%)	0/10 (0%)	3/10 (30%)
Terminal rate	29/30 (97%)	27/30 (90%)	32/37 (86%)	27/28 (96%)
First incidence (days)	420	430	367	456 (I)
Life table test	P=0.497N	P=0.419N	P=0.006N	P=0.526
Logistic regression test	P=0.259N	P=0.364N	P=0.009N	P=0.337N
Cochran-Armitage test	P=0.418N			
Fisher exact test		P=0.395N	P=0.049N	P=0.500N

(T)Terminal sacrifice
(I)Interim evaluation
[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 exposure group incidence are the P values corresponding to pairwise comparisons between the controls and that exposure 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 test regards 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 an exposure group is indicated by N.
[e] Not applicable; no neoplasms in animal group

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Feed Study of Benzyl Acetate[a]

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	10	10
Early deaths				
Moribund	18	17	13	19
Natural deaths	2	3		3
Survivors				
Terminal sacrifice	30	30	37	28
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Intestine large, colon	(10)	(10)	(10)	(10)
Parasite metazoan	2 (20%)	1 (10%)		
Intestine large, rectum	(10)	(10)	(10)	(10)
Parasite metazoan	1 (10%)	2 (20%)	1 (10%)	1 (10%)
Liver	(10)	(10)	(10)	(10)
Fatty change		4 (40%)	2 (20%)	2 (20%)
Focal cellular change				3 (30%)
Hepatodiaphragmatic nodule	2 (20%)	2 (20%)		2 (20%)
Infiltration cellular, mixed cell			1 (10%)	
Inflammation, focal	10 (100%)	10 (100%)	10 (100%)	10 (100%)
Bile duct, hyperplasia	5 (50%)	4 (40%)	4 (40%)	6 (60%)
Biliary tract, fibrosis	1 (10%)	1 (10%)	1 (10%)	
Mesentery	(2)	(1)		(2)
Fat, necrosis	2 (100%)	1 (100%)		2 (100%)
Pancreas	(10)	(10)	(10)	(10)
Atrophy, focal	3 (30%)	3 (30%)	4 (40%)	2 (20%)
Stomach, glandular	(10)	(10)	(10)	(10)
Erosion				1 (10%)
Cardiovascular System				
None				
Endocrine System				
Adrenal gland, cortex	(10)	(10)	(10)	(10)
Focal cellular change			1 (10%)	
Adrenal gland, medulla	(10)	(10)	(10)	(10)
Hyperplasia	1 (10%)			
Pituitary gland	(10)	(10)	(10)	(10)
Angiectasis		3 (30%)		
Cyst	2 (20%)	2 (20%)	2 (20%)	4 (40%)
Pars distalis, focal cellular change			2 (20%)	
Pars distalis, hyperplasia, focal		1 (10%)		
Thyroid gland	(10)	(10)	(10)	(9)
Ultimobranchial cyst	1 (10%)			1 (11%)
C-cell, hyperplasia	1 (10%)		3 (30%)	

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Feed Study of Benzyl Acetate
(continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
15-Month Interim Evaluation (continued)				
General Body System				
None				
Genital System				
Clitoral gland	(10)	(10)	(10)	(10)
Degeneration, cystic	4 (40%)	9 (90%)	7 (70%)	5 (50%)
Ovary	(10)	(10)	(10)	(10)
Follicle, cyst	1 (10%)			1 (10%)
Uterus	(10)	(10)	(10)	(10)
Hydrometra		2 (20%)		1 (10%)
Inflammation, suppurative	1 (10%)	1 (10%)	2 (20%)	1 (10%)
Endometrium, hyperplasia, cystic	7 (70%)	9 (90%)	9 (90%)	8 (80%)
Endometrium, infarct				1 (10%)
Hematopoietic System				
Lymph node	(10)	(10)	(10)	(10)
Mediastinal, angiectasis		2 (20%)	1 (10%)	
Lymph node, mesenteric	(10)	(10)	(10)	(10)
Depletion lymphoid			1 (10%)	
Hyperplasia, lymphoid		1 (10%)		
Spleen	(10)	(10)	(10)	(10)
Hematopoietic cell proliferation			1 (10%)	
Integumentary System				
Mammary gland	(10)	(10)	(10)	(10)
Dilatation	2 (20%)			
Hyperplasia			1 (10%)	
Musculoskeletal System				
Bone	(10)	(10)	(10)	(10)
Hyperostosis	1 (10%)	3 (30%)	1 (10%)	1 (10%)
Nervous System				
Brain	(10)	(10)	(10)	(10)
Compression	1 (10%)			
Respiratory System				
Lung	(10)	(10)	(10)	(10)
Alveolar epithelium, hyperplasia	2 (20%)			
Nose	(10)	(10)	(10)	(10)
Fungus	1 (10%)	1 (10%)		
Inflammation, suppurative	1 (10%)	1 (10%)		

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
15-Month Interim Evaluation (continued)				
Special Senses System				
Harderian gland			(1)	
Dilatation, focal			1 (100%)	
Urinary System				
Kidney	(10)	(10)	(10)	(10)
Mineralization	9 (90%)	10 (100%)	9 (90%)	10 (100%)
Nephropathy	2 (20%)	8 (80%)	1 (10%)	3 (30%)
2-Year Study				
Alimentary System				
Intestine large, colon	(50)	(50)	(50)	(50)
Parasite metazoan			4 (8%)	4 (8%)
Intestine large, rectum	(49)	(49)	(50)	(49)
Parasite metazoan	4 (8%)	4 (8%)		2 (4%)
Intestine small, jejunum	(49)	(50)	(50)	(50)
Dilatation			1 (2%)	
Inflammation, chronic			1 (2%)	
Ulcer			1 (2%)	
Liver	(50)	(50)	(50)	(50)
Angiectasis	1 (2%)	1 (2%)	2 (4%)	
Congestion		1 (2%)		
Cyst				1 (2%)
Degeneration, cystic			3 (6%)	
Fatty change	22 (44%)	13 (26%)	16 (32%)	20 (40%)
Fibrosis, focal	1 (2%)			1 (2%)
Focal cellular change	38 (76%)	44 (88%)	42 (84%)	42 (84%)
Hematopoietic cell proliferation	2 (4%)	2 (4%)	1 (2%)	
Hepatodiaphragmatic nodule	10 (20%)	10 (20%)	5 (10%)	5 (10%)
Hyperplasia, multifocal	21 (42%)	16 (32%)	9 (18%)	13 (26%)
Infiltration cellular, mixed cell	1 (2%)	5 (10%)	2 (4%)	2 (4%)
Inflammation, focal	35 (70%)	43 (86%)	39 (78%)	34 (68%)
Necrosis, focal	3 (6%)	1 (2%)	2 (4%)	1 (2%)
Pigmentation				1 (2%)
Bile duct, hyperplasia	38 (76%)	33 (66%)	34 (68%)	35 (70%)
Biliary tract, fibrosis	28 (56%)	22 (44%)	24 (48%)	19 (38%)
Centrilobular, atrophy	6 (12%)	4 (8%)	9 (18%)	7 (14%)
Mesentery	(9)	(4)	(7)	(10)
Inflammation, chronic			1 (14%)	
Fat, necrosis	5 (56%)	3 (75%)	2 (29%)	5 (50%)
Pancreas	(50)	(50)	(50)	(50)
Atrophy, focal	13 (26%)	17 (34%)	25 (50%)	17 (34%)
Focal cellular change	4 (8%)			1 (2%)
Infiltration cellular, lipocyte	1 (2%)			
Acinar cell, hyperplasia	1 (2%)		1 (2%)	1 (2%)
Duct, dilatation	1 (2%)		1 (2%)	1 (2%)
Salivary glands	(50)	(50)	(50)	(50)
Atrophy, focal		1 (2%)		1 (2%)
Focal cellular change		1 (2%)		
Infiltration cellular, lipocyte	1 (2%)			

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Feed Study of Benzyl Acetate
(continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Alimentary System (continued)				
Stomach, forestomach	(50)	(50)	(50)	(50)
Edema	1 (2%)			2 (4%)
Erosion				1 (2%)
Inflammation, chronic	1 (2%)		3 (6%)	3 (6%)
Ulcer			3 (6%)	1 (2%)
Mucosa, hyperplasia			2 (4%)	2 (4%)
Stomach, glandular	(50)	(50)	(50)	(50)
Developmental malformation				1 (2%)
Edema	1 (2%)		1 (2%)	
Erosion				2 (4%)
Hyperplasia, lymphoid	1 (2%)	1 (2%)		
Inflammation, chronic	1 (2%)			1 (2%)
Ulcer	1 (2%)			
Mucosa, cyst, multiple	1 (2%)			
Tooth	(1)	(3)	(1)	
Incisor, dysplasia		1 (33%)	1 (100%)	
Cardiovascular System				
Blood vessel		(1)	(1)	
Mesenteric artery, inflammation, chronic		1 (100%)	1 (100%)	
Mesenteric artery, thrombosis		1 (100%)		
Thoracic, artery, aneurysm			1 (100%)	
Thoracic, artery, inflammation, chronic			1 (100%)	
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(50)
Accessory adrenal cortical nodule			1 (2%)	2 (4%)
Angiectasis	1 (2%)	1 (2%)		
Congestion			3 (6%)	1 (2%)
Focal cellular change	10 (20%)	6 (12%)	6 (12%)	5 (10%)
Hyperplasia		1 (2%)		1 (2%)
Inflammation, focal		1 (2%)		
Vacuolization cytoplasmic	1 (2%)	1 (2%)		1 (2%)
Adrenal gland, medulla	(50)	(50)	(50)	(50)
Cyst	1 (2%)			
Fibrosis		1 (2%)		
Hyperplasia	2 (4%)	4 (8%)	1 (2%)	5 (10%)
Parathyroid gland	(48)	(50)	(49)	(49)
Cyst			1 (2%)	
Pituitary gland	(50)	(50)	(50)	(50)
Angiectasis	1 (2%)	3 (6%)	5 (10%)	4 (8%)
Cyst	3 (6%)	1 (2%)	7 (14%)	6 (12%)
Hemorrhage		1 (2%)		
Pars distalis, focal cellular change	1 (2%)	3 (6%)	6 (12%)	3 (6%)
Pars distalis, hyperplasia, focal		1 (2%)		3 (6%)

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Endocrine System (continued)				
Thyroid gland	(50)	(50)	(50)	(50)
Ultimobranchial cyst			2 (4%)	
C-cell, hyperplasia	16 (32%)	10 (20%)	11 (22%)	10 (20%)
Follicle, cyst	1 (2%)	1 (2%)		
Follicular cell, hyperplasia	1 (2%)	1 (2%)	1 (2%)	1 (2%)
General Body System				
None				
Genital System				
Clitoral gland	(50)	(50)	(50)	(49)
Degeneration, cystic	47 (94%)	45 (90%)	41 (82%)	42 (86%)
Hyperplasia	2 (4%)	1 (2%)	1 (2%)	4 (8%)
Inflammation, chronic		2 (4%)	1 (2%)	1 (2%)
Ovary	(50)	(50)	(50)	(49)
Angiectasis	2 (4%)			
Hyperplasia, histiocytic		1 (2%)	1 (2%)	
Hyperplasia, lymphoid		1 (2%)	1 (2%)	
Necrosis, focal		1 (2%)		
Follicle, cyst	5 (10%)	1 (2%)	2 (4%)	3 (6%)
Periovarian tissue, cyst	1 (2%)	1 (2%)	1 (2%)	
Uterus	(50)	(50)	(50)	(50)
Adenomyosis				1 (2%)
Cyst		1 (2%)		
Decidual reaction	1 (2%)			1 (2%)
Dilatation			1 (2%)	
Hemorrhage				1 (2%)
Hydrometra	4 (8%)	3 (6%)	3 (6%)	3 (6%)
Inflammation, suppurative	3 (6%)	2 (4%)	2 (4%)	1 (2%)
Prolapse				1 (2%)
Cervix, hyperplasia	1 (2%)			
Endometrium, angiectasis		1 (2%)		
Endometrium, hyperplasia, cystic	27 (54%)	29 (58%)	31 (62%)	35 (70%)
Endometrium, infarct		1 (2%)		
Epithelium, hyperplasia, papillary	3 (6%)	1 (2%)	1 (2%)	1 (2%)
Lumen, exudate			1 (2%)	
Vagina	(2)	(1)	(2)	(2)
Angiectasis	1 (50%)			
Cyst	1 (50%)	1 (100%)	1 (50%)	1 (50%)
Mucosa, hyperplasia	1 (50%)			
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Hypercellularity	1 (2%)			1 (2%)
Hyperplasia, histiocytic		1 (2%)		

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Hematopoietic System (continued)				
Lymph node	(50)	(50)	(50)	(50)
Axillary, angiectasis	1 (2%)			
Axillary, hyperplasia	1 (2%)			
Deep cervical, hyperplasia	1 (2%)			
Mediastinal, angiectasis	1 (2%)	2 (4%)		2 (4%)
Mediastinal, pigmentation	1 (2%)			
Pancreatic, angiectasis				1 (2%)
Pancreatic, hyperplasia, lymphoid		1 (2%)		
Lymph node, mandibular	(50)	(50)	(50)	(49)
Angiectasis	1 (2%)	2 (4%)		3 (6%)
Hyperplasia	1 (2%)	3 (6%)		
Lymph node, mesenteric	(50)	(50)	(50)	(49)
Angiectasis	1 (2%)	1 (2%)		1 (2%)
Cyst	1 (2%)			
Hyperplasia			1 (2%)	
Spleen	(50)	(50)	(50)	(50)
Developmental malformation	1 (2%)			
Fibrosis	4 (8%)	3 (6%)	3 (6%)	6 (12%)
Hematopoietic cell proliferation	4 (8%)	6 (12%)	2 (4%)	5 (10%)
Hyperplasia, histiocytic		2 (4%)		
Hyperplasia, lymphoid		2 (4%)		
Necrosis, focal				1 (2%)
Thymus	(49)	(44)	(49)	(50)
Angiectasis	1 (2%)			
Cyst	4 (8%)	1 (2%)	1 (2%)	1 (2%)
Epithelial cell, hyperplasia		1 (2%)		
Integumentary System				
Mammary gland	(50)	(50)	(50)	(50)
Dilatation	39 (78%)	36 (72%)	34 (68%)	35 (70%)
Fibrosis	1 (2%)		1 (2%)	
Hyperplasia	10 (20%)	8 (16%)	6 (12%)	6 (12%)
Skin	(50)	(50)	(50)	(50)
Hyperkeratosis, focal			1 (2%)	1 (2%)
Subcutaneous tissue, inflammation, suppurative	1 (2%)			
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Hyperostosis	11 (22%)	18 (36%)	11 (22%)	21 (42%)
Adventitia, mandible, inflammation, chronic			1 (2%)	
Nervous System				
Brain	(50)	(50)	(50)	(50)
Compression	15 (30%)	13 (26%)	8 (16%)	12 (24%)
Hemorrhage				2 (4%)

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
2-Year Study (continued)				
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Bronchiectasis		1 (2%)		
Congestion	1 (2%)	2 (4%)		1 (2%)
Fibrosis, focal		1 (2%)		1 (2%)
Granuloma				1 (2%)
Hemorrhage		1 (2%)	2 (4%)	2 (4%)
Hyperplasia, lymphoid		1 (2%)		
Hyperplasia, macrophage	1 (2%)	6 (12%)	1 (2%)	1 (2%)
Inflammation, chronic		2 (4%)	1 (2%)	
Pigmentation		2 (4%)		
Alveolar epithelium, hyperplasia	1 (2%)	3 (6%)	4 (8%)	2 (4%)
Nose	(50)	(50)	(50)	(50)
Fungus	7 (14%)	2 (4%)	3 (6%)	
Hemorrhage		1 (2%)		
Inflammation, suppurative	13 (26%)	8 (16%)	16 (32%)	13 (26%)
Special Senses System				
Eye	(2)	(4)	(2)	
Atrophy	1 (50%)			
Cataract		4 (100%)	2 (100%)	
Hemorrhage			1 (50%)	
Inflammation, chronic	1 (50%)			
Cornea, necrosis	1 (50%)			
Retina, degeneration	1 (50%)	3 (75%)	2 (100%)	
Harderian gland	(1)			(1)
Inflammation, focal				1 (100%)
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Cyst	1 (2%)		1 (2%)	
Fibrosis		1 (2%)		
Mineralization		1 (2%)		
Necrosis, focal				1 (2%)
Nephropathy	46 (92%)	47 (94%)	46 (92%)	41 (82%)
Pigmentation	1 (2%)			1 (2%)
Papilla, necrosis			1 (2%)	
Pelvis, dilatation	1 (2%)		1 (2%)	
Renal tubule, dilatation			1 (2%)	

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

APPENDIX C
SUMMARY OF LESIONS IN MALE MICE IN THE 2-YEAR FEED STUDY OF BENZYL ACETATE

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Feed Study of Benzyl Acetate[a]

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	10	10
Early deaths				
Moribund	7	3	6	7
Natural deaths	4	4	3	4
Survivors				
Terminal sacrifice	39	43	41	39
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Intestine small, jejunum	(10)	(10)	(10)	(10)
Carcinoma	1 (10%)			
Liver	(10)	(10)	(10)	(10)
Hepatocellular adenoma	1 (10%)	1 (10%)	2 (20%)	1 (10%)
Stomach, forestomach	(10)	(10)	(10)	(10)
Squamous cell papilloma				1 (10%)
Cardiovascular System				
None				
Endocrine System				
Adrenal gland, cortex	(10)	(10)	(10)	(10)
Adenoma	1 (10%)			
General Body System				
None				
Genital System				
None				
Hematopoietic System				
None				
Integumentary System				
None				
Musculoskeletal System				
None				
Nervous System				
None				

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
15-Month Interim Evaluation (continued)				
Respiratory System				
Lung	(10)	(10)	(10)	(10)
Alveolar/bronchiolar adenoma	1 (10%)		1 (10%)	
Alveolar/bronchiolar carcinoma				1 (10%)
Special Senses System				
None				
Urinary System				
None				
2-Year Study				
Alimentary System				
Gallbladder	(47)	(50)	(48)	(50)
Intestine large, rectum	(50)	(50)	(50)	(50)
Intestine small, jejunum	(50)	(49)	(50)	(49)
Carcinoma	2 (4%)	1 (2%)	1 (2%)	
Hemangiosarcoma	1 (2%)			
Liver	(50)	(50)	(50)	(50)
Cholangiocarcinoma	1 (2%)			
Hemangiosarcoma		2 (4%)	1 (2%)	1 (2%)
Hepatocellular carcinoma	8 (16%)	10 (20%)	9 (18%)	5 (10%)
Hepatocellular carcinoma, two, multiple	1 (2%)	4 (8%)	1 (2%)	3 (6%)
Hepatocellular carcinoma, three, multiple	3 (6%)			
Hepatocellular carcinoma, five, multiple			1 (2%)	
Hepatocellular adenoma	9 (18%)	11 (22%)	5 (10%)	1 (2%)
Hepatocellular adenoma, two, multiple	1 (2%)	1 (2%)	3 (6%)	
Hepatocellular adenoma, three, multiple		1 (2%)		
Mesentery	(3)	(3)	(2)	(1)
Cholangiocarcinoma, metastatic, liver	1 (33%)			
Pancreas	(50)	(50)	(50)	(50)
Salivary glands	(50)	(50)	(50)	(50)
Stomach, forestomach	(50)	(50)	(50)	(50)
Basal cell adenoma			1 (2%)	
Squamous cell carcinoma				1 (2%)
Squamous cell papilloma	3 (6%)	4 (8%)	1 (2%)	1 (2%)
Stomach, glandular	(50)	(50)	(50)	(50)
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Hemangiosarcoma			1 (2%)	
Hepatocellular carcinoma, metastatic, liver				1 (2%)
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(50)
Adenoma	1 (2%)	1 (2%)	1 (2%)	
Capsule, adenoma	3 (6%)	2 (4%)		1 (2%)

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Endocrine System (continued)				
Adrenal gland, medulla	(50)	(50)	(50)	(50)
Pheochromocytoma malignant	1 (2%)			
Pheochromocytoma benign		1 (2%)		
Islets, pancreatic	(50)	(50)	(49)	(50)
Adenoma		2 (4%)	3 (6%)	
Pituitary gland	(48)	(49)	(48)	(47)
Pars distalis, adenoma	3 (6%)			1 (2%)
Pars distalis, carcinoma			1 (2%)	
Thyroid gland	(50)	(50)	(50)	(50)
Follicular cell, adenoma	2 (4%)	1 (2%)	2 (4%)	1 (2%)
General Body System				
Tissue NOS				(1)
Genital System				
Epididymis	(50)	(50)	(50)	(50)
Hemangioma		1 (2%)		
Preputial gland	(31)	(39)	(30)	(24)
Prostate	(50)	(50)	(50)	(50)
Seminal vesicle	(50)	(50)	(50)	(50)
Testes	(50)	(50)	(50)	(50)
Interstitial cell, adenoma			1 (2%)	
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Hemangiosarcoma		2 (4%)	1 (2%)	2 (4%)
Lymph node	(50)	(50)	(50)	(50)
Lymph node, mandibular	(48)	(47)	(50)	(49)
Lymph node, mesenteric	(48)	(49)	(50)	(50)
Osteosarcoma, metastatic, bone				1 (2%)
Spleen	(50)	(50)	(50)	(50)
Hemangiosarcoma		2 (4%)	2 (4%)	1 (2%)
Thymus	(42)	(45)	(47)	(45)
Integumentary System				
Skin	(50)	(50)	(50)	(50)
Subcutaneous tissue, fibrous histiocytoma			1 (2%)	
Subcutaneous tissue, hemangiosarcoma	1 (2%)	1 (2%)	2 (4%)	
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Hemangiosarcoma		2 (4%)		1 (2%)
Osteosarcoma			1 (2%)	1 (2%)
Skeletal muscle	(50)	(50)	(50)	(50)
Hemangiosarcoma		1 (2%)		1 (2%)

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Nervous System				
Brain	(50)	(50)	(50)	(50)
Carcinoma, metastatic, pituitary gland			1 (2%)	
Oligodendroglioma malignant	1 (2%)			
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Alveolar/bronchiolar adenoma	9 (18%)	14 (28%)	7 (14%)	6 (12%)
Alveolar/bronchiolar adenoma, two, multiple		1 (2%)		
Alveolar/bronchiolar carcinoma	5 (10%)	3 (6%)	1 (2%)	2 (4%)
Cholangiocarcinoma, metastatic, liver	1 (2%)			
Hepatocellular carcinoma, metastatic, liver	1 (2%)	1 (2%)		2 (4%)
Nose	(50)	(50)	(50)	(50)
Special Senses System				
Harderian gland	(4)	(2)	(6)	(5)
Adenoma	4 (100%)	2 (100%)	6 (100%)	5 (100%)
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Urinary bladder	(50)	(50)	(50)	(50)
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Lymphoma malignant lymphocytic	1 (2%)			1 (2%)
Lymphoma malignant mixed	1 (2%)	3 (6%)	2 (4%)	
Mesothelioma malignant				1 (2%)
Neoplasm Summary				
Total animals with primary neoplasms[c]				
15-Month interim evaluation	3	1	3	2
2-Year study	42	40	35	23
Total primary neoplasms				
15-Month interim evaluation	4	1	3	3
2-Year study	61	73	55	36
Total animals with benign neoplasms				
15-Month interim evaluation	2	1	3	2
2-Year study	28	27	21	15
Total benign neoplasms				
15-Month interim evaluation	3	1	3	2
2-Year study	35	42	30	16

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Neoplasm Summary (continued)				
Total animals with malignant neoplasms				
15-Month interim evaluation	1			1
2-Year study	24	21	20	14
Total malignant neoplasms				
15-Month interim evaluation	1			1
2-Year study	26	31	25	20
Total animals with metastatic neoplasms				
2-Year study	2	1	1	4
Total metastatic neoplasms				
2-Year study	3	1	1	6

[a] Number of animals examined microscopically at site and number of animals with lesion
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 0 ppm

Number of Days on Study	4 0 8	5 0 8	5 0 8	5 7 7	6 1 8	6 4 4	6 7 0	7 1 0	7 2 0	7 2 4	7 2 5	7 2 7	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	7 2 9
Carcass ID Number	0 2 5	0 4 5	0 5 6	0 3 0	0 2 9	0 1 9	0 1 0	0 2 2	0 1 8	0 2 8	0 2 1	0 2 7	0 0 1	0 0 2	0 0 4	0 0 5	0 0 6	0 0 7	0 0 8	0 0 9	0 1 2	0 1 3	0 1 4	0 1 6	0 1 7	0 2 0
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	A	+	M	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																										
Hemangiosarcoma																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cholangiocarcinoma																										
Hepatocellular carcinoma		X	X		X												X		X						
Hepatocellular carcinoma, two, multiple						X																				
Hepatocellular carcinoma, three, multiple												X									X					
Hepatocellular adenoma										X					X							X		X	
Hepatocellular adenoma, two, multiple																										
Mesentery																										
Cholangiocarcinoma, metastatic, liver																										
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pharynx							+																			
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma							X												X							
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth																										
Cardiovascular System																										
Blood vessel																	+									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Capsule, adenoma																						X				
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant													X													

+: 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 Feed Study of Benzyl Acetate: 0 ppm (continued)

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	02 23	02 26	03 01	03 03	03 34	03 35	03 36	03 38	03 39	04 40	04 41	04 43	04 44	04 46	04 47	04 48	04 49	05 01	05 02	05 03	05 04	05 07	05 08	05 09	06 00	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma				X																				X		2
Hemangiosarcoma		X																								1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cholangiocarcinoma																							X			1
Hepatocellular carcinoma	X																X						X			8
Hepatocellular carcinoma, two, multiple																										1
Hepatocellular carcinoma, three, multiple																				X						3
Hepatocellular adenoma			X	X														X				X		X		9
Hepatocellular adenoma, two, multiple																									X	1
Mesentery				+		+																	+			3
Cholangiocarcinoma, metastatic, liver																							X			1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pharynx																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																				X						3
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth				+															+		+					3
Cardiovascular System																										
Blood vessel																										1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma													X													1
Capsule, adenoma							X								X											3
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																										1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 0 ppm (continued)

Number of Days on Study	4 0 8	5 0 8	5 0 8	5 7 7	6 1 8	6 4 4	6 7 0	7 1 0	7 2 4	7 2 5	7 2 7	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	7 2 9	7 2 9
Carcass ID Number	0 2 5	0 4 5	0 5 6	0 3 0	0 2 9	0 1 9	0 1 0	0 2 2	0 1 8	0 2 1	0 2 7	0 0 1	0 0 2	0 0 4	0 0 5	0 0 6	0 0 7	0 0 8	0 0 9	0 1 2	0 1 3	0 1 4	0 1 6	0 1 7	0 2 0
Endocrine System (continued)																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	M
Pituitary gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma													X											X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland					+			+	+	+			+	+		+	+					+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Lymph node, mesenteric	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	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	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, hemangiosarcoma										X															
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Oligodendroglioma malignant									X																
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma								X		X		X						X						X	
Alveolar/bronchiolar carcinoma			X														X					X			X
Cholangiocarcinoma, metastatic, liver																									
Hepatocellular carcinoma, metastatic, liver																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 0 ppm (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 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	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	0 2 3	0 2 6	0 3 1	0 3 3	0 3 4	0 3 5	0 3 6	0 3 8	0 3 9	0 4 0	0 4 1	0 4 3	0 4 4	0 4 6	0 4 7	0 4 8	0 4 9	0 5 1	0 5 2	0 5 3	0 5 4	0 5 7	0 5 8	0 5 9	0 6 0	Total Tissues/ Tumors
Endocrine System (continued)																										
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	M	+	M	+	I	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Pituitary gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma											X															3
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma						X	X																			2
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+		+	+	+	+	+	+	+		+	+		+	+		+	+		+	+	+		31
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mesenteric	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	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	M	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, hemangiosarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Oligodendroglioma malignant																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma			X						X	X														X		9
Alveolar/bronchiolar carcinoma						X																				5
Cholangiocarcinoma, metastatic, liver																							X			1
Hepatocellular carcinoma, metastatic, liver	X																									1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 0 ppm (continued)

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 0 ppm (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 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	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	0 2 3	0 2 6	0 3 1	0 3 3	0 3 4	0 3 5	0 3 6	0 3 8	0 3 9	0 4 0	0 4 1	0 4 3	0 4 4	0 4 6	0 4 7	0 4 8	0 4 9	0 5 1	0 5 2	0 5 3	0 5 4	0 5 7	0 5 8	0 5 9	0 6 0	Total Tissues/ Tumors
Special Senses System																										
Harderian gland					+			+															+			4
Adenoma					X			X															X			4
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 330 ppm

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 330 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	
Carcass ID Number	0 8 6	0 8 7	0 8 8	0 8 9	0 9 0	0 9 1	0 9 3	0 9 5	0 9 6	0 9 7	0 9 8	0 9 9	0 0 1	1 0 2	1 0 5	1 0 6	1 0 7	1 0 8	1 1 0	1 1 1	1 1 4	1 1 5	1 1 8	1 1 9	1 2 0	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma																										1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										2
Hepatocellular carcinoma	X			X		X			X		X															10
Hepatocellular carcinoma, two, multiple																										4
Hepatocellular adenoma	X		X				X				X											X				11
Hepatocellular adenoma, two, multiple																	X									1
Hepatocellular adenoma, three, multiple																										1
Mesentery										+							+									3
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma								X													X					4
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth	+												+													4
Cardiovascular System																										
Blood vessel	+																									1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Capsule, adenoma	X																								X	2
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign																						X				1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																								X		2
Parathyroid gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma																										1
General Body System																										
None																										

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 330 ppm (continued)

Number of Days on Study	5 0 8	5 6 1	5 6 2	5 8 9	6 0 5	7 2 2	7 2 4	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	1 1 6	0 9 4	0 6 5	1 1 3	1 1 7	1 0 3	0 7 3	0 6 2	0 6 3	0 6 4	0 6 6	0 7 9	0 8 1	0 6 8	0 6 9	0 7 0	0 7 1	0 7 4	0 7 5	0 7 6	0 7 7	0 7 8	0 8 2	0 8 3	0 8 5
Genital System																									
Coagulating gland																						+			
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Preputial gland		+	+	+	+	+	+	+		+	+	+	+		+	+	+	+	+	+		+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma			X	X																					
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma			X	X																					
Thymus	+	+	+	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																					
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma			X	X																					
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma			X																						
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma	X																					X	X		X
Alveolar/bronchiolar adenoma, two, multiple								X																	
Alveolar/bronchiolar carcinoma										X															
Hepatocellular carcinoma, metastatic, liver							X																		
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland																									
Adenoma																									

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 330 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	
Carcass ID Number	0 8 6	0 8 7	0 8 8	0 8 9	0 9 0	0 9 1	0 9 3	0 9 5	0 9 6	0 9 7	0 9 8	0 9 9	1 0 1	1 0 2	1 0 5	1 0 6	1 0 7	1 0 8	1 1 0	1 1 1	1 1 4	1 1 5	1 1 8	1 1 9	1 2 0	Total Tissues/ Tumors
Genital System																										
Coagulating gland																										1
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma	X																									1
Preputial gland	+		+	+	+	+		+	+			+			+	+	+	+		+	+	+	+	+	+	39
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										2
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	47
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										2
Thymus	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	45
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																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										2
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma	X	X	X		X						X				X				X	X	X			X		14
Alveolar/bronchiolar adenoma, two, multiple																										1
Alveolar/bronchiolar carcinoma											X					X										3
Hepatocellular carcinoma, metastatic, liver																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Harderian gland		+										+														2
Adenoma		X										X														2

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 330 ppm (continued)

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 330 ppm (continued)

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 1,000 ppm

Number of Days on Study	5 7 1	6 1 8	6 1 8	6 2 0	6 2 0	7 0 8	7 1 1	7 2 4	7 2 6	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	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1
Carcass ID Number	1 3 7	1 5 0	1 5 4	1 3 1	1 3 2	1 4 1	1 7 2	1 4 8	1 4 0	1 2 1	1 2 2	1 2 4	1 2 5	1 2 6	1 2 7	1 2 8	1 3 0	1 3 3	1 3 5	1 3 6	1 3 8	1 3 9	1 4 3	1 4 4	1 4 5
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma				X																					
Hepatocellular carcinoma						X	X											X							
Hepatocellular carcinoma, two, multiple			X																						
Hepatocellular carcinoma, five, multiple																									
Hepatocellular adenoma																									
Hepatocellular adenoma, two, multiple								X															X		
Mesentery								+																	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell adenoma																	X								
Squamous cell papilloma																				X					
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth																	+								
Cardiovascular System																									
Blood vessel											+														
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma														X											
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma							X																X		
Parathyroid gland	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, carcinoma	X																								
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																					X				

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 1,000 ppm (continued)

Number of Days on Study	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	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	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	1 4 6	1 4 9	1 5 1	1 5 3	1 5 6	1 5 7	1 5 8	1 6 0	1 6 1	1 6 2	1 6 3	1 6 4	1 6 6	1 6 7	1 6 8	1 6 9	1 7 0	1 7 1	1 7 3	1 7 4	1 7 5	1 7 7	1 7 8	1 7 9	1 8 0	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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma									X																	1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Hepatocellular carcinoma											X						X	X	X			X			X	9
Hepatocellular carcinoma, two, multiple																										1
Hepatocellular carcinoma, five, multiple						X																				1
Hepatocellular adenoma	X				X			X														X	X			5
Hepatocellular adenoma, two, multiple															X											3
Mesentery						+																				2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Basal cell adenoma																										1
Squamous cell papilloma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth																										1
Cardiovascular System																										
Blood vessel											+															2
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma					X																					1
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																						X				3
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	46
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	48
Pars distalis, carcinoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma										X																2

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 1,000 ppm (continued)

Number of Days on Study	5 7 1	6 1 8	6 1 8	6 2 0	6 2 0	7 0 8	7 1 1	7 2 4	7 2 6	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	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 3 7	1 5 0	1 5 4	1 3 1	1 3 2	1 4 1	1 7 2	1 4 8	1 4 0	1 2 1	1 2 2	1 2 4	1 2 5	1 2 6	1 2 7	1 2 8	1 3 0	1 3 3	1 3 5	1 3 6	1 3 8	1 3 9	1 4 3	1 4 4	1 4 5
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland			+					+		+		+	+	+	+	+	+	+	+		+	+				
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell, adenoma								X																		
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma		X																								
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma		X																								
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	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrous histiocytoma																										
Subcutaneous tissue, hemangiosarcoma		X																								
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma					X																					
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pituitary gland	X																									
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma						X			X	X		X		X											X	
Alveolar/bronchiolar carcinoma																										
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 1,000 ppm (continued)

Number of Days on Study	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	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	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	1 4 6	1 4 9	1 5 1	1 5 3	1 5 6	1 5 7	1 5 8	1 6 0	1 6 1	1 6 2	1 6 3	1 6 4	1 6 6	1 6 7	1 6 8	1 6 9	1 7 0	1 7 1	1 7 3	1 7 4	1 7 5	1 7 7	1 7 8	1 7 9	1 8 0	Total Tissues/ Tumors
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland		+	+	+	+	+	+			+	+	+	+	+	+		+		+		+	+		+		30
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Interstitial cell, adenoma																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma													X													2
Thymus	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
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	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrous histiocytoma			X																							1
Subcutaneous tissue, hemangiosarcoma									X																	2
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, pituitary gland																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma															X											7
Alveolar/bronchiolar carcinoma																	X									1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 1,000 ppm (continued)

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 1,000 ppm (continued)

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm

Number of Days on Study	4 7 7	5 2 4	5 5 2	5 8 4	6 0 0	6 4 7	6 5 1	6 8 3	7 0 1	7 2 4	7 2 5	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 0	7 3 0	7 3 0
Carcass ID Number	2 3 0	1 8 6	1 9 8	2 3 9	2 1 6	2 0 9	2 2 6	1 9 2	2 4 0	2 1 2	1 9 1	1 8 1	1 8 2	1 8 3	1 8 4	1 8 5	1 8 7	1 8 9	1 9 0	1 9 4	1 9 5	1 9 6	1 9 7	2 1 3	2 1 4
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma				X																					
Hepatocellular carcinoma						X	X													X					
Hepatocellular carcinoma, two, multiple				X								X													
Hepatocellular adenoma																									
Mesothelioma malignant, metastatic, mesentery								X																	
Mesentery								+																	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma								X																	
Squamous cell papilloma						X																			
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth																									
Cardiovascular System																									
Blood vessel																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic, liver							X																		
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, adenoma																									
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	M	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																									
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm (continued)

Number of Days on Study	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 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	7 3 1	7 3 1	7 3 1	
Carcass ID Number	2 1 5	2 1 7	2 1 8	2 2 9	2 3 1	2 3 2	2 3 4	2 3 5	2 3 6	2 3 7	2 3 8	2 0 0	2 0 2	2 0 3	2 0 5	2 0 6	2 0 7	2 0 8	2 1 0	2 1 9	2 2 0	2 2 2	2 2 3	2 2 5	2 2 7	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Hepatocellular carcinoma	X		X																							5
Hepatocellular carcinoma, two, multiple						X																				3
Hepatocellular adenoma															X											1
Mesothelioma malignant, metastatic, mesentery																										1
Mesentery																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma																										1
Squamous cell papilloma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth									+										+							2
Cardiovascular System																										
Blood vessel							+																			1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic, liver																										1
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, adenoma																		X								1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pars distalis, adenoma														X												1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma								X																		1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm (continued)

Number of Days on Study	4 7 7	5 2 4	5 5 2	5 8 4	6 0 0	6 4 7	6 5 1	6 8 3	7 0 1	7 2 4	7 2 5	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 0	7 3 0	7 3 0
Carcass ID Number	2 3 0	1 8 6	1 9 8	2 3 9	2 1 6	2 0 9	2 2 6	1 9 2	2 4 0	2 1 2	1 9 1	1 8 1	1 8 2	1 8 3	1 8 4	1 8 5	1 8 7	1 8 9	1 9 0	1 9 4	1 9 5	1 9 6	1 9 7	1 9 3	2 1 4	2 1 1
General Body System																										
Tissue NOS													+													
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland					+	+		+	+			+	+			+			+		+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma				X					X																	
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone			X																							
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma				X																						
Thymus	+	+	+	+	+	+	+	+	+	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	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma									X																	
Osteosarcoma			X																							
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma									X																	
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																										
Alveolar/bronchiolar carcinoma											X															
Hepatocellular carcinoma, metastatic, liver							X					X														
Mesothelioma malignant, metastatic, mesentery								X																		
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm (continued)

Number of Days on Study	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	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	2 1 5	2 1 7	2 1 8	2 2 9	2 3 1	2 3 2	2 3 4	2 3 5	2 3 6	2 3 7	2 3 8	2 0 0	2 0 2	2 0 3	2 0 5	2 0 6	2 0 7	2 0 8	2 1 0	2 1 9	2 2 0	2 2 2	2 2 3	2 2 5	2 2 7	Total Tissues/ Tumors
General Body System																										
Tissue NOS																										1
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+			+				+	+							+		+	+			24
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										2
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma, metastatic, bone																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Thymus	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
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	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Osteosarcoma																										1
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma						X	X				X				X							X			X	6
Alveolar/bronchiolar carcinoma															X											2
Hepatocellular carcinoma, metastatic, liver																										2
Mesothelioma malignant, metastatic, mesentery																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm (continued)

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm (continued)

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

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Feed Study of Benzyl Acetate

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Adrenal Cortex: Adenoma				
Overall rate[a]	5/60 (8%)	3/60 (5%)	1/60 (2%)	1/60 (2%)
Adjusted rate[b]	11.9%	7.0%	2.4%	2.6%
Interim evaluation	1/10 (10%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate[c]	4/39 (10%)	3/43 (7%)	1/41 (2%)	1/39 (3%)
First incidence (days)	457 (I)	729 (T)	729 (T)	729 (T)
Life table test[d]	P=0.095N	P=0.312N	P=0.096N	P=0.105N
Logistic regression test[d]	P=0.091N	P=0.349N	P=0.102N	P=0.104N
Cochran-Armitage test[d]	P=0.090N			
Fisher exact test[d]		P=0.359N	P=0.103N	P=0.103N
Harderian Gland: Adenoma				
Overall rate	4/60 (7%)	2/60 (3%)	6/60 (10%)	5/60 (8%)
Adjusted rate	9.9%	4.7%	13.8%	11.9%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	3/39 (8%)	2/43 (5%)	4/41 (10%)	2/39 (5%)
First incidence (days)	724	729 (T)	708	683
Life table test	P=0.288	P=0.298N	P=0.400	P=0.495
Logistic regression test	P=0.292	P=0.314N	P=0.391	P=0.493
Cochran-Armitage test	P=0.313			
Fisher exact test		P=0.340N	P=0.372	P=0.500
Liver: Hepatocellular Adenoma				
Overall rate	11/60 (18%)	14/60 (23%)	10/60 (17%)	2/60 (3%)
Adjusted rate	26.3%	31.5%	21.8%	4.2%
Interim evaluation	1/10 (10%)	1/10 (10%)	2/10 (20%)	1/10 (10%)
Terminal rate	9/39 (23%)	13/43 (30%)	7/41 (17%)	1/39 (3%)
First incidence (days)	458 (I)	458 (I)	457 (I)	456 (I)
Life table test	P=0.003N	P=0.418	P=0.460N	P=0.010N
Logistic regression test	P=0.002N	P=0.345	P=0.483N	P=0.009N
Cochran-Armitage test	P=0.002N			
Fisher exact test		P=0.327	P=0.500N	P=0.008N
Liver: Hepatocellular Carcinoma				
Overall rate	12/60 (20%)	14/60 (23%)	11/60 (18%)	8/60 (13%)
Adjusted rate	26.6%	29.6%	24.7%	18.5%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	7/39 (18%)	10/43 (23%)	8/41 (20%)	5/39 (13%)
First incidence (days)	508	508	618	584
Life table test	P=0.155N	P=0.497	P=0.454N	P=0.241N
Logistic regression test	P=0.127N	P=0.425	P=0.478N	P=0.230N
Cochran-Armitage test	P=0.125N			
Fisher exact test		P=0.412	P=0.500N	P=0.232N
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	23/60 (38%)	23/60 (38%)	20/60 (33%)	10/60 (17%)
Adjusted rate	49.5%	47.6%	41.9%	22.2%
Interim evaluation	1/10 (10%)	1/10 (10%)	2/10 (20%)	1/10 (10%)
Terminal rate	16/39 (41%)	18/43 (42%)	14/41 (34%)	6/39 (15%)
First incidence (days)	458 (I)	458 (I)	457 (I)	456 (I)
Life table test	P=0.005N	P=0.443N	P=0.302N	P=0.010N
Logistic regression test	P=0.002N	P=0.552N	P=0.322N	P=0.007N
Cochran-Armitage test	P=0.002N			
Fisher exact test		P=0.574N	P=0.352N	P=0.007N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Lung: Alveolar/bronchiolar Adenoma				
Overall rate	10/60 (17%)	15/60 (25%)	8/60 (13%)	6/60 (10%)
Adjusted rate	23.3%	33.9%	17.6%	15.4%
Interim evaluation	1/10 (10%)	0/10 (0%)	1/10 (10%)	0/10 (0%)
Terminal rate	7/39 (18%)	14/43 (33%)	5/41 (12%)	6/39 (15%)
First incidence (days)	458 (I)	508	457 (I)	729 (T)
Life table test	P=0.074N	P=0.256	P=0.367N	P=0.214N
Logistic regression test	P=0.062N	P=0.196	P=0.380N	P=0.209N
Cochran-Armitage test	P=0.061N			
Fisher exact test		P=0.184	P=0.399N	P=0.211N
Lung: Alveolar/bronchiolar Carcinoma				
Overall rate	5/60 (8%)	3/60 (5%)	1/60 (2%)	3/60 (5%)
Adjusted rate	12.1%	7.0%	2.4%	6.8%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	1/10 (10%)
Terminal rate	4/39 (10%)	3/43 (7%)	1/41 (2%)	1/39 (3%)
First incidence (days)	508	729 (T)	729 (T)	457 (I)
Life table test	P=0.419N	P=0.310N	P=0.095N	P=0.361N
Logistic regression test	P=0.402N	P=0.347N	P=0.100N	P=0.357N
Cochran-Armitage test	P=0.400N			
Fisher exact test		P=0.359N	P=0.103N	P=0.359N
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	15/60 (25%)	17/60 (28%)	9/60 (15%)	8/60 (13%)
Adjusted rate	34.2%	38.5%	19.9%	19.1%
Interim evaluation	1/10 (10%)	0/10 (0%)	1/10 (10%)	1/10 (10%)
Terminal rate	11/39 (28%)	16/43 (37%)	6/41 (15%)	6/39 (15%)
First incidence (days)	458 (I)	508	457 (I)	457 (I)
Life table test	P=0.042N	P=0.532	P=0.112N	P=0.088N
Logistic regression test	P=0.032N	P=0.443	P=0.114N	P=0.080N
Cochran-Armitage test	P=0.032N			
Fisher exact test		P=0.418	P=0.127N	P=0.082N
Pancreatic Islets: Adenoma				
Overall rate	0/60 (0%)	2/60 (3%)	3/59 (5%)	0/60 (0%)
Adjusted rate	0.0%	4.7%	7.2%	0.0%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	0/39 (0%)	2/43 (5%)	2/40 (5%)	0/39 (0%)
First incidence (days)	–[e]	729 (T)	711	–
Life table test	P=0.399N	P=0.260	P=0.129	–
Logistic regression test	P=0.395N	P=0.260	P=0.123	–
Cochran-Armitage test	P=0.385N			
Fisher exact test		P=0.248	P=0.119	–
Pituitary Gland (Pars distalis): Adenoma				
Overall rate	3/58 (5%)	0/59 (0%)	0/58 (0%)	1/57 (2%)
Adjusted rate	7.9%	0.0%	0.0%	2.6%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	3/38 (8%)	0/43 (0%)	0/39 (0%)	1/39 (3%)
First incidence (days)	729 (T)	–	–	729 (T)
Life table test	P=0.451N	P=0.100N	P=0.116N	P=0.296N
Logistic regression test	P=0.451N	P=0.100N	P=0.116N	P=0.296N
Cochran-Armitage test	P=0.451N			
Fisher exact test		P=0.119N	P=0.122N	P=0.316N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Pituitary Gland (Pars distalis): Adenoma or Carcinoma				
Overall rate	3/58 (5%)	0/59 (0%)	1/58 (2%)	1/57 (2%)
Adjusted rate	7.9%	0.0%	2.0%	2.6%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	3/38 (8%)	0/43 (0%)	0/39 (0%)	1/39 (3%)
First incidence (days)	729 (T)	–	571	729 (T)
Life table test	P=0.444N	P=0.100N	P=0.294N	P=0.296N
Logistic regression test	P=0.443N	P=0.100N	P=0.301N	P=0.296N
Cochran-Armitage test	P=0.445N			
Fisher exact test		P=0.119N	P=0.309N	P=0.316N
Small Intestine (Jejunum): Carcinoma				
Overall rate	3/60 (5%)	1/60 (2%)	1/60 (2%)	0/60 (0%)
Adjusted rate	6.9%	2.3%	2.4%	0.0%
Interim evaluation	1/10 (10%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	2/39 (5%)	1/43 (2%)	1/41 (2%)	0/39 (0%)
First incidence (days)	458 (I)	729 (T)	729 (T)	–
Life table test	P=0.120N	P=0.281N	P=0.294N	P=0.123N
Logistic regression test	P=0.116N	P=0.307N	P=0.308N	P=0.122N
Cochran-Armitage test	P=0.116N			
Fisher exact test		P=0.309N	P=0.309N	P=0.122N
Stomach (Forestomach): Squamous Cell Papilloma				
Overall rate	3/60 (5%)	4/60 (7%)	1/60 (2%)	2/60 (3%)
Adjusted rate	7.3%	8.8%	2.4%	4.1%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	1/10 (10%)
Terminal rate	2/39 (5%)	3/43 (7%)	1/41 (2%)	0/39 (0%)
First incidence (days)	670	508	729 (T)	457 (I)
Life table test	P=0.352N	P=0.541	P=0.292N	P=0.500N
Logistic regression test	P=0.338N	P=0.506	P=0.293N	P=0.501N
Cochran-Armitage test	P=0.338N			
Fisher exact test		P=0.500	P=0.309N	P=0.500N
Stomach (Forestomach): Squamous Cell Papilloma or Squamous Cell Carcinoma				
Overall rate	3/60 (5%)	4/60 (7%)	1/60 (2%)	3/60 (5%)
Adjusted rate	7.3%	8.8%	2.4%	6.3%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	1/10 (10%)
Terminal rate	2/39 (5%)	3/43 (7%)	1/41 (2%)	0/39 (0%)
First incidence (days)	670	508	729 (T)	457 (I)
Life table test	P=0.558N	P=0.541	P=0.292N	P=0.659
Logistic regression test	P=0.544N	P=0.506	P=0.293N	P=0.662
Cochran-Armitage test	P=0.544N			
Fisher exact test		P=0.500	P=0.309N	P=0.660N
All Organs: Hemangiosarcoma				
Overall rate	2/60 (3%)	2/60 (3%)	5/60 (8%)	2/60 (3%)
Adjusted rate	4.9%	4.2%	11.1%	4.5%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	1/39 (3%)	0/43 (0%)	3/41 (7%)	0/39 (0%)
First incidence (days)	725	562	618	584
Life table test	P=0.592N	P=0.675N	P=0.242	P=0.689
Logistic regression test	P=0.579N	P=0.692	P=0.226	P=0.694N
Cochran-Armitage test	P=0.579N			
Fisher exact test		P=0.691N	P=0.219	P=0.691N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
All Organs: Hemangioma or Hemangiosarcoma				
Overall rate	2/60 (3%)	3/60 (5%)	5/60 (8%)	2/60 (3%)
Adjusted rate	4.9%	6.4%	11.1%	4.5%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	1/39 (3%)	1/43 (2%)	3/41 (7%)	0/39 (0%)
First incidence (days)	725	562	618	584
Life table test	P=0.515N	P=0.526	P=0.242	P=0.689
Logistic regression test	P=0.500N	P=0.500	P=0.226	P=0.694N
Cochran-Armitage test	P=0.500N			
Fisher exact test		P=0.500	P=0.219	P=0.691N
All Organs: Malignant Lymphoma or Histiocytic Sarcoma				
Overall rate	2/60 (3%)	3/60 (5%)	2/60 (3%)	1/60 (2%)
Adjusted rate	4.4%	7.0%	4.4%	2.6%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	0/39 (0%)	3/43 (7%)	0/41 (0%)	1/39 (3%)
First incidence (days)	577	729 (T)	618	729 (T)
Life table test	P=0.319N	P=0.530	P=0.676N	P=0.505N
Logistic regression test	P=0.305N	P=0.507	P=0.692	P=0.500N
Cochran-Armitage test	P=0.303N			
Fisher exact test		P=0.500	P=0.691N	P=0.500N
All Organs: Benign Neoplasms				
Overall rate	30/60 (50%)	28/60 (47%)	24/60 (40%)	17/60 (28%)
Adjusted rate	66.3%	62.0%	49.4%	37.1%
Interim evaluation	2/10 (20%)	1/10 (10%)	3/10 (30%)	2/10 (20%)
Terminal rate	24/39 (62%)	26/43 (60%)	17/41 (41%)	11/39 (28%)
First incidence (days)	457 (I)	458 (I)	457 (I)	456 (I)
Life table test	P=0.012N	P=0.250N	P=0.139N	P=0.016N
Logistic regression test	P=0.006N	P=0.376N	P=0.138N	P=0.010N
Cochran-Armitage test	P=0.007N			
Fisher exact test		P=0.428N	P=0.179N	P=0.012N
All Organs: Malignant Neoplasms				
Overall rate	25/60 (42%)	21/60 (35%)	20/60 (33%)	15/60 (25%)
Adjusted rate	50.8%	42.8%	40.6%	31.5%
Interim evaluation	1/10 (10%)	0/10 (0%)	0/10 (0%)	1/10 (10%)
Terminal rate	15/39 (38%)	15/43 (35%)	12/41 (29%)	7/39 (18%)
First incidence (days)	458 (I)	508	571	457 (I)
Life table test	P=0.075N	P=0.214N	P=0.202N	P=0.062N
Logistic regression test	P=0.042N	P=0.266N	P=0.200N	P=0.039N
Cochran-Armitage test	P=0.042N			
Fisher exact test		P=0.287N	P=0.225N	P=0.040N
All Organs: Benign or Malignant Neoplasms				
Overall rate	45/60 (75%)	41/60 (68%)	38/60 (63%)	25/60 (42%)
Adjusted rate	86.5%	81.9%	71.6%	50.7%
Interim evaluation	3/10 (30%)	1/10 (10%)	3/10 (30%)	2/10 (20%)
Terminal rate	32/39 (82%)	34/43 (79%)	26/41 (63%)	15/39 (38%)
First incidence (days)	457 (I)	458 (I)	457 (I)	456 (I)
Life table test	P<0.001N	P=0.128N	P=0.107N	P=0.002N
Logistic regression test	P<0.001N	P=0.202N	P=0.078N	P<0.001N
Cochran-Armitage test	P<0.001N			
Fisher exact test		P=0.272N	P=0.118N	P<0.001N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

(T)Terminal sacrifice
(I)Interim evaluation
[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 exposure group incidence are the P values corresponding to pairwise comparisons between the controls and that exposure 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 test regards 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 an exposure group is indicated by N.
[e] Not applicable; no neoplasms in animal group

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Feed Study of Benzyl Acetate[a]

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	10	10
Early deaths				
Moribund	7	3	6	7
Natural deaths	4	4	3	4
Survivors				
Terminal sacrifice	39	43	41	39
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Intestine small, jejunum	(10)	(10)	(10)	(10)
Hyperplasia, lymphoid		1 (10%)		
Liver	(10)	(10)	(10)	(10)
Basophilic focus	1 (10%)	1 (10%)		
Clear cell focus	1 (10%)		2 (20%)	
Inflammation, subacute			1 (10%)	
Hepatocyte, cytomegaly	2 (20%)		1 (10%)	
Hepatocyte, vacuolization cytoplasmic	2 (20%)		1 (10%)	
Lobules, necrosis			1 (10%)	
Pancreas	(10)	(10)	(10)	(10)
Atrophy	1 (10%)		1 (10%)	
Focal cellular change	2 (20%)	1 (10%)	1 (10%)	1 (10%)
Acinar cell, cytoplasmic alteration				1 (10%)
Salivary glands	(10)	(10)	(10)	(10)
Hyperplasia, lymphoid	1 (10%)	1 (10%)		1 (10%)
Stomach, glandular	(10)	(10)	(10)	(10)
Cyst	3 (30%)	2 (20%)		2 (20%)
Tongue	(10)	(10)	(10)	(10)
Inflammation, chronic		1 (10%)		
Cardiovascular System				
None				
Endocrine System				
Adrenal gland, cortex	(10)	(10)	(10)	(10)
Accessory adrenal cortical nodule	2 (20%)		1 (10%)	
Hyperplasia, diffuse			1 (10%)	
Hyperplasia, focal	3 (30%)	3 (30%)	3 (30%)	5 (50%)
Capsule, hyperplasia		1 (10%)	1 (10%)	
Islets, pancreatic	(10)	(10)	(10)	(10)
Hyperplasia	1 (10%)	2 (20%)	2 (20%)	1 (10%)
Parathyroid gland	(10)	(10)	(9)	(10)
Cyst	1 (10%)			
Pituitary gland	(10)	(10)	(10)	(10)
Pars distalis, cyst	1 (10%)			
General Body System				
None				

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
15-Month Interim Evaluation (continued)				
Genital System				
Preputial gland	(7)	(3)	(5)	(1)
Atrophy	1 (14%)			
Ectasia	4 (57%)	3 (100%)	4 (80%)	1 (100%)
Inflammation, chronic	2 (29%)	2 (67%)	1 (20%)	
Prostate	(10)	(10)	(10)	(10)
Hemorrhage	1 (10%)	1 (10%)		1 (10%)
Inflammation, chronic				1 (10%)
Seminal vesicle	(10)	(10)	(10)	(10)
Fibrosis			1 (10%)	
Hemorrhage			1 (10%)	
Testes	(10)	(10)	(10)	(10)
Granuloma sperm				1 (10%)
Mineralization				1 (10%)
Seminiferous tubule, atrophy				1 (10%)
Hematopoietic System				
Lymph node	(10)	(10)	(10)	(10)
Mediastinal, hyperplasia, lymphoid				1 (10%)
Lymph node, mesenteric	(10)	(10)	(10)	(10)
Hemorrhage	1 (10%)	3 (30%)		
Spleen	(10)	(10)	(10)	(10)
Red pulp, hyperplasia			1 (10%)	
Thymus	(10)	(10)	(10)	(9)
Cyst	2 (20%)			1 (11%)
Integumentary System				
None				
Musculoskeletal System				
Skeletal muscle	(10)	(10)	(10)	(10)
Inflammation, chronic			1 (10%)	
Nervous System				
Brain	(10)	(10)	(10)	(10)
Ectopic tissue		1 (10%)		
Thalamus, mineralization	10 (100%)	7 (70%)	10 (100%)	10 (100%)
Respiratory System				
Lung	(10)	(10)	(10)	(10)
Hemorrhage		1 (10%)		1 (10%)
Infiltration cellular, histiocyte				1 (10%)
Alveolar epithelium, hyperplasia				1 (10%)
Nose	(10)	(10)	(10)	(10)
Exudate			1 (10%)	5 (50%)
Glands, hyperplasia, cystic	2 (20%)	3 (30%)	1 (10%)	10 (100%)
Mucosa, atrophy		8 (80%)	10 (100%)	10 (100%)
Mucosa, degeneration	5 (50%)	5 (50%)	10 (100%)	10 (100%)
Mucosa, pigmentation		7 (70%)	10 (100%)	10 (100%)

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Feed Study of Benzyl Acetate
(continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
15-Month Interim Evaluation (continued)				
Special Senses System				
None				
Urinary System				
Kidney	(10)	(10)	(10)	(10)
Casts protein		1 (10%)		
Cyst			1 (10%)	1 (10%)
Hyperplasia, lymphoid		2 (20%)	1 (10%)	1 (10%)
Mineralization	6 (60%)	6 (60%)	1 (10%)	7 (70%)
Renal tubule, dilatation	1 (10%)	1 (10%)		
Renal tubule, regeneration	8 (80%)	5 (50%)	4 (40%)	5 (50%)
Urinary bladder	(10)	(10)	(10)	(10)
Hyperplasia, lymphoid	1 (10%)			
2-Year Study				
Alimentary System				
Gallbladder	(47)	(50)	(48)	(50)
Cyst				1 (2%)
Inflammation, subacute		1 (2%)		1 (2%)
Mucosa, hyperplasia		1 (2%)		1 (2%)
Intestine large, cecum	(49)	(49)	(50)	(48)
Edema				1 (2%)
Intestine small, ileum	(48)	(49)	(50)	(48)
Hyperplasia, lymphoid		1 (2%)		1 (2%)
Inflammation, chronic			1 (2%)	
Intestine small, jejunum	(50)	(49)	(50)	(49)
Hyperplasia, lymphoid		1 (2%)	1 (2%)	1 (2%)
Liver	(50)	(50)	(50)	(50)
Basophilic focus	1 (2%)	1 (2%)		2 (4%)
Clear cell focus	6 (12%)	4 (8%)	3 (6%)	2 (4%)
Hematopoietic cell proliferation		2 (4%)	1 (2%)	1 (2%)
Hyperplasia, focal	2 (4%)	3 (6%)	1 (2%)	
Hyperplasia, lymphoid	1 (2%)	1 (2%)		
Inflammation, subacute	1 (2%)	3 (6%)	1 (2%)	3 (6%)
Mixed cell focus	3 (6%)	2 (4%)	2 (4%)	2 (4%)
Nuclear alteration	1 (2%)	1 (2%)		
Thrombosis		1 (2%)		
Bile duct, hyperplasia				1 (2%)
Centrilobular, necrosis	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Hepatocyte, vacuolization cytoplasmic	2 (4%)	1 (2%)	1 (2%)	2 (4%)
Kupffer cell, hyperplasia	3 (6%)	2 (4%)	2 (4%)	4 (8%)
Kupffer cell, pigmentation			1 (2%)	2 (4%)
Lobules, necrosis	4 (8%)	1 (2%)	1 (2%)	4 (8%)
Mesentery	(3)	(3)	(2)	(1)
Inflammation, suppurative		1 (33%)		
Fat, hemorrhage		1 (33%)		
Fat, necrosis	2 (67%)	1 (33%)	2 (100%)	
Pancreas	(50)	(50)	(50)	(50)
Atrophy	1 (2%)	2 (4%)	1 (2%)	
Cyst		1 (2%)		
Focal cellular change	1 (2%)	1 (2%)		

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Alimentary System (continued)				
Pancreas (continued)	(50)	(50)	(50)	(50)
Hyperplasia, lymphoid			1 (2%)	1 (2%)
Acinar cell, cytoplasmic alteration	3 (6%)	2 (4%)		4 (8%)
Acinar cell, hyperplasia, focal				1 (2%)
Pharynx	(1)			
Ulcer	1 (100%)			
Salivary glands	(50)	(50)	(50)	(50)
Hyperplasia, lymphoid	7 (14%)	3 (6%)	5 (10%)	6 (12%)
Stomach, forestomach	(50)	(50)	(50)	(50)
Diverticulum		3 (6%)		3 (6%)
Erosion				1 (2%)
Inflammation, subacute	3 (6%)	3 (6%)	3 (6%)	1 (2%)
Mucosa, hyperplasia	5 (10%)	4 (8%)	5 (10%)	3 (6%)
Stomach, glandular	(50)	(50)	(50)	(50)
Cyst	2 (4%)	4 (8%)	2 (4%)	4 (8%)
Erosion	3 (6%)			
Ulcer				1 (2%)
Tongue	(50)	(50)	(50)	(50)
Epithelium, degeneration, ballooning				1 (2%)
Tooth	(3)	(4)	(1)	(2)
Dysplasia	3 (100%)	3 (75%)	1 (100%)	2 (100%)
Inflammation, chronic		1 (25%)		
Cardiovascular System				
Blood vessel	(1)	(1)	(2)	(1)
Inflammation, chronic active	1 (100%)	1 (100%)	2 (100%)	1 (100%)
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy				2 (4%)
Myocardium, hemorrhage				1 (2%)
Myocardium, inflammation, chronic				2 (4%)
Myocardium, mineralization		1 (2%)		1 (2%)
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(50)
Accessory adrenal cortical nodule	7 (14%)	10 (20%)	7 (14%)	8 (16%)
Angiectasis	1 (2%)	1 (2%)		
Cyst	1 (2%)			
Hyperplasia, focal	4 (8%)	10 (20%)	5 (10%)	2 (4%)
Hypertrophy, focal	29 (58%)	22 (44%)	23 (46%)	26 (52%)
Vacuolization cytoplasmic, focal	5 (10%)	4 (8%)	2 (4%)	5 (10%)
Capsule, hyperplasia	11 (22%)	7 (14%)	8 (16%)	7 (14%)
Adrenal gland, medulla	(50)	(50)	(50)	(50)
Hyperplasia	2 (4%)		1 (2%)	1 (2%)
Islets, pancreatic	(50)	(50)	(49)	(50)
Cyst	1 (2%)			
Hyperplasia	10 (20%)	11 (22%)	9 (18%)	3 (6%)
Parathyroid gland	(42)	(48)	(46)	(49)
Cyst		2 (4%)	2 (4%)	
Ectopic thymus			1 (2%)	

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Feed Study of Benzyl Acetate
(continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Endocrine System (continued)				
Pituitary gland	(48)	(49)	(48)	(47)
Pars distalis, cyst	3 (6%)	1 (2%)	3 (6%)	
Pars distalis, hyperplasia	2 (4%)	1 (2%)	2 (4%)	
Pars intermedia, hyperplasia				1 (2%)
Thyroid gland	(50)	(50)	(50)	(50)
Degeneration, cystic	5 (10%)	4 (8%)	8 (16%)	8 (16%)
Follicle, cyst	6 (12%)	2 (4%)	3 (6%)	5 (10%)
Follicular cell, hyperplasia	6 (12%)	8 (16%)	7 (14%)	2 (4%)
General Body System				
None				
Genital System				
Coagulating gland		(1)		
Dilatation		1 (100%)		
Epididymis	(50)	(50)	(50)	(50)
Atypia cellular	1 (2%)	1 (2%)	2 (4%)	2 (4%)
Hypospermia			1 (2%)	
Inflammation, chronic	1 (2%)	1 (2%)	1 (2%)	
Spermatocele			1 (2%)	
Preputial gland	(31)	(39)	(30)	(24)
Ectasia	29 (94%)	37 (95%)	28 (93%)	23 (96%)
Inflammation, chronic	16 (52%)	23 (59%)	17 (57%)	11 (46%)
Inflammation, suppurative	3 (10%)	4 (10%)	1 (3%)	
Prostate	(50)	(50)	(50)	(50)
Fibrosis	1 (2%)			
Inflammation, chronic	1 (2%)	4 (8%)		
Inflammation, suppurative	1 (2%)			
Epithelium, hyperplasia	1 (2%)			
Seminal vesicle	(50)	(50)	(50)	(50)
Depletion cellular		1 (2%)		
Dilatation	1 (2%)	1 (2%)		
Inflammation, chronic		1 (2%)		
Testes	(50)	(50)	(50)	(50)
Angiectasis			1 (2%)	
Granuloma sperm				1 (2%)
Seminiferous tubule, atrophy	1 (2%)		3 (6%)	5 (10%)
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Hypercellularity	8 (16%)	6 (12%)	3 (6%)	4 (8%)
Necrosis	1 (2%)			
Pigmentation, hemosiderin	2 (4%)	1 (2%)	2 (4%)	
Lymph node	(50)	(50)	(50)	(50)
Inguinal, hyperplasia, lymphoid	2 (4%)	1 (2%)		
Mediastinal, hyperplasia, plasma cell		2 (4%)		
Lymph node, mandibular	(48)	(47)	(50)	(49)
Depletion cellular	1 (2%)			
Hyperplasia, lymphoid	1 (2%)	3 (6%)	4 (8%)	
Hyperplasia, plasma cell	3 (6%)	1 (2%)		1 (2%)
Pigmentation			2 (4%)	

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Hematopoietic System (continued)				
Lymph node, mesenteric	(48)	(49)	(50)	(50)
Angiectasis				1 (2%)
Depletion cellular	1 (2%)			
Ectasia		1 (2%)	1 (2%)	
Hematopoietic cell proliferation	3 (6%)	5 (10%)	8 (16%)	1 (2%)
Hemorrhage	17 (35%)	21 (43%)	19 (38%)	23 (46%)
Hyperplasia, lymphoid	4 (8%)	5 (10%)	1 (2%)	4 (8%)
Hyperplasia, plasma cell	1 (2%)	1 (2%)	1 (2%)	
Necrosis			1 (2%)	
Pigmentation		1 (2%)		1 (2%)
Spleen	(50)	(50)	(50)	(50)
Hematopoietic cell proliferation	13 (26%)	14 (28%)	9 (18%)	8 (16%)
Hyperplasia, reticulum cell	1 (2%)			
Necrosis	1 (2%)			
Lymphoid follicle, atrophy	1 (2%)	1 (2%)	1 (2%)	3 (6%)
Lymphoid follicle, hyperplasia	1 (2%)	1 (2%)	1 (2%)	3 (6%)
Red pulp, atrophy	1 (2%)		1 (2%)	1 (2%)
Thymus	(42)	(45)	(47)	(45)
Cyst	10 (24%)	12 (27%)	15 (32%)	9 (20%)
Depletion cellular	4 (10%)	4 (9%)	4 (9%)	5 (11%)
Ectopic parathyroid gland				1 (2%)
Hyperplasia, lymphoid				2 (4%)
Integumentary System				
Skin	(50)	(50)	(50)	(50)
Acanthosis	2 (4%)	1 (2%)		2 (4%)
Granuloma		1 (2%)		
Hemorrhage		1 (2%)		
Inflammation, chronic			2 (4%)	1 (2%)
Subcutaneous tissue, edema	1 (2%)	1 (2%)	1 (2%)	2 (4%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Dysplasia				1 (2%)
Hyperostosis			2 (4%)	
Skeletal muscle	(50)	(50)	(50)	(50)
Inflammation, chronic		1 (2%)	2 (4%)	2 (4%)
Sarcolemmal nuclei, hyperplasia	1 (2%)	2 (4%)	1 (2%)	2 (4%)
Sarcoplasm, atrophy	1 (2%)	1 (2%)		
Nervous System				
Brain	(50)	(50)	(50)	(50)
Compression			1 (2%)	
Hydrocephalus			1 (2%)	
Vacuolization cytoplasmic			1 (2%)	1 (2%)
Glial cell, proliferation			1 (2%)	
Thalamus, mineralization	36 (72%)	41 (82%)	44 (88%)	37 (74%)

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Feed Study of Benzyl Acetate
(continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Angiectasis		1 (2%)		
Congestion				1 (2%)
Hemorrhage		1 (2%)	2 (4%)	4 (8%)
Hyperplasia, lymphoid	5 (10%)	2 (4%)		2 (4%)
Infiltration cellular, histiocyte	7 (14%)	8 (16%)	8 (16%)	3 (6%)
Inflammation, suppurative		1 (2%)		
Thrombosis	1 (2%)			
Alveolar epithelium, hyperplasia	1 (2%)	3 (6%)	6 (12%)	
Nose	(50)	(50)	(50)	(50)
Cyst	1 (2%)			
Developmental malformation				1 (2%)
Exudate	8 (16%)	18 (36%)	38 (76%)	26 (52%)
Glands, hyperplasia, cystic	22 (44%)	43 (86%)	47 (94%)	50 (100%)
Mucosa, atrophy	30 (60%)	49 (98%)	50 (100%)	50 (100%)
Mucosa, degeneration	31 (62%)	50 (100%)	50 (100%)	50 (100%)
Mucosa, metaplasia, squamous	1 (2%)			
Mucosa, pigmentation		45 (90%)	50 (100%)	50 (100%)
Special Senses System				
Eye			(3)	(1)
Inflammation, chronic			3 (100%)	1 (100%)
Cornea, hyperplasia			3 (100%)	1 (100%)
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Casts protein	10 (20%)	15 (30%)	13 (26%)	7 (14%)
Cyst	21 (42%)	16 (32%)	15 (30%)	16 (32%)
Glomerulosclerosis	1 (2%)	4 (8%)	1 (2%)	2 (4%)
Hyperplasia, lymphoid	18 (36%)	15 (30%)	14 (28%)	11 (22%)
Inflammation, suppurative	2 (4%)			
Mineralization	23 (46%)	42 (84%)	41 (82%)	31 (62%)
Renal tubule, atrophy	6 (12%)	3 (6%)	5 (10%)	2 (4%)
Renal tubule, dilatation	1 (2%)		1 (2%)	2 (4%)
Renal tubule, hyperplasia	2 (4%)	1 (2%)		1 (2%)
Renal tubule, pigmentation				1 (2%)
Renal tubule, regeneration	49 (98%)	46 (92%)	43 (86%)	46 (92%)
Transitional epithelium, hyperplasia	1 (2%)	1 (2%)		
Urinary bladder	(50)	(50)	(50)	(50)
Dilatation		1 (2%)		1 (2%)
Hyperplasia, lymphoid	1 (2%)	2 (4%)	2 (4%)	
Inflammation, chronic	1 (2%)			
Inflammation, suppurative	2 (4%)			
Mucosa, hyperplasia	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 FEED STUDY OF BENZYL ACETATE

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Feed Study of Benzyl Acetate[a]

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	10	10
Early deaths				
Moribund	12	16	7	3
Natural deaths	9	6	6	3
Survivors				
Terminal sacrifice	29	28	37	44
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Liver	(10)	(10)	(10)	(10)
Hepatocellular adenoma	1 (10%)		1 (10%)	
Cardiovascular System				
None				
Endocrine System				
Thyroid gland	(10)	(10)	(10)	(10)
Follicular cell, adenoma	1 (10%)			
General Body System				
None				
Genital System				
Ovary	(10)	(10)	(10)	(10)
Cystadenoma	1 (10%)			1 (10%)
Uterus	(10)	(10)	(10)	(10)
Sarcoma stromal			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 Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
15-Month Interim Evaluation (continued)				
Respiratory System				
Lung	(10)	(10)	(10)	(10)
Alveolar/bronchiolar adenoma				1 (10%)
Special Senses System				
None				
Urinary System				
None				
2-Year Study				
Alimentary System				
Intestine small, duodenum	(49)	(48)	(49)	(49)
Carcinoma		1 (2%)		
Intestine small, ileum	(48)	(48)	(49)	(49)
Intestine small, jejunum	(48)	(50)	(49)	(49)
Carcinoma	1 (2%)			
Liver	(50)	(50)	(50)	(50)
Fibrous histiocytoma			1 (2%)	
Hepatocellular carcinoma	8 (16%)	8 (16%)	5 (10%)	6 (12%)
Hepatocellular carcinoma, two, multiple	1 (2%)		1 (2%)	1 (2%)
Hepatocellular carcinoma, five, multiple	1 (2%)			
Hepatocellular adenoma	5 (10%)	8 (16%)	7 (14%)	7 (14%)
Hepatocellular adenoma, two, multiple	1 (2%)	2 (4%)		1 (2%)
Histiocytic sarcoma				1 (2%)
Histiocytic sarcoma, metastatic, uterus		1 (2%)		
Sarcoma stromal, metastatic, uterus		1 (2%)		
Mesentery	(9)	(7)	(7)	(2)
Carcinoma, metastatic, pancreas	1 (11%)			
Carcinoma, metastatic, intestine small	1 (11%)			
Fibrous histiocytoma		1 (14%)		
Fibrous histiocytoma, metastatic, liver			1 (14%)	
Hemangioma	1 (11%)			
Pancreas	(50)	(50)	(50)	(49)
Carcinoma	1 (2%)			
Fibrous histiocytoma		1 (2%)		
Pharynx			(1)	
Squamous cell carcinoma			1 (100%)	
Salivary glands	(50)	(50)	(50)	(50)
Stomach, forestomach	(49)	(50)	(50)	(50)
Squamous cell papilloma		1 (2%)	2 (4%)	1 (2%)
Stomach, glandular	(50)	(50)	(50)	(50)
Carcinoma, metastatic, pancreas	1 (2%)			
Tongue	(50)	(50)	(50)	(50)
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Carcinoma, metastatic, pancreas	1 (2%)			
Hepatocellular carcinoma, metastatic, liver	1 (2%)			

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(50)
Capsule, adenoma		2 (4%)		
Capsule, carcinoma			1 (2%)	
Adrenal gland, medulla	(50)	(50)	(50)	(50)
Pheochromocytoma benign	1 (2%)	1 (2%)	1 (2%)	
Islets, pancreatic	(50)	(50)	(50)	(49)
Adenoma	3 (6%)	2 (4%)	2 (4%)	
Pituitary gland	(48)	(46)	(50)	(49)
Pars distalis, adenoma	9 (19%)	11 (24%)	4 (8%)	5 (10%)
Pars intermedia, adenoma			1 (2%)	1 (2%)
Thyroid gland	(50)	(50)	(50)	(50)
C-cell, adenoma			1 (2%)	
Follicular cell, adenoma	1 (2%)			1 (2%)
General Body System				
Tissue NOS	(1)	(1)		(1)
Genital System				
Ovary	(49)	(48)	(49)	(49)
Choriocarcinoma		1 (2%)		
Cystadenoma			1 (2%)	
Granulosa cell tumor benign	1 (2%)			
Histiocytic sarcoma, metastatic, uterus		1 (2%)		
Teratoma malignant			1 (2%)	
Uterus	(50)	(49)	(50)	(50)
Adenoma			1 (2%)	
Carcinoma *in situ*		1 (2%)		
Hemangioma		1 (2%)		
Hemangiosarcoma			1 (2%)	
Histiocytic sarcoma		1 (2%)		
Leiomyosarcoma		1 (2%)		
Polyp stromal	8 (16%)	2 (4%)	1 (2%)	6 (12%)
Sarcoma stromal		1 (2%)	1 (2%)	
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Fibrosarcoma, metastatic, skin		1 (2%)		
Hemangiosarcoma			2 (4%)	1 (2%)
Lymph node	(50)	(50)	(50)	(49)
Axillary, hepatocellular carcinoma, metastatic, liver	1 (2%)			
Mediastinal, carcinoma, metastatic, pancreas	1 (2%)			
Mediastinal, fibrous histiocytoma		1 (2%)		
Mediastinal, hepatocellular carcinoma, metastatic, liver	1 (2%)			
Pancreatic, histiocytic sarcoma, metastatic, uterus		1 (2%)		
Renal, fibrous histiocytoma		1 (2%)		

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Hematopoietic System (continued)				
Lymph node, mandibular	(50)	(50)	(50)	(49)
Histiocytic sarcoma, metastatic, uterus		1 (2%)		
Lymph node, mesenteric	(50)	(46)	(49)	(48)
Carcinoma, metastatic, pancreas	1 (2%)			
Fibrous histiocytoma		1 (2%)		
Histiocytic sarcoma, metastatic, uterus		1 (2%)		
Spleen	(50)	(50)	(50)	(50)
Hemangiosarcoma			1 (2%)	
Thymus	(45)	(47)	(46)	(49)
Histiocytic sarcoma, metastatic, liver				1 (2%)
Thymoma benign	1 (2%)			
Integumentary System				
Mammary gland	(50)	(49)	(50)	(50)
Skin	(50)	(50)	(49)	(50)
Basal cell adenoma				1 (2%)
Subcutaneous tissue, fibrosarcoma		2 (4%)	3 (6%)	
Subcutaneous tissue, hemangioma	1 (2%)			
Subcutaneous tissue, hemangiosarcoma			1 (2%)	
Subcutaneous tissue, schwannoma benign				1 (2%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma		1 (2%)		
Skeletal muscle	(50)	(50)	(50)	(50)
Carcinoma, metastatic, pancreas	1 (2%)			
Fibrosarcoma				1 (2%)
Fibrosarcoma, metastatic, skin			2 (4%)	
Hemangiosarcoma			1 (2%)	
Nervous System				
Brain	(50)	(50)	(50)	(50)
Histiocytic sarcoma, metastatic, liver				1 (2%)
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Alveolar/bronchiolar adenoma	1 (2%)	5 (10%)		4 (8%)
Alveolar/bronchiolar adenoma, two, multiple			1 (2%)	
Alveolar/bronchiolar carcinoma			1 (2%)	
Carcinoma, metastatic, pancreas	1 (2%)			
Hepatocellular carcinoma, metastatic, liver	1 (2%)	1 (2%)		1 (2%)
Histiocytic sarcoma, metastatic, liver				1 (2%)
Histiocytic sarcoma, metastatic, uterus		1 (2%)		
Osteosarcoma, metastatic, bone		1 (2%)		
Nose	(50)	(50)	(50)	(50)

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Special Senses System				
Harderian gland	(3)	(4)	(2)	(1)
Adenoma	3 (100%)	4 (100%)	2 (100%)	1 (100%)
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Fibroma			1 (2%)	
Hepatocellular carcinoma, metastatic, liver	1 (2%)			
Renal tubule, adenoma	1 (2%)			
Renal tubule, carcinoma		1 (2%)		
Urinary bladder	(50)	(49)	(50)	(50)
Histiocytic sarcoma, metastatic, uterus		1 (2%)		
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Histiocytic sarcoma		1 (2%)		1 (2%)
Lymphoma malignant histiocytic			1 (2%)	
Lymphoma malignant lymphocytic	1 (2%)	1 (2%)	1 (2%)	2 (4%)
Lymphoma malignant mixed	7 (14%)	6 (12%)	6 (12%)	7 (14%)
Lymphoma malignant undifferentiated cell			1 (2%)	
Neoplasm Summary				
Total animals with primary neoplasms[c]				
15-Month interim evaluation	3		2	2
2-Year study	35	40	33	33
Total primary neoplasms				
15-Month interim evaluation	3		2	2
2-Year study	57	69	55	48
Total animals with benign neoplasms				
15-Month interim evaluation	3		1	2
2-Year study	29	29	16	22
Total benign neoplasms				
15-Month interim evaluation	3		1	2
2-Year study	37	39	25	29
Total animals with malignant neoplasms				
15-Month interim evaluation			1	
2-Year study	17	24	24	16
Total malignant neoplasms				
15-Month interim evaluation			1	
2-Year study	20	30	30	19
Total animals with metastatic neoplasms				
2-Year study	3	5	3	2
Total metastatic neoplasms				
2-Year study	13	11	3	4

[a] Number of animals examined microscopically at site and number of animals with lesion
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplams except metastatic neoplasms

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 0 ppm

Number of Days on Study	4 9 4	5 2 0	5 3 3	5 3 3	5 4 1	5 4 4	5 8 4	5 9 7	6 0 0	6 0 3	6 1 4	6 3 3	6 3 9	6 5 6	6 5 6	6 5 9	6 7 5	6 9 1	6 9 7	7 2 2	7 2 5	7 2 9	7 2 9	7 2 9
Carcass ID Number	2 7 4	2 8 2	2 7 3	2 9 1	2 5 4	2 6 4	2 7 1	3 0 0	2 7 0	2 6 5	2 8 3	2 7 9	2 5 0	2 4 2	2 4 3	2 6 3	2 9 7	2 5 6	2 8 5	2 4 4	2 8 7	2 4 1	2 4 5	2 4 6	2 4 7
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	A	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+
Carcinoma															X										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma		X							X			X							X					
Hepatocellular carcinoma, two, multiple																				X					
Hepatocellular carcinoma, five, multiple																	X								
Hepatocellular adenoma														X							X	X	X		
Hepatocellular adenoma, two, multiple																									
Mesentery	+							+		+	+			+	+				+		+				
Carcinoma, metastatic, pancreas																			X						
Carcinoma, metastatic, intestine small															X										
Hemangioma																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																			X						
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pancreas																			X						
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel										+															
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pancreas																			X						
Hepatocellular carcinoma, metastatic, liver												X													
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																									

+: 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 Feed Study of Benzyl Acetate: 0 ppm
(continued)

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	24 8	25 1	25 2	25 3	25 5	25 7	25 9	26 0	26 1	26 6	26 7	26 8	27 6	27 7	28 0	28 1	28 8	28 6	28 8	28 9	29 0	29 2	29 3	29 4	29 6	29 8	Total Tissues/ Tumors
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma																											1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma									X	X				X											X		8
Hepatocellular carcinoma, two, multiple																											1
Hepatocellular carcinoma, five, multiple																											1
Hepatocellular adenoma										X																	5
Hepatocellular adenoma, two, multiple																									X		1
Mesentery			+																								9
Carcinoma, metastatic, pancreas																											1
Carcinoma, metastatic, intestine small																											1
Hemangioma			X																								1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																											1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, pancreas																											1
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																											
Blood vessel														+													2
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, pancreas																											1
Hepatocellular carcinoma, metastatic, liver																											1
Endocrine System																											
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign									X																		1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 0 ppm
(continued)

Number of Days on Study	4 9 4	5 2 0	5 3 3	5 3 3	5 4 1	5 4 4	5 8 4	5 9 7	6 0 0	6 0 3	6 1 4	6 3 3	6 3 9	6 5 6	6 5 6	6 5 9	6 7 5	6 9 1	6 9 7	7 2 2	7 2 5	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	2 7 4	2 8 2	2 7 3	2 9 1	2 5 4	2 6 4	2 7 1	3 0 0	2 7 0	2 6 5	2 8 3	2 7 9	2 5 0	2 4 2	2 4 3	2 6 3	2 9 7	2 5 6	2 8 5	2 4 4	2 8 7	2 4 1	2 4 5	2 4 6	2 4 7
Endocrine System (continued)																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma				X																				X	
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Pituitary gland	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																				X	X				
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									
General Body System																									
Tissue NOS									+																
Genital System																									
Ovary	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor benign																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal														X					X						X
Vagina									+																
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Axillary, hepatocellular carcinoma, metastatic, liver												X													
Mediastinal, carcinoma, metastatic, pancreas																			X						
Mediastinal, hepatocellular carcinoma, metastatic, liver												X													
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pancreas																			X						
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	M	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	M	M	+	+	+	+	+
Thymoma benign																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, hemangioma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pancreas																			X						
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 0 ppm
(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 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	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	2 4 8	2 5 1	2 5 2	2 5 3	2 5 5	2 5 7	2 5 9	2 6 0	2 6 1	2 6 7	2 6 8	2 7 6	2 7 7	2 8 0	2 8 1	2 8 4	2 8 6	2 8 8	2 8 9	2 9 0	2 9 2	2 9 3	2 9 4	2 9 6	2 9 8	Total Tissues/ Tumors
Endocrine System (continued)																										
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma														X												3
Parathyroid gland	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma				X	X	X			X	X		X									X					9
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma																				X						1
General Body System																										
Tissue NOS																										1
Genital System																										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Granulosa cell tumor benign																X										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal	X						X							X	X				X							8
Vagina																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Axillary, hepatocellular carcinoma, metastatic, liver																										1
Mediastinal, carcinoma, metastatic, pancreas																										1
Mediastinal, hepatocellular carcinoma, metastatic, liver																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, pancreas																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Thymoma benign																						X				1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, hemangioma											X															1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, pancreas																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 0 ppm
(continued)

Number of Days on Study	4 9 4	5 2 0	5 3 3	5 3 3	5 4 1	5 4 4	5 8 4	5 9 7	6 0 0	6 0 3	6 1 4	6 3 3	6 3 9	6 5 6	6 5 6	6 5 9	6 7 5	6 9 1	6 9 7	7 2 2	7 2 5	7 2 9	7 2 9	7 2 9
Carcass ID Number	2 7 4	2 8 2	2 7 3	2 9 1	2 5 4	2 6 4	2 7 1	3 0 0	2 7 0	2 6 5	2 8 3	2 7 9	2 5 0	2 4 2	2 4 3	2 6 3	2 9 7	2 5 6	2 8 5	2 4 4	2 8 7	2 4 1	2 4 5	2 4 6	2 4 7
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Carcinoma, metastatic, pancreas																			X						
Hepatocellular carcinoma, metastatic, liver												X													
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																									
Harderian gland									+					+									+		
Adenoma									X					X									X		
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic, liver												X													
Renal tubule, adenoma		X																							
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic	X																								
Lymphoma malignant mixed						X															X			X	

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 0 ppm
(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 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	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	2 4 8	2 5 1	2 5 2	2 5 3	2 5 5	2 5 7	2 5 9	2 6 0	2 6 1	2 6 7	2 6 8	2 6 6	2 7 7	2 7 6	2 8 0	2 8 1	2 8 4	2 8 6	2 8 8	2 8 9	2 9 0	2 9 2	2 9 3	2 9 4	2 9 6	2 9 8	Total Tissues/ Tumors
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma											X															1
Carcinoma, metastatic, pancreas																										1
Hepatocellular carcinoma, metastatic, liver																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye											M															
Harderian gland																										3
Adenoma																										3
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic, liver																										1
Renal tubule, adenoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed	X							X							X	X										7

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 330 ppm

Number of Days on Study	0 1 7	4 2 8	5 0 7	5 2 1	5 4 4	5 4 4	6 2 8	6 3 8	6 3 8	6 4 7	6 5 6	6 5 9	6 5 9	6 7 8	6 8 1	6 9 1	7 0 1	7 0 1	7 1 4	7 1 8	7 2 3	7 2 3	7 3 2	7 3 2	7 3 2
Carcass ID Number	3 1 8	3 1 3	3 1 0	3 3 2	3 1 7	3 6 0	3 3 6	3 4 9	3 5 5	3 1 1	3 2 9	3 0 3	3 3 9	3 0 5	3 4 2	3 2 7	3 5 7	3 5 2	3 5 1	3 2 2	3 2 6	3 4 4	3 0 2	3 0 4	3 0 6
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	A	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+
Carcinoma							X																		
Intestine small, ileum	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma			X				X	X					X	X											
Hepatocellular adenoma			X			X					X												X	X	
Hepatocellular adenoma, two, multiple													X												
Histiocytic sarcoma, metastatic, uterus															X										
Sarcoma stromal, metastatic, uterus					X																				
Mesentery		+	+			+			+																
Fibrous histiocytoma									X																
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma									X																
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth																					+				
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, adenoma																					X	X			
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	M	+	+	+	+	+	+	+
Pars distalis, adenoma				X					X															X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																									
Tissue NOS															+										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 330 ppm
(continued)

Number of Days on Study	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	3 0 7	3 0 9	3 1 2	3 1 4	3 1 5	3 1 6	3 1 9	3 2 0	3 2 3	3 2 5	3 3 0	3 3 1	3 3 3	3 3 5	3 3 7	3 4 1	3 4 3	3 4 5	3 4 6	3 4 7	3 4 8	3 5 4	3 5 6	3 5 8	3 5 9	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma	X													X											X	8
Hepatocellular adenoma																X		X			X					8
Hepatocellular adenoma, two, multiple																									X	2
Histiocytic sarcoma, metastatic, uterus																										1
Sarcoma stromal, metastatic, uterus																										1
Mesentery		+					+		+																	7
Fibrous histiocytoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma														X												1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, adenoma																										2
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign																	X									1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma												X			X											2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	46
Pars distalis, adenoma				X	X		X			X										X			X	X	X	11
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
General Body System																										
Tissue NOS																										1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 330 ppm
(continued)

Number of Days on Study	0 1 7	4 2 8	5 0 7	5 2 1	5 4 4	5 4 4	6 2 8	6 3 8	6 3 8	6 4 7	6 5 6	6 5 9	6 5 9	6 7 8	6 8 1	6 9 1	7 0 1	7 0 6	7 1 4	7 1 8	7 2 3	7 2 3	7 3 2	7 3 2	7 3 2
Carcass ID Number	3 1 8	3 1 3	3 1 0	3 3 2	3 1 7	3 6 0	3 3 6	3 4 9	3 5 5	3 1 1	3 2 9	3 0 3	3 3 9	3 0 5	3 4 2	3 2 7	3 5 7	3 5 2	3 5 1	3 2 2	3 2 6	3 4 4	3 0 2	3 0 4	3 0 6
Genital System																									
Clitoral gland																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Choriocarcinoma	X																								
Histiocytic sarcoma, metastatic, uterus															X										
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Carcinoma *in situ*																									
Hemangioma																									
Histiocytic sarcoma															X										
Leiomyosarcoma																						X			
Polyp stromal																									
Sarcoma stromal					X																				
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma, metastatic, skin											X														
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, fibrous histiocytoma									X																
Pancreatic, histiocytic sarcoma, metastatic, uterus															X										
Renal, fibrous histiocytoma									X																
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, uterus															X										
Lymph node, mesenteric	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	M	+	+	+	+	+	+
Fibrous histiocytoma									X																
Histiocytic sarcoma, metastatic, uterus															X										
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma											X														
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma																			X						
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma							X										X						X		
Hepatocellular carcinoma, metastatic, liver																									
Histiocytic sarcoma, metastatic, uterus															X										
Osteosarcoma, metastatic, bone																			X						
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 330 ppm
(continued)

Number of Days on Study	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	3 0 7	3 0 9	3 1 2	3 1 4	3 1 5	3 1 6	3 1 9	3 2 0	3 2 3	3 2 5	3 3 0	3 3 1	3 3 3	3 3 5	3 3 7	3 4 1	3 4 3	3 4 5	3 4 6	3 4 7	3 4 8	3 5 4	3 5 6	3 5 8	3 5 9	Total Tissues/ Tumors
Genital System																										
Clitoral gland																									+	1
Ovary	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Choriocarcinoma																										1
Histiocytic sarcoma, metastatic, uterus																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma *in situ*																	X									1
Hemangioma																								X		1
Histiocytic sarcoma																										1
Leiomyosarcoma																										1
Polyp stromal							X							X												2
Sarcoma stromal																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma, metastatic, skin																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mediastinal, fibrous histiocytoma																										1
Pancreatic, histiocytic sarcoma, metastatic, uterus																										1
Renal, fibrous histiocytoma																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma, metastatic, uterus																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Fibrous histiocytoma																										1
Histiocytic sarcoma, metastatic, uterus																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	47
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrosarcoma	X																									2
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma			X																		X					5
Hepatocellular carcinoma, metastatic, liver														X												1
Histiocytic sarcoma, metastatic, uterus																										1
Osteosarcoma, metastatic, bone																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 330 ppm
(continued)

Number of Days on Study	0 1 7	4 2 8	5 0 7	5 2 1	5 4 4	5 4 4	6 2 8	6 3 8	6 3 8	6 4 7	6 5 6	6 5 9	6 5 9	6 7 8	6 8 1	6 9 1	7 0 1	7 0 6	7 1 4	7 1 8	7 2 3	7 2 3	7 3 2	7 3 2	7 3 2
Carcass ID Number	3 1 8	3 1 3	3 1 0	3 3 2	3 1 7	3 6 0	3 3 6	3 4 9	3 5 5	3 1 1	3 2 9	3 0 3	3 3 9	3 0 5	3 4 2	3 2 7	3 5 7	3 5 2	3 5 1	3 2 2	3 2 6	3 4 4	3 0 2	3 0 4	3 0 6
Special Senses System																									
Harderian gland																					+	+			
Adenoma																					X	X			
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, carcinoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, uterus															X										
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma															X										
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed																X				X					

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 330 ppm
(continued)

Number of Days on Study	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	3 0 7	3 0 9	3 1 2	3 1 4	3 1 5	3 1 6	3 1 9	3 2 0	3 2 3	3 2 5	3 3 0	3 3 1	3 3 3	3 3 5	3 3 7	3 4 1	3 4 3	3 4 5	3 4 6	3 4 7	3 4 8	3 5 4	3 5 6	3 5 8	3 5 9	Total Tissues/ Tumors
Special Senses System																										
Harderian gland					+																		+			4
Adenoma					X																		X			4
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Renal tubule, carcinoma						X																				1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma, metastatic, uterus																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymphoma malignant lymphocytic									X																	1
Lymphoma malignant mixed			X				X						X			X										6

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 1,000 ppm

Number of Days on Study	1 1 4	5 6 8	6 4 9	6 8 3	7 0 2	7 0 8	7 1 2	7 1 6	7 2 0	7 2 2	7 2 2	7 2 3	7 2 3	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	7 3 1	7 3 1
Carcass ID Number	4 0 0 6	4 0 8	3 6 3	3 9 6	4 0 4	4 0 9	3 7 2	3 8 9	4 0 0	3 7 6	4 0 7	3 7 0	4 1 1	3 6 1	3 6 4	3 6 5	3 6 6	3 6 7	3 6 9	3 7 1	3 7 3	3 7 5	3 7 7	3 7 8	3 7 9
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	M	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Hepatocellular carcinoma		X							X														X		X
Hepatocellular carcinoma, two, multiple						X																			
Hepatocellular adenoma										X								X			X	X			
Mesentery			+	+					+			+													
Fibrous histiocytoma, metastatic, liver																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pharynx																									
Squamous cell carcinoma																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																						X	X		
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel						+																			
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, carcinoma					X																				
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																						X			
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma					X																				
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																							X	X	
Pars intermedia, adenoma																X									
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																							X		
General Body System																									
None																									

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 1,000 ppm
(continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	4 0 3	4 0 5	4 1 2	4 1 4	3 8 0	3 8 2	3 8 3	3 8 4	3 8 6	3 8 8	3 9 0	3 9 1	3 9 2	3 9 4	3 9 5	3 9 7	3 9 8	3 9 9	4 0 1	4 0 2	4 1 5	4 1 7	4 1 8	4 1 9	4 2 0	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma									X																	1
Hepatocellular carcinoma															X											5
Hepatocellular carcinoma, two, multiple																										1
Hepatocellular adenoma								X		X															X	7
Mesentery				+			+		+																	7
Fibrous histiocytoma, metastatic, liver									X																	1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pharynx												+														1
Squamous cell carcinoma												X														1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																										2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Blood vessel			+																							2
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, carcinoma																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma								X																		2
Parathyroid gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma								X															X			4
Pars intermedia, adenoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma																										1
General Body System																										
None																										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 1,000 ppm
(continued)

Number of Days on Study	1 1 4	5 6 8	6 4 9	6 8 3	7 0 2	7 0 8	7 1 2	7 1 6	7 2 0	7 2 2	7 2 2	7 2 3	7 2 3	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	7 3 1	7 3 1
Carcass ID Number	4 0 6	4 0 8	3 6 3	3 9 6	4 0 4	4 0 9	3 7 2	3 8 9	4 0 0	3 7 6	4 0 7	3 7 0	4 1 1	3 6 1	3 6 4	3 6 5	3 6 6	3 6 7	3 6 9	3 7 1	3 7 3	3 7 5	3 7 7	3 7 8	3 7 9
Genital System																									
Clitoral gland																									
Ovary	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma																									
Teratoma malignant	X																								
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma									X																
Hemangiosarcoma																									
Polyp stromal															X										
Sarcoma stromal																									X
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																	X								
Thymus	+	+	+	+	+	+	+	M	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma							X				X		X												
Subcutaneous tissue, hemangiosarcoma										X															
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma, metastatic, skin											X		X												
Hemangiosarcoma										X															
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma, two, multiple												X													
Alveolar/bronchiolar carcinoma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear								+																	
Harderian gland												+											+		
Adenoma												X											X		

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 1,000 ppm
(continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	4 0 3	4 0 5	4 1 2	4 1 4	3 8 0	3 8 2	3 8 3	3 8 4	3 8 6	3 8 8	3 9 0	3 9 1	3 9 2	3 9 4	3 9 5	3 9 7	3 9 8	3 9 9	4 0 1	4 0 2	4 1 5	4 1 7	4 1 8	4 1 9	4 2 0	Total Tissues/ Tumors
Genital System																										
Clitoral gland										+																1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cystadenoma								X																		1
Teratoma malignant																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Hemangiosarcoma												X														1
Polyp stromal																										1
Sarcoma stromal																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma										X		X														2
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	46
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Subcutaneous tissue, fibrosarcoma																										3
Subcutaneous tissue, hemangiosarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma, metastatic, skin																										2
Hemangiosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma, two, multiple																										1
Alveolar/bronchiolar carcinoma							X																			1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																										1
Harderian gland																										2
Adenoma																										2

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 1,000 ppm
(continued)

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

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 1,000 ppm
(continued)

Number of Days on Study	731	731	731	731	732	732	732	732	732	732	732	732	732	732	732	732	732	732	732	732	732	732	732	732	
Carcass ID Number	40313	40055	41212	41444	38800	38822	38833	38844	38866	38888	39900	39911	39922	39944	39955	39977	39988	39999	40101	40122	41155	41177	41188	41199	41220	Total Tissues/ Tumors
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroma					X																					1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic							X																			1
Lymphoma malignant mixed											X				X	X		X			X				X	6
Lymphoma malignant undifferentiated cell type																										1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm

Number of Days on Study	3 0 2	5 4 4	5 5 2	5 7 4	5 9 0	5 9 4	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 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0
Carcass ID Number	4 4 7	4 2 6	4 4 1	4 6 0	4 4 0	4 2 1	4 2 2	4 2 4	4 2 5	4 2 7	4 2 9	4 3 0	4 3 1	4 3 2	4 3 4	4 3 5	4 3 6	4 3 7	4 3 8	4 3 9	4 4 2	4 4 3	4 4 4	4 4 6	4 4 8
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma														X						X		X			
Hepatocellular carcinoma, two, multiple																									
Hepatocellular adenoma		X				X	X																		X
Hepatocellular adenoma, two, multiple																				X					
Histiocytic sarcoma				X																					
Mesentery						+						+													
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel		+	+																+				+		
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	M	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma		X																							
Pars intermedia, adenoma																									
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									
General Body System																									
Tissue NOS	+																								
Genital System																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal																X					X		X		X

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm
(continued)

Number of Days on Study	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 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 0	7 3 0	7 3 0	
Carcass ID Number	4 5 0	4 5 1	4 5 3	4 5 4	4 5 5	4 5 7	4 5 8	4 5 9	4 6 1	4 6 3	4 6 4	4 6 5	4 6 6	4 6 7	4 6 8	4 7 0	4 7 1	4 7 2	4 7 3	4 7 4	4 7 5	4 7 7	4 7 8	4 7 9	4 8 0	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma							X			X												X				6
Hepatocellular carcinoma, two, multiple																				X						1
Hepatocellular adenoma				X				X						X												7
Hepatocellular adenoma, two, multiple																										1
Histiocytic sarcoma																										1
Mesentery																										2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	49
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																						X				1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Blood vessel							+																			5
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	49
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	46
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma										X					X	X		X								5
Pars intermedia, adenoma								X																		1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma																			X							1
General Body System																										
Tissue NOS																										1
Genital System																										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal														X										X		6

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm
(continued)

Number of Days on Study	3 0 2	5 4 4	5 5 2	5 7 4	5 9 0	5 9 4	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 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0
Carcass ID Number	4 4 7	4 2 6	4 4 1	4 6 0	4 4 0	4 2 1	4 2 2	4 2 4	4 2 5	4 2 7	4 2 9	4 3 0	4 3 1	4 3 2	4 3 4	4 3 5	4 3 6	4 3 7	4 3 8	4 3 9	4 4 2	4 4 3	4 4 4	4 4 6	4 4 8
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma														X											
Lymph node	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver				X																					
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell adenoma																		X							
Subcutaneous tissue, schwannoma benign																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma					X																				
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver				X																					
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma			X																				X		
Hepatocellular carcinoma, metastatic, liver																									
Histiocytic sarcoma, metastatic, liver				X																					
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																									
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																					
Lymphoma malignant lymphocytic	X												X												
Lymphoma malignant mixed														X			X	X					X		

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Feed Study of Benzyl Acetate: 3,000 ppm
(continued)

Number of Days on Study	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 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 0	7 3 0	7 3 0	
Carcass ID Number	4 5 0	4 5 1	4 5 3	4 5 4	4 5 5	4 5 7	4 5 8	4 5 9	4 6 1	4 6 3	4 6 4	4 6 5	4 6 6	4 6 7	4 6 8	4 7 0	4 7 1	4 7 2	4 7 3	4 7 4	4 7 5	4 7 7	4 7 8	4 7 9	4 8 0	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma, metastatic, liver																										1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Basal cell adenoma																										1
Subcutaneous tissue, schwannoma benign																	X									1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma, metastatic, liver																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma	X			X																						4
Hepatocellular carcinoma, metastatic, liver																						X				1
Histiocytic sarcoma, metastatic, liver																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																	+									1
Harderian gland																	+									1
Adenoma																	X									1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymphoma malignant lymphocytic																										2
Lymphoma malignant mixed									X	X											X					7

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Feed Study of Benzyl Acetate

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Harderian Gland: Adenoma				
Overall rate[a]	3/60 (5%)	4/60 (7%)	2/60 (3%)	1/60 (2%)
Adjusted rate[b]	8.3%	13.3%	5.2%	2.3%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate[c]	1/29 (3%)	2/28 (7%)	1/37 (3%)	1/44 (2%)
First incidence (days)	600	723	723	729 (T)
Life table test[d]	P=0.085N	P=0.501	P=0.400N	P=0.220N
Logistic regression test[d]	P=0.129N	P=0.514	P=0.463N	P=0.287N
Cochran-Armitage test[d]	P=0.165N			
Fisher exact test[d]		P=0.500	P=0.500N	P=0.309N
Liver: Hepatocellular Adenoma				
Overall rate	7/60 (12%)	10/60 (17%)	8/60 (13%)	8/60 (13%)
Adjusted rate	20.8%	28.5%	19.8%	17.3%
Interim evaluation	1/10 (10%)	0/10 (0%)	1/10 (10%)	0/10 (0%)
Terminal rate	5/29 (17%)	6/28 (21%)	6/37 (16%)	6/44 (14%)
First incidence (days)	456 (I)	507	458 (I)	544
Life table test	P=0.235N	P=0.297	P=0.545N	P=0.455N
Logistic regression test	P=0.486N	P=0.304	P=0.566	P=0.553
Cochran-Armitage test	P=0.537N			
Fisher exact test		P=0.301	P=0.500	P=0.500
Liver: Hepatocellular Carcinoma				
Overall rate	10/60 (17%)	8/60 (13%)	6/60 (10%)	7/60 (12%)
Adjusted rate	27.0%	20.9%	14.1%	15.9%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	4/29 (14%)	3/28 (11%)	3/37 (8%)	7/44 (16%)
First incidence (days)	520	507	568	729 (T)
Life table test	P=0.121N	P=0.387N	P=0.106N	P=0.107N
Logistic regression test	P=0.262N	P=0.396N	P=0.166N	P=0.220N
Cochran-Armitage test	P=0.315N			
Fisher exact test		P=0.399N	P=0.211N	P=0.301N
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	15/60 (25%)	15/60 (25%)	14/60 (23%)	14/60 (23%)
Adjusted rate	38.5%	39.6%	32.3%	30.3%
Interim evaluation	1/10 (10%)	0/10 (0%)	1/10 (10%)	0/10 (0%)
Terminal rate	7/29 (24%)	8/28 (29%)	9/37 (24%)	12/44 (27%)
First incidence (days)	456 (I)	507	458 (I)	544
Life table test	P=0.120N	P=0.567N	P=0.260N	P=0.171N
Logistic regression test	P=0.378N	P=0.579N	P=0.421N	P=0.412N
Cochran-Armitage test	P=0.457N			
Fisher exact test		P=0.583N	P=0.500N	P=0.500N
Lung: Alveolar/bronchiolar Adenoma				
Overall rate	1/60 (2%)	5/60 (8%)	1/60 (2%)	5/60 (8%)
Adjusted rate	3.4%	15.3%	2.6%	10.3%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	1/10 (10%)
Terminal rate	1/29 (3%)	3/28 (11%)	0/37 (0%)	3/44 (7%)
First incidence (days)	729 (T)	628	723	456 (I)
Life table test	P=0.330	P=0.109	P=0.703N	P=0.185
Logistic regression test	P=0.193	P=0.111	P=0.695N	P=0.104
Cochran-Armitage test	P=0.176			
Fisher exact test		P=0.103	P=0.752N	P=0.103

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	1/60 (2%)	5/60 (8%)	2/60 (3%)	5/60 (8%)
Adjusted rate	3.4%	15.3%	5.2%	10.3%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	1/10 (10%)
Terminal rate	1/29 (3%)	3/28 (11%)	1/37 (3%)	3/44 (7%)
First incidence (days)	729 (T)	628	723	456 (I)
Life table test	P=0.361	P=0.109	P=0.586	P=0.185
Logistic regression test	P=0.212	P=0.111	P=0.608	P=0.104
Cochran-Armitage test	P=0.190			
Fisher exact test		P=0.103	P=0.500	P=0.103
Pancreatic Islets: Adenoma				
Overall rate	3/60 (5%)	2/60 (3%)	2/60 (3%)	0/59 (0%)
Adjusted rate	8.8%	7.1%	4.8%	0.0%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	2/29 (7%)	2/28 (7%)	1/37 (3%)	0/43 (0%)
First incidence (days)	533	729 (T)	702	–[e]
Life table test	P=0.054N	P=0.517N	P=0.398N	P=0.079N
Logistic regression test	P=0.085N	P=0.492N	P=0.467N	P=0.120N
Cochran-Armitage test	P=0.101N			
Fisher exact test		P=0.500N	P=0.500N	P=0.125N
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	9/58 (16%)	11/56 (20%)	4/60 (7%)	5/59 (8%)
Adjusted rate	29.0%	36.3%	10.8%	10.9%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	7/29 (24%)	9/27 (33%)	4/37 (11%)	4/44 (9%)
First incidence (days)	722	521	729 (T)	544
Life table test	P=0.014N	P=0.345	P=0.047N	P=0.051N
Logistic regression test	P=0.040N	P=0.370	P=0.033N	P=0.104N
Cochran-Armitage test	P=0.082N			
Fisher exact test		P=0.370	P=0.107N	P=0.187N
Skin (Subcutaneous Tissue): Fibrosarcoma				
Overall rate	0/60 (0%)	2/60 (3%)	3/60 (5%)	0/60 (0%)
Adjusted rate	0.0%	6.0%	7.1%	0.0%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	0/29 (0%)	1/28 (4%)	0/37 (0%)	0/44 (0%)
First incidence (days)	–	656	712	–
Life table test	P=0.284N	P=0.244	P=0.182	–
Logistic regression test	P=0.342N	P=0.242	P=0.163	–
Cochran-Armitage test	P=0.385N			
Fisher exact test		P=0.248	P=0.122	–
Uterus: Stromal Polyp				
Overall rate	8/60 (13%)	2/60 (3%)	1/60 (2%)	6/60 (10%)
Adjusted rate	25.2%	7.1%	2.7%	13.6%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	6/29 (21%)	2/28 (7%)	1/37 (3%)	6/44 (14%)
First incidence (days)	656	729 (T)	729 (T)	729 (T)
Life table test	P=0.411N	P=0.050N	P=0.006N	P=0.139N
Logistic regression test	P=0.547N	P=0.038N	P=0.006N	P=0.223N
Cochran-Armitage test	P=0.478			
Fisher exact test		P=0.047N	P=0.016N	P=0.389N

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Uterus: Stromal Polyp or Stromal Sarcoma				
Overall rate	8/60 (13%)	3/60 (5%)	3/60 (5%)	6/60 (10%)
Adjusted rate	25.2%	9.2%	7.0%	13.6%
Interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	0/10 (0%)
Terminal rate	6/29 (21%)	2/28 (7%)	2/37 (5%)	6/44 (14%)
First incidence (days)	656	544	457 (I)	729 (T)
Life table test	P=0.333N	P=0.106N	P=0.048N	P=0.139N
Logistic regression test	P=0.535N	P=0.090N	P=0.070N	P=0.223N
Cochran-Armitage test	P=0.553			
Fisher exact test		P=0.102N	P=0.102N	P=0.389N
All Organs: Hemangiosarcoma				
Overall rate	0/60 (0%)	0/60 (0%)	4/60 (7%)	1/60 (2%)
Adjusted rate	0.0%	0.0%	10.3%	2.3%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	0/29 (0%)	0/28 (0%)	3/37 (8%)	1/44 (2%)
First incidence (days)	–	–	722	729 (T)
Life table test	P=0.562	–	P=0.101	P=0.583
Logistic regression test	P=0.525	–	P=0.108	P=0.583
Cochran-Armitage test	P=0.410			
Fisher exact test		–	P=0.059	P=0.500
All Organs: Hemangioma or Hemangiosarcoma				
Overall rate	2/60 (3%)	1/60 (2%)	4/60 (7%)	1/60 (2%)
Adjusted rate	6.9%	3.6%	10.3%	2.3%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	2/29 (7%)	1/28 (4%)	3/37 (8%)	1/44 (2%)
First incidence (days)	729 (T)	729 (T)	722	729 (T)
Life table test	P=0.281N	P=0.512N	P=0.457	P=0.356N
Logistic regression test	P=0.310N	P=0.512N	P=0.485	P=0.356N
Cochran-Armitage test	P=0.459N			
Fisher exact test		P=0.500N	P=0.340	P=0.500N
All Organs: Malignant Lymphoma (Histiocytic, Lymphocytic, Mixed, or Undifferentiated Cell Type)				
Overall rate	8/60 (13%)	7/60 (12%)	9/60 (15%)	9/60 (15%)
Adjusted rate	23.3%	22.8%	22.8%	19.5%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	5/29 (17%)	5/28 (18%)	7/37 (19%)	8/44 (18%)
First incidence (days)	494	691	716	302
Life table test	P=0.350N	P=0.521N	P=0.512N	P=0.407N
Logistic regression test	P=0.493	P=0.479N	P=0.587N	P=0.544
Cochran-Armitage test	P=0.399			
Fisher exact test		P=0.500N	P=0.500	P=0.500
All Organs: Malignant Lymphoma or Histiocytic Sarcoma				
Overall rate	8/60 (13%)	8/60 (13%)	9/60 (15%)	10/60 (17%)
Adjusted rate	23.3%	24.9%	22.8%	21.3%
Interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/10 (0%)
Terminal rate	5/29 (17%)	5/28 (18%)	7/37 (19%)	8/44 (18%)
First incidence (days)	494	681	716	302
Life table test	P=0.413N	P=0.589	P=0.512N	P=0.508N
Logistic regression test	P=0.413	P=0.588N	P=0.587N	P=0.431
Cochran-Armitage test	P=0.333			
Fisher exact test		P=0.605N	P=0.500	P=0.399

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
All Organs: Benign Neoplasms				
Overall rate	32/60 (53%)	29/60 (48%)	17/60 (28%)	24/60 (40%)
Adjusted rate	81.1%	75.2%	39.8%	48.6%
Interim evaluation	3/10 (30%)	0/10 (0%)	1/10 (10%)	2/10 (20%)
Terminal rate	22/29 (76%)	19/28 (68%)	12/37 (32%)	19/44 (43%)
First incidence (days)	456 (I)	507	458 (I)	456 (I)
Life table test	P=0.002N	P=0.392N	P<0.001N	P=0.002N
Logistic regression test	P=0.053N	P=0.315N	P<0.001N	P=0.052N
Cochran-Armitage test	P=0.112N			
Fisher exact test		P=0.358N	P=0.004N	P=0.100N
All Organs: Malignant Neoplasms				
Overall rate	17/60 (28%)	24/60 (40%)	25/60 (42%)	16/60 (27%)
Adjusted rate	42.8%	56.4%	50.6%	33.7%
Interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	0/10 (0%)
Terminal rate	8/29 (28%)	11/28 (39%)	13/37 (35%)	13/44 (30%)
First incidence (days)	494	17	114	302
Life table test	P=0.025N	P=0.163	P=0.353	P=0.163N
Logistic regression test	P=0.174N	P=0.122	P=0.119	P=0.443N
Cochran-Armitage test	P=0.212N			
Fisher exact test		P=0.124	P=0.090	P=0.500N
All Organs: Benign or Malignant Neoplasms				
Overall rate	38/60 (63%)	40/60 (67%)	35/60 (58%)	35/60 (58%)
Adjusted rate	85.7%	86.7%	69.7%	67.1%
Interim evaluation	3/10 (30%)	0/10 (0%)	2/10 (20%)	2/10 (20%)
Terminal rate	23/29 (79%)	22/28 (79%)	22/37 (59%)	27/44 (61%)
First incidence (days)	456 (I)	17	114	302
Life table test	P=0.003N	P=0.427	P=0.060N	P=0.014N
Logistic regression test	P=0.160N	P=0.417	P=0.232N	P=0.262N
Cochran-Armitage test	P=0.247N			
Fisher exact test		P=0.424	P=0.354N	P=0.354N

(T)Terminal sacrifice
(I)Interim evaluation
[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, 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 exposure group incidence are the P values corresponding to pairwise comparisons between the controls and that exposure 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 test regards 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 an exposure 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 Feed Study of Benzyl Acetate[a]

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim sacrifice	10	10	10	10
Early deaths				
Moribund	12	16	7	3
Natural deaths	9	6	6	3
Survivors				
Terminal sacrifice	29	28	37	44
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Liver	(10)	(10)	(10)	(10)
Basophilic focus		1 (10%)		1 (10%)
Clear cell focus	1 (10%)	1 (10%)		
Hematopoietic cell proliferation	1 (10%)			
Hyperplasia, lymphoid	1 (10%)	1 (10%)	1 (10%)	
Inflammation, subacute	2 (20%)	1 (10%)	2 (20%)	3 (30%)
Mineralization	1 (10%)		1 (10%)	
Kupffer cell, hyperplasia	1 (10%)			
Kupffer cell, pigmentation	1 (10%)			
Lobules, necrosis	1 (10%)	1 (10%)		
Mesentery				(1)
Capillary, fat, congestion				1 (100%)
Pancreas	(10)	(10)	(10)	(10)
Focal cellular change			1 (10%)	
Hyperplasia, lymphoid	1 (10%)		1 (10%)	
Salivary glands	(10)	(10)	(10)	(10)
Hyperplasia, lymphoid	3 (30%)	1 (10%)		1 (10%)
Stomach, forestomach	(10)	(10)	(10)	(10)
Diverticulum		1 (10%)	1 (10%)	
Inflammation, subacute			1 (10%)	
Mucosa, hyperplasia			1 (10%)	
Stomach, glandular	(10)	(10)	(10)	(10)
Cyst				1 (10%)
Inflammation, subacute		1 (10%)		
Mucosa, dysplasia		1 (10%)		
Tongue	(10)	(10)	(10)	(10)
Inflammation, chronic	1 (10%)	2 (20%)		
Cardiovascular System				
Heart	(10)	(10)	(10)	(10)
Myocardium, inflammation, chronic	1 (10%)			

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
15-Month Interim Evaluation (continued)				
Endocrine System				
Adrenal gland, cortex	(10)	(10)	(10)	(10)
Accessory adrenal cortical nodule	2 (20%)		5 (50%)	4 (40%)
Angiectasis				1 (10%)
Developmental malformation				1 (10%)
Hematopoietic cell proliferation	1 (10%)			
Inflammation, subacute	1 (10%)			
Islets, pancreatic	(10)	(10)	(10)	(10)
Hyperplasia	3 (30%)			
Pituitary gland	(9)	(10)	(10)	(10)
Pars distalis, hyperplasia	2 (22%)	1 (10%)		
Thyroid gland	(10)	(10)	(10)	(10)
Degeneration, cystic	3 (30%)	1 (10%)	4 (40%)	2 (20%)
Follicular cell, hyperplasia		1 (10%)		
General Body System				
None				
Genital System				
Clitoral gland	(1)			
Ectasia	1 (100%)			
Pigmentation	1 (100%)			
Ovary	(10)	(10)	(10)	(10)
Angiectasis				1 (10%)
Cyst	1 (10%)	2 (20%)	2 (20%)	3 (30%)
Inflammation, suppurative	1 (10%)	1 (10%)		
Interstitial cell, hyperplasia	1 (10%)			
Uterus	(10)	(10)	(10)	(10)
Hyperplasia, cystic	10 (100%)	10 (100%)	10 (100%)	10 (100%)
Inflammation, suppurative	1 (10%)			
Epithelium, metaplasia, squamous		1 (10%)		
Hematopoietic System				
Bone marrow	(10)	(10)	(10)	(10)
Hypercellularity	1 (10%)	1 (10%)		
Lymph node	(10)	(10)	(10)	(10)
Lumbar, hyperplasia, lymphoid			1 (10%)	
Lumbar, hyperplasia, plasma cell	1 (10%)			
Mediastinal, hyperplasia, plasma cell	1 (10%)			
Lymph node, mesenteric	(10)	(10)	(10)	(10)
Hematopoietic cell proliferation	1 (10%)			
Hyperplasia, plasma cell	1 (10%)			
Spleen	(10)	(10)	(10)	(9)
Hematopoietic cell proliferation	1 (10%)		1 (10%)	
Lymphoid follicle, hyperplasia	1 (10%)		1 (10%)	
Thymus	(10)	(9)	(10)	(8)
Cyst	3 (30%)	1 (11%)	1 (10%)	2 (25%)
Depletion cellular	1 (10%)			

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
15-Month Interim Evaluation (continued)				
Integumentary System				
Mammary gland	(10)	(10)	(10)	(10)
Hyperplasia, lobular	1 (10%)			
Skin	(10)	(10)	(10)	(10)
Inflammation, chronic	1 (10%)			
Musculoskeletal System				
None				
Nervous System				
Brain	(10)	(10)	(10)	(10)
Thalamus, mineralization	8 (80%)	9 (90%)	9 (90%)	10 (100%)
Respiratory System				
Lung	(10)	(10)	(10)	(10)
Hyperplasia, lymphoid			1 (10%)	1 (10%)
Bronchiole, foreign body			2 (20%)	1 (10%)
Nose	(10)	(10)	(10)	(10)
Exudate				2 (20%)
Glands, cyst				1 (10%)
Glands, hyperplasia, cystic	8 (80%)	9 (90%)	10 (100%)	10 (100%)
Mucosa, atrophy	5 (50%)	9 (90%)	10 (100%)	10 (100%)
Mucosa, degeneration	10 (100%)	9 (90%)	10 (100%)	10 (100%)
Mucosa, pigmentation		7 (70%)	10 (100%)	10 (100%)
Special Senses System				
None				
Urinary System				
Kidney	(10)	(10)	(10)	(10)
Casts protein	7 (70%)	8 (80%)	6 (60%)	6 (60%)
Cyst	1 (10%)	1 (10%)		
Hyperplasia, lymphoid	3 (30%)	4 (40%)	2 (20%)	3 (30%)
Inflammation, suppurative	1 (10%)			
Metaplasia, osseous		1 (10%)		
Mineralization				1 (10%)
Renal tubule, dilatation	2 (20%)			
Renal tubule, regeneration	1 (10%)		1 (10%)	
Urinary bladder	(10)	(10)	(10)	(10)
Hyperplasia, lymphoid	1 (10%)	2 (20%)	3 (30%)	3 (30%)

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Feed Study of Benzyl Acetate
(continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study				
Alimentary System				
Gallbladder	(50)	(48)	(48)	(50)
Dilatation	2 (4%)	1 (2%)		
Inflammation, subacute			1 (2%)	
Intestine large, cecum	(49)	(50)	(50)	(48)
Edema		1 (2%)		
Intestine small, duodenum	(49)	(48)	(49)	(49)
Dilatation	1 (2%)			
Intestine small, ileum	(48)	(48)	(49)	(49)
Hyperplasia, lymphoid				1 (2%)
Intestine small, jejunum	(48)	(50)	(49)	(49)
Dilatation	1 (2%)			
Hyperplasia, lymphoid		1 (2%)		2 (4%)
Liver	(50)	(50)	(50)	(50)
Angiectasis		2 (4%)	2 (4%)	
Basophilic focus	4 (8%)	1 (2%)		4 (8%)
Clear cell focus	1 (2%)	1 (2%)	2 (4%)	
Cyst	1 (2%)	1 (2%)		
Fibrosis			1 (2%)	
Hematopoietic cell proliferation	12 (24%)	7 (14%)	10 (20%)	1 (2%)
Hemorrhage			1 (2%)	
Hyperplasia, focal	2 (4%)	2 (4%)	2 (4%)	
Hyperplasia, lymphoid	2 (4%)	4 (8%)	4 (8%)	2 (4%)
Inflammation, subacute	10 (20%)	3 (6%)	5 (10%)	10 (20%)
Metaplasia, osseous			1 (2%)	
Mixed cell focus	2 (4%)	2 (4%)		1 (2%)
Nuclear alteration			3 (6%)	
Bile duct, hyperplasia	2 (4%)			
Centrilobular, necrosis		1 (2%)		
Hepatocyte, cytomegaly	1 (2%)			
Hepatocyte, karyomegaly	1 (2%)			
Hepatocyte, vacuolization cytoplasmic	3 (6%)	1 (2%)		
Kupffer cell, hyperplasia	6 (12%)	6 (12%)	11 (22%)	5 (10%)
Kupffer cell, pigmentation	1 (2%)		5 (10%)	2 (4%)
Lobules, necrosis	6 (12%)	7 (14%)	4 (8%)	6 (12%)
Mesentery	(9)	(7)	(7)	(2)
Inflammation, suppurative	3 (33%)	3 (43%)	4 (57%)	1 (50%)
Fat, necrosis	2 (22%)	2 (29%)	1 (14%)	
Pancreas	(50)	(50)	(50)	(49)
Atrophy	4 (8%)		5 (10%)	2 (4%)
Cyst		1 (2%)	4 (8%)	1 (2%)
Focal cellular change			1 (2%)	
Hyperplasia, lymphoid	3 (6%)	2 (4%)	7 (14%)	4 (8%)
Necrosis	2 (4%)			
Acinar cell, cytoplasmic alteration	8 (16%)	2 (4%)	3 (6%)	
Salivary glands	(50)	(50)	(50)	(50)
Atrophy		1 (2%)		
Hyperplasia, lymphoid	8 (16%)	12 (24%)	13 (26%)	14 (28%)
Stomach, forestomach	(49)	(50)	(50)	(50)
Diverticulum		1 (2%)	1 (2%)	2 (4%)
Edema	1 (2%)			1 (2%)
Inflammation, subacute	4 (8%)		6 (12%)	2 (4%)
Ulcer	2 (4%)			
Mucosa, hyperplasia	8 (16%)	6 (12%)	8 (16%)	3 (6%)

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Alimentary System (continued)				
Stomach, glandular	(50)	(50)	(50)	(50)
Cyst	6 (12%)	3 (6%)	3 (6%)	1 (2%)
Edema	1 (2%)			1 (2%)
Erosion	4 (8%)	1 (2%)	1 (2%)	
Inflammation, chronic	2 (4%)			
Inflammation, subacute	1 (2%)		1 (2%)	
Ulcer		1 (2%)		
Tongue	(50)	(50)	(50)	(50)
Inflammation, chronic		1 (2%)	2 (4%)	
Mineralization				1 (2%)
Tooth		(1)		
Dysplasia		1 (100%)		
Cardiovascular System				
Blood vessel	(2)		(2)	(5)
Inflammation, chronic active	2 (100%)		2 (100%)	5 (100%)
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	1 (2%)			1 (2%)
Thrombosis	1 (2%)			
Myocardium, inflammation, chronic	1 (2%)	2 (4%)		
Myocardium, mineralization	1 (2%)			
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(50)
Accessory adrenal cortical nodule	15 (30%)	6 (12%)	9 (18%)	10 (20%)
Angiectasis			1 (2%)	
Cyst			2 (4%)	2 (4%)
Hematopoietic cell proliferation	2 (4%)	2 (4%)	4 (8%)	
Hyperplasia, diffuse		1 (2%)	1 (2%)	
Hyperplasia, focal	1 (2%)		1 (2%)	1 (2%)
Hypertrophy, focal		1 (2%)		2 (4%)
Vacuolization cytoplasmic, focal		1 (2%)		
Capsule, hyperplasia	1 (2%)	1 (2%)	5 (10%)	5 (10%)
X-zone, degeneration, fatty		1 (2%)		1 (2%)
Adrenal gland, medulla	(50)	(50)	(50)	(50)
Hyperplasia	2 (4%)	4 (8%)	5 (10%)	3 (6%)
Islets, pancreatic	(50)	(50)	(50)	(49)
Hyperplasia	2 (4%)	1 (2%)		
Parathyroid gland	(48)	(50)	(48)	(46)
Cyst	2 (4%)		1 (2%)	1 (2%)
Ectopic thymus		1 (2%)		2 (4%)
Hyperplasia	1 (2%)		1 (2%)	
Pituitary gland	(48)	(46)	(50)	(49)
Pars distalis, angiectasis	5 (10%)	4 (9%)	6 (12%)	
Pars distalis, cyst	1 (2%)		1 (2%)	1 (2%)
Pars distalis, hyperplasia	16 (33%)	13 (28%)	15 (30%)	14 (29%)
Pars intermedia, hyperplasia	1 (2%)			

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Feed Study of Benzyl Acetate
(continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Endocrine System (continued)				
Thyroid gland	(50)	(50)	(50)	(50)
Degeneration, cystic	7 (14%)	8 (16%)	10 (20%)	11 (22%)
Ectopic thymus	2 (4%)			1 (2%)
Inflammation, subacute	1 (2%)			
Follicle, cyst	5 (10%)	3 (6%)	2 (4%)	5 (10%)
Follicular cell, hyperplasia	11 (22%)	9 (18%)	12 (24%)	17 (34%)
General Body System				
Tissue NOS	(1)	(1)		(1)
Infiltration cellular, lymphocyte	1 (100%)			
Genital System				
Clitoral gland		(1)	(1)	
Pigmentation			1 (100%)	
Ovary	(49)	(48)	(49)	(49)
Angiectasis	8 (16%)	8 (17%)	9 (18%)	4 (8%)
Cyst	10 (20%)	12 (25%)	14 (29%)	14 (29%)
Hemorrhage	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Inflammation, suppurative	12 (24%)	6 (13%)	10 (20%)	4 (8%)
Pigmentation	1 (2%)			2 (4%)
Thrombosis		1 (2%)		
Interstitial cell, hyperplasia	3 (6%)		1 (2%)	1 (2%)
Uterus	(50)	(49)	(50)	(50)
Angiectasis	2 (4%)	2 (4%)	3 (6%)	3 (6%)
Granuloma			1 (2%)	1 (2%)
Hemorrhage			1 (2%)	
Hydrometra	1 (2%)	3 (6%)	4 (8%)	2 (4%)
Hyperplasia, cystic	46 (92%)	45 (92%)	48 (96%)	48 (96%)
Inflammation, suppurative	13 (26%)	6 (12%)	10 (20%)	6 (12%)
Necrosis			1 (2%)	2 (4%)
Endometrium, pigmentation	1 (2%)		1 (2%)	
Epithelium, metaplasia, squamous	7 (14%)	7 (14%)	15 (30%)	7 (14%)
Myometrium, hyperplasia		1 (2%)	1 (2%)	1 (2%)
Vagina	(1)			
Granuloma	1 (100%)			
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Hypercellularity	18 (36%)	10 (20%)	20 (40%)	8 (16%)
Myelofibrosis	16 (32%)	12 (24%)	14 (28%)	15 (30%)
Necrosis		1 (2%)		
Pigmentation, hemosiderin	3 (6%)	2 (4%)	7 (14%)	4 (8%)
Lymph node	(50)	(50)	(50)	(49)
Iliac, angiectasis	1 (2%)			
Iliac, hematopoietic cell proliferation	2 (4%)			
Iliac, hyperplasia, lymphoid		2 (4%)		
Iliac, hyperplasia, plasma cell	2 (4%)	3 (6%)		1 (2%)
Lumbar, hyperplasia, plasma cell	1 (2%)			

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Hematopoietic System (continued)				
Lymph node (continued)	(50)	(50)	(50)	(49)
Mediastinal, hyperplasia, plasma cell	4 (8%)	4 (8%)	2 (4%)	
Mediastinal, inflammation, suppurative	1 (2%)	2 (4%)		
Renal, ectasia	1 (2%)			
Renal, hematopoietic cell proliferation	2 (4%)		1 (2%)	
Renal, hemorrhage			1 (2%)	
Renal, hyperplasia, lymphoid	3 (6%)	1 (2%)		
Renal, hyperplasia, plasma cell	5 (10%)	5 (10%)	3 (6%)	1 (2%)
Lymph node, mandibular	(50)	(50)	(50)	(49)
Hematopoietic cell proliferation	2 (4%)	1 (2%)	2 (4%)	
Hyperplasia, lymphoid	5 (10%)	5 (10%)	5 (10%)	
Hyperplasia, plasma cell	6 (12%)	4 (8%)	1 (2%)	1 (2%)
Pigmentation	1 (2%)	2 (4%)	1 (2%)	
Lymph node, mesenteric	(50)	(46)	(49)	(48)
Angiectasis	2 (4%)		1 (2%)	
Ectasia				2 (4%)
Hematopoietic cell proliferation	10 (20%)	5 (11%)	4 (8%)	2 (4%)
Hemorrhage	7 (14%)	3 (7%)	5 (10%)	6 (13%)
Hyperplasia, lymphoid	3 (6%)	3 (7%)	3 (6%)	3 (6%)
Hyperplasia, plasma cell	1 (2%)		1 (2%)	
Necrosis		1 (2%)		
Spleen	(50)	(50)	(50)	(50)
Hematopoietic cell proliferation	26 (52%)	24 (48%)	26 (52%)	15 (30%)
Hyperplasia, reticulum cell	2 (4%)			
Pigmentation, hemosiderin	8 (16%)	7 (14%)	6 (12%)	2 (4%)
Lymphoid follicle, atrophy	1 (2%)	1 (2%)	1 (2%)	
Lymphoid follicle, hyperplasia	3 (6%)	6 (12%)	5 (10%)	6 (12%)
Red pulp, hyperplasia	3 (6%)	1 (2%)	1 (2%)	1 (2%)
Thymus	(45)	(47)	(46)	(49)
Angiectasis	4 (9%)	2 (4%)		1 (2%)
Cyst	6 (13%)	2 (4%)	10 (22%)	11 (22%)
Depletion cellular	7 (16%)	9 (19%)	6 (13%)	2 (4%)
Ectopic parathyroid gland	2 (4%)			
Hyperplasia, lymphoid	3 (7%)	2 (4%)		2 (4%)
Integumentary System				
Mammary gland	(50)	(49)	(50)	(50)
Hyperplasia, cystic	5 (10%)	4 (8%)		2 (4%)
Hyperplasia, lobular				1 (2%)
Skin	(50)	(50)	(49)	(50)
Acanthosis	2 (4%)	1 (2%)	4 (8%)	3 (6%)
Cyst epithelial inclusion				1 (2%)
Inflammation, chronic	2 (4%)	1 (2%)	3 (6%)	2 (4%)
Ulcer			1 (2%)	1 (2%)
Subcutaneous tissue, edema	2 (4%)	2 (4%)	2 (4%)	

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Feed Study of Benzyl Acetate
(continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Musculoskeletal System				
Skeletal muscle	(50)	(50)	(50)	(50)
Foreign body			1 (2%)	
Inflammation, chronic	7 (14%)	2 (4%)	7 (14%)	1 (2%)
Sarcolemmal nuclei, hyperplasia	1 (2%)	1 (2%)	4 (8%)	
Sarcoplasm, atrophy			1 (2%)	
Nervous System				
Brain	(50)	(50)	(50)	(50)
Compression	3 (6%)	3 (6%)		1 (2%)
Cyst		1 (2%)		
Hydrocephalus	1 (2%)			
Inflammation, chronic	1 (2%)		1 (2%)	1 (2%)
Vacuolization cytoplasmic	1 (2%)		1 (2%)	
Glial cell, proliferation	1 (2%)			
Thalamus, mineralization	30 (60%)	44 (88%)	38 (76%)	32 (64%)
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Adenomatosis	1 (2%)			
Bacterium	1 (2%)	1 (2%)	1 (2%)	
Congestion	1 (2%)			
Edema	1 (2%)			1 (2%)
Hemorrhage	1 (2%)	6 (12%)	4 (8%)	4 (8%)
Hyperplasia, lymphoid	9 (18%)	7 (14%)	9 (18%)	13 (26%)
Infiltration cellular, histiocyte	7 (14%)	4 (8%)	3 (6%)	1 (2%)
Inflammation, subacute		1 (2%)	3 (6%)	
Inflammation, suppurative	2 (4%)			
Thrombosis	2 (4%)			
Alveolar epithelium, hyperplasia	1 (2%)	1 (2%)	1 (2%)	
Artery, hypertrophy	1 (2%)	1 (2%)		
Bronchiole, foreign body	1 (2%)		1 (2%)	
Nose	(50)	(50)	(50)	(50)
Exudate	15 (30%)	26 (52%)	36 (72%)	43 (86%)
Glands, hyperplasia, cystic	39 (78%)	45 (90%)	49 (98%)	50 (100%)
Mucosa, atrophy	41 (82%)	48 (96%)	49 (98%)	50 (100%)
Mucosa, degeneration	48 (96%)	48 (96%)	50 (100%)	50 (100%)
Mucosa, pigmentation		46 (92%)	48 (96%)	48 (96%)
Special Senses System				
None				
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Bacterium	1 (2%)	1 (2%)	1 (2%)	
Casts protein	32 (64%)	31 (62%)	32 (64%)	25 (50%)
Cyst	1 (2%)	1 (2%)		2 (4%)
Glomerulosclerosis	7 (14%)		5 (10%)	1 (2%)

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
2-Year Study (continued)				
Urinary System (continued)				
Kidney (continued)	(50)	(50)	(50)	(50)
Hydronephrosis			1 (2%)	
Hyperplasia, lymphoid	25 (50%)	23 (46%)	20 (40%)	20 (40%)
Inflammation, suppurative	4 (8%)			
Metaplasia, osseous		1 (2%)	2 (4%)	
Mineralization		2 (4%)	1 (2%)	2 (4%)
Interstitial tissue, pigmentation	2 (4%)			
Renal tubule, atrophy	2 (4%)	1 (2%)		1 (2%)
Renal tubule, cytoplasmic alteration		1 (2%)		
Renal tubule, dilatation	4 (8%)	1 (2%)	2 (4%)	
Renal tubule, necrosis	1 (2%)	1 (2%)		
Renal tubule, pigmentation	1 (2%)	2 (4%)		
Renal tubule, regeneration	21 (42%)	9 (18%)	14 (28%)	14 (28%)
Transitional epithelium, hyperplasia	1 (2%)			
Urinary bladder	(50)	(49)	(50)	(50)
Edema	1 (2%)	1 (2%)		
Hyperplasia, lymphoid	23 (46%)	13 (27%)	19 (38%)	14 (28%)
Inflammation, chronic	1 (2%)			
Mucosa, hyperplasia	2 (4%)			

[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). Benzyl acetate was sent to the laboratory as a coded aliquot from Radian Corporation (Austin, TX). It 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 of at least five doses of benzyl acetate. The high dose was limited by toxicity. All trials were repeated.

In this test, 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 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.

MOUSE LYMPHOMA CELL MUTAGENICITY TEST PROTOCOL

The experimental protocol is presented in detail by McGregor *et al.* (1988). Benzyl acetate was supplied as a coded aliquot by Radian Corporation. The high dose of 1,700 μg/mL was determined by toxicity. L5178Y mouse lymphoma cells were maintained at 37° C as suspension cultures in Fischer's medium supplemented with *l*-glutamine, sodium pyruvate, pluronic F68, antibiotics, and heat-inactivated horse serum; normal cycling time was approximately 10 hours. To reduce the number of spontaneously occurring trifluorothymidine-resistant cells, subcultures were exposed to medium containing THMG (thymidine, hypoxanthine, methotrexate, glycine) for 1 day, to medium containing THG (thymidine, hypoxanthine, and glycine) for 1 day, and to normal medium for 3 to 5 days. For cloning, the horse serum content was increased and Noble agar was added.

All treatment levels within an experiment, including concurrent positive and solvent controls, were replicated. Treated cultures contained 6×10^6 cells in 10 mL medium. This volume included the S9 fraction in those experiments performed with metabolic activation. The cells were incubated with benzyl acetate for 4 hours, after which time the medium plus benzyl acetate was removed and the cells were resuspended in fresh medium and incubated for an additional 2 days to express the mutant phenotype. Cell density was monitored so that log phase growth was maintained. After the 48-hour expression period, 3×10^6 cells were plated in medium and soft agar supplemented with trifluorothymidine (TFT) for selection of TFT-resistant ($TK^{-/-}$) cells; 600 cells were plated in nonselective medium and soft agar to determine cloning efficiency. Plates were incubated at 37° C in 5% CO_2 for 10 to 12 days. The test was initially performed without S9. If a clearly positive response was not obtained, the test was repeated using freshly prepared S9 from the livers of Aroclor 1254-induced male Fischer 344 rats.

Minimum criteria for accepting an experiment as valid and a detailed description of the statistical analysis and data evaluation are presented in Caspary *et al.* (1988). All data were evaluated statistically for trend and peak responses. Both responses had to be significant ($P \leq 0.05$) for benzyl acetate to be considered positive, i.e., capable of inducing TFT resistance. A single significant response led to a

"questionable" conclusion, and the absence of both a trend and peak response resulted in a "negative" call.

CHINESE HAMSTER OVARY CELL CYTOGENETICS PROTOCOLS

Testing was performed as reported by Galloway *et al.* (1987). Benzyl acetate was sent to the laboratory as a coded aliquot by Radian Corporation. It 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 three doses of benzyl acetate; the high dose was 5,000 μg/mL. 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 benzyl acetate 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 benzyl acetate was removed and replaced with fresh medium plus BrdU and Colcemid, and incubation was continued for 2 hours. Cells were harvested by mitotic shake-off, fixed, and stained with Hoechst 33258 and Giemsa. In the SCE test with S9, cells were incubated with benzyl acetate, serum-free medium, and S9 for 2 hours. The medium was then removed and replaced with medium containing serum and BrdU and no benzyl acetate, and incubation proceeded for an additional 26 to 28 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 of both the slopes of the dose-response curves and the individual dose points were conducted (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 benzyl acetate for 12 hours; Colcemid was added and incubation continued for 2 hours. The cells were harvested by mitotic shake-off, fixed, and stained with Giemsa. For the Abs test with S9, cells were treated with benzyl acetate and S9 for 2 hours, after which the treatment medium was removed and the cells were incubated for 12 hours in fresh medium, with Colcemid present for the final 2 hours. Harvesting and staining were the same as for cells treated without S9.

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).

DROSOPHILA MELANOGASTER TEST PROTOCOL

The assays for induction of sex-linked recessive lethal (SLRL) mutations were performed with adult flies as described by Valencia *et al.* (1985). Benzyl acetate was supplied as a coded aliquot by Radian Corporation. It was assayed in the SLRL mutation test by feeding for 3 days to adult Canton-S wild-type males no more than 24 hours old at the beginning of treatment. Because no response was obtained, benzyl acetate was retested by injection into adult males.

To administer a chemical by injection, a glass Pasteur pipette is drawn out in a flame to a microfine filament, and the tip is broken off to allow delivery of the test solution. Injection is performed either manually, by attaching a rubber bulb to the other end of the pipette and forcing through sufficient solution (0.2 to 0.3 μL) to slightly distend the abdomen of the fly, or by attaching the pipette to a microinjector, which automatically delivers a calibrated volume. Flies are anesthetized with ether and immobilized on a strip of tape. Injection into the thorax, under the wing, is performed with the aid of a dissecting microscope.

Toxicity tests were performed to set concentrations of benzyl acetate at a level that would induce 30% mortality after 72 hours of feeding or 24 hours after injection, while keeping induced sterility at an acceptable level. Oral exposure was achieved by allowing Canton-S males to feed for 72 hours on a solution of benzyl acetate in 5% sucrose. In the injection experiments, 24- to 72-hour-old Canton-S males were treated with a solution of benzyl acetate dissolved in saline and allowed to recover for 24 hours. In the adult exposures, treated males were mated to three *Basc* females for 3 days and given fresh females at 2-day intervals to produce three matings of 3, 2, and 2 days (in each case, sample sperm from successive matings were treated at successively earlier post-meiotic stages). A concurrent saline control group was also included. F_1 heterozygous females were mated with their siblings and then placed in individual vials. F_1 daughters from the same parental male were kept together to identify clusters. (A cluster occurs when a number of mutants from a given male results from a single spontaneous premeiotic mutation event and is identified when the number of mutants from that male exceeds the number predicted by a Poisson distribution.) A cluster was identified in the feeding experiment and all data from the male in question were discarded. Presumptive lethal mutations were identified as vials containing fewer than 5% of the expected number of wild-type males after 17 days; these were retested to confirm the response.

SLRL mutation data were analyzed by simultaneous comparison with the concurrent and historical controls using a normal approximation to the binomial test (Margolin *et al.*, 1983). A test result was considered positive if the P value was less than 0.01 and the mutation frequency in the tested group was greater than 0.10%, or if the P value was less than 0.05 and the frequency in the treatment group was greater than 0.15%. A test was considered to be inconclusive if (a) the P value was between 0.05 and 0.01 but the frequency in the treatment group was between 0.10% and 0.15% or (b) the P value was between 0.10 and 0.05 but the frequency in the treatment group was greater than 0.10%. A test was considered negative if the P value was greater than 0.10 or if the frequency in the treatment group was less than 0.10%.

MOUSE BONE MARROW SISTER CHROMATID EXCHANGE TEST PROTOCOL

A dose range-finding study was performed in the absence of adequate toxicity information from the literature. The highest dose (1,700 mg/kg) was limited by toxicity and induction of cell cycle delay. Benzyl acetate was tested for the induction of SCEs in mouse bone marrow cells using two protocols. Male $B6C3F_1$ mice (five animals per dose group) were injected intraperitoneally with benzyl acetate

dissolved in corn oil (injection volume=0.4 mL). Solvent control mice received equivalent injections of corn oil only. The positive control was dimethylbenzanthracene.

The first experiment had a (standard) harvest time of 24 hours, and the second had an extended harvest of 42 hours. The mice were implanted subcutaneously with a BrdU tablet (McFee *et al.*, 1983) 24 hours before harvest (1 hour before benzyl acetate treatment in the case of the standard protocol). The use of BrdU allowed selection of the appropriate cell population cells in the second metaphase following benzyl acetate treatment for scoring. Two hours before sacrifice, the mice received an intraperitoneal injection of colchicine in saline. The animals were killed by cervical dislocation 24 or 42 hours after treatment. One or both femurs were removed, and the marrow was flushed out with phosphate-buffered saline (pH 7.0). The cells were treated with a hypotonic salt solution, fixed, and dropped onto chilled slides. After a 24-hour drying period, the slides were stained using fluorescence-plus-Giemsa and scored.

Twenty-five second-division metaphase cells were scored from each of four animals per treatment. Responses were evaluated as SCEs/cell, and the data were analyzed by a trend test (Margolin *et al.*, 1986).

Mouse Bone Marrow Chromosomal Aberrations Test Protocol

A dose range-finding study was performed in the absence of adequate toxicity information from the literature. The highest dose (1,700 mg/kg) was limited by toxicity and induction of cell cycle delay. Benzyl acetate was tested for induction of Abs in mouse bone marrow using two different protocols. The first experiment used a standard harvest time of 17 hours and the second used an extended harvest time of 36 hours.

Male B6C3F$_1$ mice (10 animals per dose group) were injected intraperitoneally with benzyl acetate dissolved in corn oil (injection volume=0.4 mL). Solvent control mice received equivalent injections of corn oil only. The positive control was dimethylbenzanthracene. The mice were subcutaneously implanted with a BrdU tablet (McFee *et al.*, 1983) 17 hours before the scheduled harvest. (For the standard protocol, this required BrdU implantation to precede injection with benzyl acetate by 1 hour.) The use of BrdU allowed selection of the appropriate cell population for scoring. (Abs induced by chemical administration are present in maximum number at the first metaphase following treatment; they decline in number during subsequent nuclear divisions due to cell death.) Two hours before sacrifice, the mice received an intraperitoneal injection of colchicine in saline. The animals were killed by cervical dislocation 17 or 36 hours after benzyl acetate injection (18 hours after BrdU dosing). One or both femurs were removed and the marrow was flushed out with phosphate-buffered saline (pH 7.0). Cells were treated with a hypotonic salt solution, fixed, and dropped onto chilled slides. After a 24-hour drying period, the slides were stained and scored.

Fifty first-division metaphase cells were scored from each of four animals per treatment. Responses were evaluated as the percentage of aberrant metaphase cells, excluding gaps. The data were analyzed by a trend test (Margolin *et al.*, 1986).

Mouse Bone Marrow Micronucleus Test Protocol

Preliminary range-finding studies were performed. Factors affecting dose selection included chemical solubility, toxicity, and the extent of cell cycle delay induced by benzyl acetate exposure. Male mice were injected intraperitoneally three times at 24-hour intervals with benzyl acetate dissolved in corn oil; the total dosing volume was 0.4 mL. Solvent control animals were injected with 0.4 mL of corn oil only. The positive control mice received injections of dimethylbenzanthracene. The mice were killed by cervical dislocation 24 hours after the third injection, and smears were prepared from bone marrow cells

obtained from the femurs. Air-dried smears were fixed and stained; 2,000 polychromatic erythrocytes (PCEs) were scored for the frequency of micronucleated cells in each of five animals per dose group. The results were tabulated as the mean of the pooled results from all animals within a treatment group plus or minus the standard error of the mean.

MOUSE PERIPHERAL BLOOD MICRONUCLEUS TEST PROTOCOL

A detailed discussion of this assay can be found in MacGregor *et al.* (1990). Peripheral blood samples were obtained from male and female $B6C3F_1$ mice at the end of the 13-week study. Smears were immediately prepared and fixed in absolute methanol, stained with a chromatin-specific fluorescent dye mixture of Hoechst 33258/pyronin Y (MacGregor *et al.*, 1983), and coded. Slides were scanned to determine the frequency of micronuclei in 2,000 PCEs and 10,000 normochromatic erythrocytes (NCEs) in each animal per dose group. The criteria of Schmid (1976) were used to define micronuclei, with the additional requirement that the micronuclei exhibit the characteristic fluorescent emissions of DNA (blue with 360 nm and orange with 540 nm UV illumination); the minimum size limit was approximately one-twentieth the diameter of the NCE cell. In addition, the percentage of PCEs among the total erythrocyte population was determined.

Log transformation of the NCE data and testing for normality by the Shapiro-Wilk test and for heterogeneity of variance by Cochran's test were performed before statistical analyses. The frequency of micronucleated cells among NCEs was analyzed by analysis of variance using the SAS GLM procedure. The NCE data for each dose group was compared with the concurrent solvent control using Student's t-test. The frequency of micronucleated cells among PCEs was analyzed by the Cochran-Armitage trend test, and individual dose groups were compared to the concurrent solvent control by Kastenbaum-Bowman's binomial test. The percentage of PCEs among total erythrocytes was analyzed by an analysis of variance on ranks (classed by sex), and individual dose groups were compared with the concurrent solvent control using a *t*-test on ranks.

RESULTS

Benzyl acetate was tested for mutagenicity in a variety of systems, both *in vitro* and *in vivo*, and, with one exception, all results were negative. Benzyl acetate (33 to 10,000 μg/plate) did not induce mutations in *S. typhimurium* strains TA98, TA100, TA1535, or TA1537 when tested in a preincubation protocol, with or without induced hamster or rat liver S9 (Mortelmans *et al.*, 1986; Table E1). Benzyl acetate was tested in two laboratories for induction of trifluorothymidine resistance in L5178Y mouse lymphoma cells (McGregor *et al.*, 1988; Table E2). In one laboratory, a positive response was observed only in the presence of Aroclor 1254-induced male Fischer 344 rat liver S9; in the second laboratory, a positive response was observed in two of three trials without S9, and no tests were conducted with S9. Benzyl acetate did not induce significant increases in SCEs or Abs in CHO cells *in vitro*, with or without induced S9 (Galloway *et al.*, 1987; Tables E3, E4). No induction of SLRL mutations was observed in germ cells of male *D. melanogaster* administered benzyl acetate by feeding or by injection (Table E5).

No induction of SCEs (Table E6) or Abs (Table E7) was observed in bone marrow cells of male mice treated by intraperitoneal injection with benzyl acetate, where both standard and extended harvest times were employed. The highest dose tested was 1,700 mg/kg for the standard harvest protocol, and 1,300 mg/kg for the extended harvest experiments. *In vivo* mouse bone marrow chromosome damage tests conducted with benzyl acetate yielded uniformly negative results. No increase in micronucleated polychromatic erythrocytes was observed in bone marrow smears of male mice treated with benzyl acetate (312.5 to 1,250 mg/kg) by intraperitoneal injection three times at 24-hour intervals (Table E8). No increases in the frequencies of micronucleated PCEs or NCEs were seen in peripheral blood smears prepared from male and female mice at the termination of the 13-week toxicity study, where benzyl acetate was administered in feed (3,130 to 50,000 ppm benzyl acetate) (Table E9).

TABLE E1
Mutagenicity of Benzyl Acetate 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
TA100							
	0	75 ± 7.9	97 ± 3.5	96 ± 8.0	102 ± 7.3	112 ± 14.5	105 ± 14.9
	33		102 ± 6.7				
	100	83 ± 0.3	101 ± 4.0	123 ± 1.2	67 ± 2.7	134 ± 6.3	122 ± 2.9
	333	81 ± 4.7	85 ± 5.8	110 ± 4.0	97 ± 9.6	97 ± 7.0	110 ± 12.3
	1,000	78 ± 9.8	91 ± 14.4	98 ± 8.4	93 ± 2.7	95 ± 12.7	99 ± 12.1
	3,333	70 ± 9.5	58 ± 11.7	90 ± 5.8	104 ± 15.5	96 ± 5.2	78 ± 4.1
	10,000	Toxic		73 ± 11.2	84 ± 9.0	107 ± 6.5	95 ± 6.5
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control[c]		705 ± 51.8	481 ± 29.2	1,759 ± 39.8	1,770 ± 31.1	1,040 ± 101.7	961 ± 89.2
TA1535							
	0	4 ± 0.9	8 ± 0.3	8 ± 1.2	7 ± 1.5	8 ± 2.2	6 ± 1.3
	33		5 ± 0.9				
	100	5 ± 1.7	4 ± 0.6	8 ± 0.9	6 ± 1.2	9 ± 2.0	6 ± 1.5
	333	7 ± 2.4	5 ± 0.6	12 ± 1.8	8 ± 1.2	5 ± 0.9	6 ± 1.2
	1,000	6 ± 2.0	4 ± 0.6	7 ± 1.7	2 ± 0.9	5 ± 1.2	5 ± 0.3
	3,333	4 ± 0.7	3 ± 0.3	6 ± 1.9	3 ± 1.2	8 ± 2.0	8 ± 3.0
	10,000	0 ± 0.0		3 ± 0.9	1 ± 0.7	5 ± 0.9	5 ± 2.3
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		407 ± 40.8	724 ± 63.9	63 ± 18.0	106 ± 2.6	51 ± 6.2	43 ± 3.5
TA1537							
	0	3 ± 0.7	2 ± 0.0	11 ± 2.8	6 ± 1.2	5 ± 0.6	7 ± 1.3
	33						
	100	6 ± 2.1	2 ± 1.0	6 ± 1.2	8 ± 2.3	11 ± 3.0	6 ± 1.2
	333	4 ± 1.5	5 ± 1.0	7 ± 2.3	4 ± 0.9	5 ± 1.8	9 ± 0.3
	1,000	5 ± 0.3	1 ± 0.7	4 ± 0.0	4 ± 1.2	4 ± 0.7	7 ± 3.2
	3,333	3 ± 2.1	5	5 ± 0.9	3 ± 0.3	5 ± 1.2	5 ± 1.5
	10,000	Toxic	Toxic	6 ± 1.2	6 ± 1.2	7 ± 1.5	4 ± 1.3
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		104 ± 24.3	224 ± 32.4	123 ± 14.6	79 ± 9.2	74 ± 7.7	82 ± 14.2
TA98							
	0	11 ± 2.3	12 ± 2.8	18 ± 5.6	16 ± 2.6	19 ± 2.5	20 ± 1.2
	33						
	100	12 ± 3.1	11 ± 1.2	18 ± 1.2	20 ± 1.8	16 ± 0.7	23 ± 2.5
	333	13 ± 1.0	13 ± 0.3	10 ± 0.7	20 ± 3.8	16 ± 2.2	24 ± 1.9
	1,000	8 ± 1.2	15 ± 3.5	12 ± 2.6	16 ± 1.9	13 ± 1.3	20 ± 3.2
	3,333	8 ± 1.2	12 ± 2.3	8 ± 1.5	19 ± 2.3	10 ± 0.9	19 ± 4.8
	10,000	1 ± 0.6	8 ± 1.0	7 ± 1.5	12 ± 1.3	9 ± 1.5	18 ± 4.1
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		87 ± 10.7	140 ± 3.7	1,169 ± 48.5	1,169 ± 69.6	431 ± 22.2	524 ± 49.4

[a] Study performed at Case Western Reserve University. 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] 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 Trifluorothymidine Resistance in L5178Y Mouse Lymphoma Cells by Benzyl Acetate[a]

Compound	Concentration (μL/mL)	Cloning Efficiency (%)	Relative Total Growth (%)	Mutant Count	Mutant Fraction[b]	Average Mutant Fraction
Experiment performed at SRI, International:						
-S9						
Dimethylsulfoxide						
		60	108	130	72	
		60	92	130	72	72
Ethyl methanesulfonate						
	500 μg/mL	25	43	570	776	
		26	37	575	752	764*
Hycanthone						
	10 μg/mL	32	48	387	405	
Benzyl acetate						
	0.25	62	116	173	93	
		68	127	130	64	78
	0.5	62	100	96	51	
		63	104	130	69	60
	0.75	57	77	128	75	
		62	103	170	92	83
	1	61	59	186	102	
		57	49	139	82	92
	1.25	Lethal				
		Lethal				

TABLE E2
Induction of Trifluorothymidine Resistance in L5178Y Mouse Lymphoma Cells by Benzyl Acetate
(continued)

Compound	Concentration (μL/mL)	Cloning Efficiency (%)	Relative Total Growth (%)	Mutant Count	Mutant Fraction	Average Mutant Fraction
Experiment performed at SRI, International:						
+S9						
Trial 1						
Dimethylsulfoxide		62	97	215	115	
		60	101	271	152	
		67	102	224	112	126
Hycanthone	10 μg/mL	37	34	555	498	
Benzyl acetate	0.25	56	86	338	202	
		62	107	316	169	185
	0.5	58	86	383	219	
		58	82	468	269	244*
	0.75	52	63	557	355	
		53	77	521	330	342*
	1	55	65	688	420	
		53	51	734	459	439*
	1.25	32	22	773	801	
		31	19	736	804	803*
	1.75	Lethal				
		Lethal				
Trial 2						
Dimethylsulfoxide		70	101	285	136	
		79	112	222	93	
		63	86	216	114	114
Methylcholanthrene	6 μg/mL	23	8	392	564	
Benzyl acetate	0.25	83	120	242	98	
		67	100	229	114	106
	0.5	68	72	287	141	
		66	85	460	232	186*
	0.75	62	64	517	279	
		59	67	408	231	255*
	1	70	69	511	243	
		61	58	480	264	254*
	1.25	40	31	618	519	
		59	54	663	374	446*

TABLE E2
Induction of Trifluorothymidine Resistance in L5178Y Mouse Lymphoma Cells by Benzyl Acetate
(continued)

Compound	Concentration (μg/mL)	Cloning Efficiency (%)	Relative Total Growth (%)	Mutant Count	Mutant Fraction	Average Mutant Fraction
Experiment performed at Inveresk Research, International:						
-S9						
Trial 1						
Dimethylsulfoxide		83	102	53	21	
		94	81	95	34	
		86	98	89	35	
		98	120	155	53	36
Methyl methanesulfonate						
	15	44	34	298	226	
		51	37	280	182	204*
Benzyl acetate	700	118	75	187	53	
		109	86	213	65	59*
	900	69	50	173	84	
		71	50	187	88	86*
	1,100	76	54	189	83	
		71	54	142	67	75*
	1,300	73	43	223	102	
		65	42	198	102	102*
	1,500	69	23	203	99	
		73	17	245	112	105*
	1,700	Lethal				
		Lethal				
Trial 2						
Dimethylsulfoxide		61	99	158	86	
		70	98	141	67	
		78	102	132	57	
		68	102	159	78	72
Methyl methanesulfonate						
	15	37	33	251	224	
		42	28	302	239	231*
Benzyl acetate	800	68	109	148	73	
		74	111	110	50	61
	1,000	90	116	125	46	
		76	74	132	58	52
	1,200	85	74	131	51	
		72	70	154	72	62
	1,400	85	69	148	58	
		71	67	131	61	60
	1,600	64	17	152	79	
		Lethal				

TABLE E2
Induction of Trifluorothymidine Resistance in L5178Y Mouse Lymphoma Cells by Benzyl Acetate
(continued)

Compound	Concentration (μL/mL)	Cloning Efficiency (%)	Relative Total Growth (%)	Mutant Count	Mutant Fraction	Average Mutant Fraction
-S9						
Trial 3						
Dimethylsulfoxide		55	75	58	35	
		54	125	58	36	
		67	100	65	32	35
Methyl methanesulfonate						
	15 μg/mL	42	37	176	140	
		29	32	223	258	199*
Benzyl acetate	600	65	95	113	58	
		60	100	63	35	46
	800	73	114	114	52	
		66	89	84	43	47
	1,000	66	80	145	73	
		73	87	144	66	70*
	1,200	70	76	125	59	
		74	62	165	75	67*
	1,400	72	43	128	59	
		85	52	174	69	64*
	1,600	Lethal				
		Lethal				

* Significant positive response ($P \leq 0.05$)

[a] The experimental protocol and data for the study performed at SRI, International, are presented in detail by Caspary *et al.* (1988); the experimental protocol and data for the Inveresk Research, International study are presented in detail by McGregor *et al.* (1988). All doses are tested in triplicate; the average of the three tests is presented in the table.

[b] Mutant fraction (frequency) is a ratio of the mutant count to the cloning efficiency, divided by 3 (to arrive at MF 10^6 cells treated).

TABLE E3
Induction of Sister Chromatid Exchanges in Chinese Hamster Ovary Cells by Benzyl Acetate[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	1,049	518	0.49	10.4	26.0	
Mitomycin-C	0.005	50	1,050	1,174	1.11	23.5	26.0	126.43
Benzyl acetate	50	50	1,048	449	0.42	9.0	26.0	-13.24
	160	50	1,048	473	0.45	9.5	26.0	-8.60
	500	50	1,050	487	0.46	9.7	26.0	-6.08
								P=0.764[c]
+S9								
Summary: Negative								
Dimethylsulfoxide		50	1,051	461	0.43	9.2	26.0	
Cyclophosphamide	1	50	1,049	862	0.82	17.2	26.0	87.34
Benzyl acetate	500	50	1,050	484	0.46	9.7	26.0	5.09
	1,600	50	1,047	493	0.47	9.9	26.0	7.35
	5,000	50	1,048	515	0.49	10.3	28.0	12.04
								P=0.037

[a] Study performed at Columbia University. 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 benzyl acetate relative to those of culture exposed to solvent
[c] Significance of relative SCEs/chromosomes tested by the linear regression trend test vs. log of the dose

TABLE E4
Induction of Chromosomal Aberrations in Chinese Hamster Ovary Cells by Benzyl Acetate[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: 14.0 hours Summary: Negative					**Trial 1** - Harvest time: 14.0 hours Summary: Negative				
Dimethylsulfoxide					Dimethylsulfoxide				
	100	5	0.05	5.0		100	10	0.10	7.0
Mitomycin-C					Cyclophosphamide				
0.15	100	37	0.37	30.0	15	100	21	0.21	20.0
Benzyl acetate					Benzyl acetate				
160	100	4	0.04	3.0	500	100	5	0.05	5.0
500	100	3	0.03	3.0	1,600	100	12	0.12	11.0
1,600	100	13	0.13	12.0	5,000	100	9	0.09	7.0
				P=0.021[b]					P=0.303
Trial 2 - Harvest time: 14.0 hours Summary: Negative					**Trial 2** - Harvest time: 14.0 hours Summary: Negative				
Dimethylsulfoxide					Dimethylsulfoxide				
	100	8	0.08	8.0		100	4	0.04	4.0
Mitomycin-C					Cyclophosphamide				
0.15	50	26	0.52	40.0	15	100	18	0.18	14.0
Benzyl acetate					Benzyl acetate				
800	100	13	0.13	12.0	3,000	100	10	0.10	9.0
1,200	100	12	0.12	8.0	4,000	100	9	0.09	8.0
1,600	100	6	0.06	6.0	5,000	100	9	0.09	9.0
				P=0.788					P=0.118
Trial 3 - Harvest time: 14.0 hours Summary: Negative									
Dimethylsulfoxide									
	100	4	0.04	3.0					
Mitomycin-C									
0.15	50	17	0.34	30.0					
Benzyl acetate									
500	100	5	0.05	5.0					
1,000	100	5	0.05	5.0					
1,500	100	11	0.11	9.0					
				P=0.046					

[a] Study performed at Columbia University. Abs=aberrations. A detailed presentation of the protocol and these data are 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

TABLE E5
Induction of Sex-Linked Recessive Lethal Mutations in *Drosophila melanogaster* by Benzyl Acetate[a]

Route of Exposure	Dose (ppm)	Incidence of Deaths (%)	Incidence of Sterility (%)	No. of Lethals/No. of X chromosomes Tested			
				Mating 1	Mating 2	Mating 3	Total[b]
Feeding	300	2	0	1/3,303	4/3,317	2/3,232	17/9,852 (0.17%)
	0			2/3,255	4/2,783	4/2,865	10/8,903 (0.11%)
Injection	20,000	23	17	2/1,814	6/1,605	6/1,398	14/4,817 (0.29%)
	0			1/2,053	8/1,711	4/1,897	13/5,661 (0.23%)

[a] Study performed at University of Wisconsin, Madison. A detailed description of the protocol is presented in Zimmering *et al.* (1985). Results were not significant at the 5% level (Margolin *et al.*, 1983) ($P<0.001$).
[b] Combined total number of lethal mutations/number of X chromosomes tested for three mating trials.

TABLE E6
Induction of Sister Chromatid Exchanges in Mouse Bone Marrow Cells by Benzyl Acetate[a]

Treatment	Dose (mg/kg)	SCEs/Cell	
		Standard harvest	Extended harvest
Corn oil		4.01 ± 0.49	4.60 ± 0.81
Dimethylbenzanthracene[b]	2.5	5.79 ± 0.41	8.58 ± 0.70
Benzyl acetate	325		4.09 ± 0.70
	425	3.87 ± 0.77	
	650		6.54 ± 1.68
	850	4.62 ± 1.18	
	1,300		4.13 ± 0.48
	1,700	3.97 ± 0.21	
		P=0.450[c]	P>0.500

[a] Data are presented as mean ± standard error.
[b] Positive control
[c] Significance of mean SCEs/cell tested by the one-tailed trend test; significant at P=0.05 (Margolin *et al.*, 1986)

TABLE E7
Induction of Chromosomal Aberrations in Mouse Bone Marrow Cells by Benzyl Acetate[a]

Treatment	Dose (mg/kg)	% Aberrant Cells	
		Standard harvest	Extended harvest
Corn oil		2.75 ± 0.65	2.75 ± 1.06
Dimethylbenzanthracene[b]	12.5	17.50 ± 1.40	20.00 ± 2.75
Benzyl acetate	325		1.50 ± 0.82
	425	2.25 ± 0.45	
	650		2.00 ± 0.85
	850	1.00 ± 0.53	
	1,300		2.50 ± 1.24
	1,700	4.00 ± 1.07	
		P=0.117[c]	P=0.475

[a] Data are presented as mean ± standard error.
[b] Positive control
[c] One-tailed trend test (Margolin, *et al.*, 1986); significant at P=0.05.

TABLE E8
Induction of Micronuclei in Mouse Bone Marrow Cells by Benzyl Acetate[a]

Compound	Dose (mg/kg)	Micronucleated PCEs/1,000 Cells	PCEs (%)
Dimethylbenzanthracene[b]			
	12.5	8.60 ± 0.64	51.70 ± 4.61
Benzyl acetate			
	0	3.00 ± 0.69	69.90 ± 2.37
	312.5	2.90 ± 0.60	65.80 ± 3.18
	625.0	3.20 ± 0.60	64.30 ± 5.41
	1,250.0	1.80 ± 0.46	60.70 ± 3.08
		Trend Test: P=-0.076[b] ANOVA:	P=0.0412

[a] PCE=polychromatic erythrocyte. Data are presented as mean ± standard error.
[b] Positive control

TABLE E9
Frequency of Micronuclei in Mouse Peripheral Blood Erythrocytes Following Treatment with Benzyl Acetate for 13 Weeks[a]

Dose (ppm)	Micronucleated Cells/1,000 Cells		PCE (%)	Number of Mice
	PCE	NCE		
Male				
0	1.87 ± 0.33	1.67 ± 0.18	1.91 ± 0.09	9
3,130	1.54 ± 0.25	1.32 ± 0.11	1.86 ± 0.11	8
6,250	1.63 ± 0.34	1.24 ± 0.08	1.63 ± 0.10	9
12,500	1.64 ± 0.31	1.45 ± 0.15	1.82 ± 0.11	9
25,000	1.38 ± 0.17	1.52 ± 0.12	2.03 ± 0.21	8
50,000	1.98 ± 0.30	1.71 ± 0.11	2.02 ± 0.09	8
Female				
0	1.16 ± 0.14	1.02 ± 0.09	1.77 ± 0.09	7
3,130	0.92 ± 0.19	0.93 ± 0.09	1.78 ± 0.11	7
6,250	1.17 ± 0.15	0.99 ± 0.06	1.87 ± 0.12	9
12,500	1.25 ± 0.17	0.98 ± 0.06	1.64 ± 0.12	9
25,000	1.52 ± 0.34	0.98 ± 0.06	1.88 ± 0.09	8
50,000	1.54 ± 0.32	1.28 ± 0.10	1.65 ± 0.06	8

[a] PCE=polychromatic erythrocyte; NCE=normochromatic erythrocyte. Two thousand PCEs and 10,000 NCEs scored per animal; data presented as mean ± standard error.

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 13-Week Feed Study of Benzyl Acetate[a]

	0 ppm	3,130 ppm	6,250 ppm	12,500 ppm	25,000 ppm
Male					
n	9	9	9	9	9
Necropsy body wt	365 ± 6	369 ± 6	364 ± 8	356 ± 6	328 ± 9**
Brain					
Absolute	1.978 ± 0.011	1.991 ± 0.026	1.990 ± 0.030	2.000 ± 0.018	1.946 ± 0.015
Relative	5.47 ± 0.09	5.44 ± 0.08	5.51 ± 0.09	5.62 ± 0.08	5.82 ± 0.06**
R. Kidney					
Absolute	1.243 ± 0.042	1.354 ± 0.032	1.318 ± 0.039	1.347 ± 0.038	1.220 ± 0.029
Relative	3.44 ± 0.14	3.70 ± 0.06	3.65 ± 0.10	3.78 ± 0.08*	3.64 ± 0.03
Liver					
Absolute	13.294 ± 0.292	14.660 ± 0.343	13.939 ± 0.548	13.881 ± 0.438	12.557 ± 0.373
Relative	36.74 ± 0.65	40.01 ± 0.68**	38.45 ± 0.81	38.87 ± 0.64	37.47 ± 0.76
Pancreas					
Absolute	0.605 ± 0.050	0.647 ± 0.028	0.615 ± 0.041	0.611 ± 0.038	0.606 ± 0.036
Relative	1.67 ± 0.13	1.77 ± 0.08	1.70 ± 0.09	1.71 ± 0.10	1.81 ± 0.11
Prostate Gland					
Absolute	0.718 ± 0.093	0.672 ± 0.037	0.746 ± 0.035	0.719 ± 0.060	0.642 ± 0.034
Relative	1.98 ± 0.25	1.84 ± 0.11	2.07 ± 0.11	2.01 ± 0.15	1.92 ± 0.10
Seminal Vesicle					
Absolute	1.124 ± 0.078	1.036 ± 0.084	1.016 ± 0.071	1.040 ± 0.078	0.942 ± 0.072
Relative	3.12 ± 0.23	2.84 ± 0.25	2.79 ± 0.16	2.92 ± 0.21	2.81 ± 0.21
Spleen					
Absolute	0.787 ± 0.023	0.768 ± 0.016	0.814 ± 0.026	0.740 ± 0.021[b]	0.708 ± 0.019*
Relative	2.18 ± 0.08	2.10 ± 0.03	2.26 ± 0.07	2.09 ± 0.05	2.11 ± 0.04
R. Testis					
Absolute	1.525 ± 0.030[b]	1.490 ± 0.031	1.554 ± 0.041	1.513 ± 0.026	1.497 ± 0.021
Relative	4.24 ± 0.11	4.07 ± 0.09	4.30 ± 0.10	4.25 ± 0.08	4.48 ± 0.06
Thymus					
Absolute	0.329 ± 0.024	0.365 ± 0.023	0.364 ± 0.021	0.343 ± 0.023	0.383 ± 0.018
Relative	0.91 ± 0.06	1.00 ± 0.06	1.00 ± 0.05	0.97 ± 0.07	1.14 ± 0.05**

TABLE F1
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 13-Week Feed Study of Benzyl Acetate (continued)

	0 ppm	3,130 ppm	6,250 ppm	12,500 ppm	25,000 ppm
Female					
n	9	9	9	8	9
Necropsy body wt	202 ± 3	202 ± 3	198 ± 3	197 ± 3	194 ± 4
Brain					
Absolute	1.801 ± 0.012	1.810 ± 0.034	1.818 ± 0.024	1.805 ± 0.020	1.784 ± 0.020
Relative	8.98 ± 0.09	9.01 ± 0.21	9.18 ± 0.18	9.15 ± 0.11	9.23 ± 0.19
R. Kidney					
Absolute	0.716 ± 0.029	0.764 ± 0.023	0.758 ± 0.026	0.774 ± 0.034	0.720 ± 0.023
Relative	3.56 ± 0.13	3.80 ± 0.12	3.81 ± 0.10	3.91 ± 0.12	3.71 ± 0.07
Pancreas					
Absolute	0.516 ± 0.031	0.508 ± 0.016	0.502 ± 0.042	0.513 ± 0.025	0.479 ± 0.024
Relative	2.58 ± 0.18	2.53 ± 0.09	2.53 ± 0.22	2.60 ± 0.11	2.47 ± 0.11
Spleen					
Absolute	0.454 ± 0.010	0.550 ± 0.070	0.484 ± 0.014	0.464 ± 0.020	0.497 ± 0.017
Relative	2.27 ± 0.06	2.72 ± 0.33	2.44 ± 0.06	2.34 ± 0.06	2.58 ± 0.14
Thymus					
Absolute	0.258 ± 0.020	0.243 ± 0.015	0.279 ± 0.016	0.288 ± 0.009	0.270 ± 0.017
Relative	1.28 ± 0.08	1.21 ± 0.07	1.40 ± 0.06	1.46 ± 0.05	1.39 ± 0.08
Uterus					
Absolute	0.609 ± 0.088	0.506 ± 0.030	0.498 ± 0.047	0.511 ± 0.054	0.439 ± 0.041*
Relative	3.02 ± 0.41	2.52 ± 0.16	2.52 ± 0.25	2.58 ± 0.27	2.24 ± 0.18

* 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); no measurements taken for males or females receiving 50,000 ppm because of high mortality in these groups.
[b] n=8

TABLE F2
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats at the 15-Month Interim Evaluation in the 2-Year Feed Study of Benzyl Acetate[a]

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Male				
n	10	10	10	10
Necropsy body wt	440 ± 11	427 ± 11	423 ± 9	406 ± 6*
Brain				
Absolute	2.127 ± 0.016	2.109 ± 0.034	2.102 ± 0.040	2.045 ± 0.018
Relative	4.87 ± 0.15	4.95 ± 0.09	4.98 ± 0.08	5.05 ± 0.07
R. Kidney				
Absolute	1.547 ± 0.016	1.518 ± 0.043	1.508 ± 0.046	1.435 ± 0.030*
Relative	3.54 ± 0.10	3.56 ± 0.08	3.57 ± 0.09	3.54 ± 0.06
Liver				
Absolute	12.606 ± 0.385	12.416 ± 0.564	12.052 ± 0.284	12.046 ± 0.427
Relative	28.73 ± 0.84	29.04 ± 1.01	28.60 ± 0.74	29.66 ± 0.90
Female				
n	10	10	10	10
Necropsy body wt	266 ± 8	257 ± 6	250 ± 6	252 ± 6
Brain				
Absolute	1.921 ± 0.019	1.905 ± 0.018	1.886 ± 0.013	1.903 ± 0.016
Relative	7.26 ± 0.20	7.43 ± 0.14	7.59 ± 0.16	7.59 ± 0.18
R. Kidney				
Absolute	0.926 ± 0.030	0.903 ± 0.029	0.874 ± 0.019	0.873 ± 0.026
Relative	3.48 ± 0.09	3.51 ± 0.10	3.51 ± 0.06	3.47 ± 0.07
Liver				
Absolute	7.410 ± 0.306	7.109 ± 0.183	6.844 ± 0.141	7.203 ± 0.211
Relative	27.82 ± 0.78	27.63 ± 0.39	27.46 ± 0.44	28.71 ± 0.94

* Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
[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 F3
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 13-Week Feed Study of Benzyl Acetate[a]

	0 ppm	3,130 ppm	6,250 ppm	12,500 ppm	25,000 ppm	50,000 ppm
Male						
n	10	10	10	10	10	9
Necropsy body wt	31.4 ± 0.6	27.8 ± 0.7**	26.4 ± 0.8**	25.7 ± 0.3**	23.4 ± 0.3**	20.6 ± 0.3**
Brain						
Absolute	0.463 ± 0.005	0.458 ± 0.008	0.448 ± 0.006	0.451 ± 0.003	0.447 ± 0.005*	0.434 ± 0.004**
Relative	14.79 ± 0.22	16.53 ± 0.38**	17.11 ± 0.53**	17.60 ± 0.27**	19.15 ± 0.24**	21.10 ± 0.30**
R. Kidney						
Absolute	0.253 ± 0.007	0.238 ± 0.010	0.219 ± 0.008**	0.216 ± 0.006**	0.188 ± 0.008**	0.167 ± 0.004**
Relative	8.07 ± 0.18	8.54 ± 0.19	8.31 ± 0.25	8.42 ± 0.26	8.04 ± 0.27	8.10 ± 0.22
Liver						
Absolute	1.105 ± 0.025	1.039 ± 0.025	0.967 ± 0.034**	0.946 ± 0.010**	0.884 ± 0.017**	0.919 ± 0.029**
Relative	35.22 ± 0.32	37.39 ± 0.33	36.66 ± 0.80	36.88 ± 0.38	37.83 ± 0.43*	44.68 ± 1.67**
Pancreas						
Absolute	0.162 ± 0.013	0.168 ± 0.005	0.155 ± 0.010	0.151 ± 0.008	0.144 ± 0.011	0.118 ± 0.006**[b]
Relative	5.16 ± 0.40	6.06 ± 0.17	5.90 ± 0.45	5.88 ± 0.33	6.13 ± 0.41	5.74 ± 0.28[b]
Prostate Gland						
Absolute	0.038 ± 0.009[c]	0.023 ± 0.004*[c]	0.022 ± 0.004	0.022 ± 0.003	0.026 ± 0.005	0.016 ± 0.002*
Relative	1.20 ± 0.28[c]	0.84 ± 0.15[c]	0.86 ± 0.16	0.88 ± 0.12	1.11 ± 0.19	0.76 ± 0.11
Seminal Vesicle						
Absolute	0.314 ± 0.010	0.293 ± 0.012	0.267 ± 0.009**	0.239 ± 0.011**	0.202 ± 0.016**	0.143 ± 0.006**
Relative	10.03 ± 0.30	10.54 ± 0.39	10.15 ± 0.38	9.31 ± 0.43	8.62 ± 0.63*	6.95 ± 0.30**
Spleen						
Absolute	0.058 ± 0.003	0.056 ± 0.005	0.051 ± 0.005	0.050 ± 0.003	0.045 ± 0.003*	0.042 ± 0.003**
Relative	1.85 ± 0.10	2.01 ± 0.18	1.95 ± 0.19	1.95 ± 0.11	1.93 ± 0.15	2.05 ± 0.13
R. Testis						
Absolute	0.118 ± 0.002	0.113 ± 0.003	0.116 ± 0.001	0.115 ± 0.003	0.112 ± 0.001	0.103 ± 0.002**
Relative	3.76 ± 0.08	4.06 ± 0.07*	4.44 ± 0.13**	4.48 ± 0.11**	4.81 ± 0.08**	4.99 ± 0.11**
Thymus						
Absolute	0.041 ± 0.001	0.039 ± 0.002	0.036 ± 0.002	0.035 ± 0.002*	0.035 ± 0.001*	0.028 ± 0.001**
Relative	1.30 ± 0.03	1.40 ± 0.08	1.37 ± 0.07	1.35 ± 0.08	1.52 ± 0.06	1.37 ± 0.06

TABLE F3
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 13-Week Feed Study of Benzyl Acetate (continued)

	0 ppm	3,130 ppm	6,250 ppm	12,500 ppm	25,000 ppm	50,000 ppm
Female						
n	10	10	10	10	10	9
Necropsy body wt	26.8 ± 0.6	22.8 ± 0.7**	21.2 ± 0.5**	20.9 ± 0.5**	19.4 ± 0.3**	17.9 ± 0.5**
Brain						
Absolute	0.478 ± 0.007	0.460 ± 0.004*	0.455 ± 0.007**	0.456 ± 0.006**	0.447 ± 0.006**	0.432 ± 0.005**
Relative	17.92 ± 0.37	20.28 ± 0.51**	21.54 ± 0.50**	21.94 ± 0.49**	23.06 ± 0.43**	24.23 ± 0.51**
R. Kidney						
Absolute	0.188 ± 0.007	0.155 ± 0.005*	0.174 ± 0.009*	0.146 ± 0.005**	0.143 ± 0.008**	0.139 ± 0.004**
Relative	7.02 ± 0.18	6.82 ± 0.22	8.24 ± 0.46	7.01 ± 0.24	7.35 ± 0.36	7.76 ± 0.11
Liver						
Absolute	1.057 ± 0.039	0.864 ± 0.018**	0.874 ± 0.029**	0.855 ± 0.037**	0.780 ± 0.020**	0.807 ± 0.043**
Relative	39.48 ± 1.12	37.98 ± 0.70	41.23 ± 1.12	40.90 ± 1.10	40.14 ± 0.65	44.92 ± 1.69**
Pancreas						
Absolute	0.190 ± 0.013	0.157 ± 0.012	0.152 ± 0.012*	0.146 ± 0.018*	0.128 ± 0.012**	0.112 ± 0.008**
Relative	7.06 ± 0.41	6.83 ± 0.40	7.20 ± 0.63	6.90 ± 0.70	6.56 ± 0.59	6.25 ± 0.33
Spleen						
Absolute	0.077 ± 0.004	0.060 ± 0.002*	0.064 ± 0.007*	0.054 ± 0.003**	0.053 ± 0.006**	0.046 ± 0.003**
Relative	2.88 ± 0.14	2.64 ± 0.09	3.03 ± 0.36	2.59 ± 0.14	2.72 ± 0.28	2.53 ± 0.15
Thymus						
Absolute	0.051 ± 0.002	0.044 ± 0.003*	0.041 ± 0.003**	0.040 ± 0.001**	0.040 ± 0.002**	0.038 ± 0.002**
Relative	1.89 ± 0.06	1.91 ± 0.11	1.93 ± 0.14	1.92 ± 0.08	2.07 ± 0.14	2.11 ± 0.08

* 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=7
[c] n=9

TABLE F4
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice at the 15-Month Interim Evaluation in the 2-Year Feed Study of Benzyl Acetate[a]

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Male				
n	10	10	10	10
Necropsy body wt	41.5 ± 1.6	39.0 ± 1.3	38.7 ± 1.2	36.9 ± 1.7*
Brain				
Absolute	0.465 ± 0.004	0.457 ± 0.005	0.454 ± 0.007	0.447 ± 0.004*
Relative	11.35 ± 0.41	11.80 ± 0.31	11.82 ± 0.33	12.37 ± 0.59
R. Kidney				
Absolute	0.371 ± 0.011	0.351 ± 0.011	0.332 ± 0.017*	0.301 ± 0.009**
Relative	9.01 ± 0.32	9.02 ± 0.21	8.59 ± 0.37	8.29 ± 0.38
Liver				
Absolute	1.393 ± 0.068	1.270 ± 0.039	1.264 ± 0.041	1.186 ± 0.032**
Relative	33.60 ± 0.88	32.62 ± 0.66	32.79 ± 0.92	32.53 ± 0.94
Female				
n	9	10	10	10
Necropsy body wt	39.6 ± 1.8	35.8 ± 1.1	32.9 ± 1.6*	36.0 ± 1.4
Brain				
Absolute	0.482 ± 0.005	0.476 ± 0.006	0.478 ± 0.006	0.474 ± 0.005
Relative	12.42 ± 0.66	13.39 ± 0.41	14.85 ± 0.73*	13.40 ± 0.60
R. Kidney				
Absolute	0.249 ± 0.008	0.227 ± 0.005*	0.229 ± 0.009	0.219 ± 0.006**
Relative	6.42 ± 0.41	6.37 ± 0.18	7.06 ± 0.32	6.11 ± 0.26
Liver				
Absolute	1.378 ± 0.022	1.220 ± 0.035*	1.245 ± 0.060*	1.199 ± 0.023**
Relative	35.34 ± 1.53	34.24 ± 1.16	38.17 ± 1.58	33.70 ± 1.09

* 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)

APPENDIX G
HEMATOLOGY AND CLINICAL CHEMISTRY RESULTS

TABLE G1
Hematology and Clinical Chemistry Data for Rats in the 13-Week Feed Study of Benzyl Acetate[a]

	0 ppm	3,130 ppm	6,250 ppm	12,500 ppm	25,000 ppm	50,000 ppm
Male						
Hematology						
n	9	8	10	10	10	1[b]
Hematocrit (%)	36.6 ± 0.8	36.7 ± 0.4	36.4 ± 0.6	36.7 ± 0.5	36.1 ± 0.4	29.1
Hemoglobin (g/dL)	14.5 ± 0.2	14.6 ± 0.1	14.3 ± 0.2	14.7 ± 0.1	14.6 ± 0.1	13.9
Erythrocytes (10^6/μL)	8.91 ± 0.15	8.95 ± 0.06	8.75 ± 0.11	8.91 ± 0.10	8.91 ± 0.10	7.90
Mean cell volume (fL)	41.1 ± 0.3	41.0 ± 0.4	41.5 ± 0.3	41.1 ± 0.2	40.6 ± 0.2	37.0
Mean cell hemoglobin (pg)	16.2 ± 0.1	16.3 ± 0.1	16.4 ± 0.1	16.5 ± 0.1	16.4 ± 0.1	17.6
Mean cell hemoglobin concentration (g/dL)	39.6 ± 0.4	39.8 ± 0.4	39.5 ± 0.3	40.0 ± 0.4	40.5 ± 0.3	47.8
Platelets (10^3/μL)	628.0 ± 14.3	648.3 ± 23.3	630.4 ± 27.3	602.8 ± 17.3	565.5 ± 9.8*	336.0
Reticulocytes (10^6/μL)	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1
Leukocytes (10^3/μL)	5.64 ± 0.24	5.38 ± 0.31	5.65 ± 0.28	5.30 ± 0.17	5.30 ± 0.15	3.80
Segmented neutrophils (10^3/μL)	0.76 ± 0.09	0.83 ± 0.11	0.83 ± 0.06	0.75 ± 0.08	0.75 ± 0.06	0.57
Lymphocytes (10^3/μL)	4.71 ± 0.20	4.38 ± 0.27	4.67 ± 0.30	4.48 ± 0.18	4.47 ± 0.16	3.19
Atypical lymphocytes (10^3/μL)	0.04 ± 0.02	0.04 ± 0.02	0.04 ± 0.02	0.01 ± 0.01	0.03 ± 0.02	0.04
Monocytes (10^3/μL)	0.03 ± 0.01	0.06 ± 0.02	0.08 ± 0.02	0.04 ± 0.01	0.03 ± 0.01	0.00
Clinical Chemistry						
n	10	10	10	10	10	1[b]
Cholesterol (mg/dL)	62.95 ± 1.67	65.28 ± 2.65	68.20 ± 2.67	62.06 ± 2.99	63.68 ± 2.97	64.40
Triglyceride (mg/dL)	197 ± 12	196 ± 27	211 ± 15	199 ± 8	197 ± 15	39
Female						
Hematology						
n	10	9	8	8	9	0[c]
Hematocrit (%)	36.65 ± 0.86	37.34 ± 0.79	36.85 ± 1.03	38.60 ± 1.18	38.31 ± 1.13	–
Hemoglobin (g/dL)	14.4 ± 0.4	15.0 ± 0.4	14.6 ± 0.4	15.3 ± 0.4	14.9 ± 0.5	–
Erythrocytes (10^6/μL)	8.18 ± 0.17	8.42 ± 0.16	8.32 ± 0.23	8.39 ± 0.17	8.39 ± 0.17	–
Mean cell volume (fL)	44.8 ± 0.1	44.6 ± 0.3	44.3 ± 0.3	44.4 ± 0.4	44.6 ± 0.2	–
Mean cell hemoglobin (pg)	17.6 ± 0.2	17.7 ± 0.4	17.6 ± 0.1	17.6 ± 0.1	17.3 ± 0.1	–
Mean cell hemoglobin concentration (g/dL)	39.3 ± 0.3	40.1 ± 0.8	39.7 ± 0.3	39.6 ± 0.4	38.9 ± 0.2	–
Platelets (10^3/μL)	660.0 ± 22.5[d]	677.8 ± 21.5	586.1 ± 52.9	626.9 ± 30.1	611.2 ± 30.3	–
Reticulocytes (10^6/μL)	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0[e]	0.1 ± 0.0	0.1 ± 0.0	–
Leukocytes (10^3/μL)	3.54 ± 0.18	3.09 ± 0.18	3.29 ± 0.16	3.19 ± 0.14	3.83 ± 0.19	–
Segmented neutrophils (10^3/μL)	0.55 ± 0.08	0.62 ± 0.04	0.72 ± 0.10	0.67 ± 0.09	0.63 ± 0.07	–
Lymphocytes (10^3/μL)	2.92 ± 0.17	2.39 ± 0.16	2.46 ± 0.17	2.35 ± 0.13	3.11 ± 0.19	–
Atypical lymphocytes (10^3/μL)	0.02 ± 0.01	0.02 ± 0.01	0.03 ± 0.02	0.06 ± 0.02	0.03 ± 0.01	–
Monocytes (10^3/μL)	0.04 ± 0.02	0.03 ± 0.01	0.04 ± 0.03	0.04 ± 0.01	0.03 ± 0.01	–
Clinical Chemistry						
n	10	10	10	9	10	1[b]
Cholesterol (mg/dL)	85.95 ± 3.71	82.69 ± 3.72	75.84 ± 4.66	71.11 ± 5.02*	68.54 ± 3.34**	84.40
Triglyceride (mg/dL)	63 ± 5	62 ± 4	69 ± 6	63 ± 5	54 ± 3	31

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Mean ± standard error
[b] No standard error calculated due to high mortality in this group
[c] No measurements taken due to 100% mortality
[d] n=9
[e] n=7

TABLE G2
Hematology and Clinical Chemistry Data for Rats at the 15-Month Interim Evaluation in the 2-Year Feed Study of Benzyl Acetate[a]

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
Male				
n	10	10	10	10
Hematology				
Hematocrit (%)	48.2 ± 0.8	50.3 ± 1.8	47.2 ± 1.0	47.9 ± 0.3
Hemoglobin (g/dL)	15.9 ± 0.2	16.6 ± 0.6	15.7 ± 0.3	16.0 ± 0.1
Erythrocytes (10^6/μL)	9.53 ± 0.20	9.92 ± 0.37	9.23 ± 0.19	9.50 ± 0.09
Mean cell volume (fL)	50.7 ± 0.8	50.7 ± 0.3	51.2 ± 0.2	50.6 ± 0.3
Mean cell hemoglobin (pg)	16.7 ± 0.3	16.7 ± 0.1	17.1 ± 0.1	16.8 ± 0.2
Mean cell hemoglobin concentration (g/dL)	33.0 ± 0.2	33.0 ± 0.2	33.4 ± 0.1	33.4 ± 0.1
Platelets (10^3/μL)	690.9 ± 11.5	651.1 ± 18.1	664.7 ± 13.8	663.2 ± 14.3
Reticulocytes (10^6/μL)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Leukocytes (10^3/μL)	6.69 ± 0.29	5.93 ± 0.32	6.17 ± 0.46	6.13 ± 0.40
Segmented neutrophils (10^3/μL)	2.71 ± 0.23	2.19 ± 0.18	2.48 ± 0.29	2.32 ± 0.29
Lymphocytes (10^3/μL)	3.93 ± 0.13	3.63 ± 0.28	3.57 ± 0.23	3.71 ± 0.22
Monocytes (10^3/μL)	0.00 ± 0.00	0.00 ± 0.00	0.01 ± 0.01	0.00 ± 0.00
Eosinophils (10^3/μL)	0.05 ± 0.02	0.11 ± 0.03	0.12 ± 0.02	0.10 ± 0.03
Clinical Chemistry				
Cholesterol (mg/dL)	91 ± 10	82 ± 4	97 ± 6	88 ± 4
Triglyceride (mg/dL)	126 ± 12	124 ± 7	121 ± 10	139 ± 11
Alkaline phosphatase (IU/L)	86 ± 4	90 ± 4	91 ± 5	97 ± 2*
Creatine kinase (IU/L)	336 ± 58	323 ± 48	291 ± 44	379 ± 71
Sorbitol dehydrogenase (IU/L)	6 ± 0	7 ± 0	8 ± 0*	6 ± 1
Female				
n	10	10	10	10
Hematology				
Hematocrit (%)	47.8 ± 0.5	47.4 ± 0.7	47.2 ± 0.5	47.1 ± 0.5
Hemoglobin (g/dL)	16.0 ± 0.1	15.8 ± 0.2	16.0 ± 0.2	15.9 ± 0.2
Erythrocytes (10^6/μL)	8.66 ± 0.10	8.59 ± 0.15	8.57 ± 0.12	8.62 ± 0.12
Mean cell volume (fL)	55.2 ± 0.3	55.3 ± 0.5	55.4 ± 0.5	54.6 ± 0.3
Mean cell hemoglobin (pg)	18.5 ± 0.1	18.5 ± 0.2	18.6 ± 0.1	18.4 ± 0.1
Mean cell hemoglobin concentration (g/dL)	33.6 ± 0.3	33.4 ± 0.3	33.8 ± 0.2	33.7 ± 0.1
Platelets (10^3/μL)	609.6 ± 14.4	635.7 ± 18.8	589.6 ± 16.7	622.8 ± 14.3
Reticulocytes (10^6/μL)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Leukocytes (10^3/μL)	3.72 ± 0.20	3.87 ± 0.23	3.52 ± 0.24	3.76 ± 0.12
Segmented neutrophils (10^3/μL)	1.02 ± 0.09	1.20 ± 0.20	1.03 ± 0.06	1.09 ± 0.09
Lymphocytes (10^3/μL)	2.67 ± 0.14	2.61 ± 0.11	2.44 ± 0.22	2.63 ± 0.14
Monocytes (10^3/μL)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Eosinophils (10^3/μL)	0.03 ± 0.02	0.06 ± 0.01	0.05 ± 0.02	0.04 ± 0.01
Clinical Chemistry				
Cholesterol (mg/dL)	125 ± 5	130 ± 10	115.1 ± 4.5	120.9 ± 5.2
Triglyceride (mg/dL)	106 ± 8	110 ± 11	95 ± 7	90 ± 12
Alkaline phosphatase (IU/L)	81 ± 6	85 ± 4	74 ± 3	72 ± 3
Creatine kinase (IU/L)	156 ± 13	225 ± 29	146 ± 13	235 ± 48
Sorbitol dehydrogenase (IU/L)	5 ± 0	4 ± 0	5 ± 0	4 ± 0

* Significantly different ($P \leq 0.05$) from the control group by Dunn's or Shirley's test
[a] Mean ± standard error

TABLE G3
Hematology and Clinical Chemistry Data for Mice in the 13-Week Feed Study of Benzyl Acetate[a]

	0 ppm	3,130 ppm	6,250 ppm	12,500 ppm	25,000 ppm	50,000 ppm
Male						
Hematology						
n	10	9	10	10	9	8
Hematocrit (%)	43.9 ± 0.5	44.7 ± 1.5	44.3 ± 1.5	44.3 ± 0.6	44.3 ± 0.4	44.2 ± 0.6
Hemoglobin (g/dL)	14.9 ± 0.1	15.3 ± 0.4	15.7 ± 0.2[b]	15.3 ± 0.2	15.3 ± 0.2	15.2 ± 0.2
Erythrocytes (10^6/μL)	9.49 ± 0.09	9.69 ± 0.31	9.74 ± 0.33	9.80 ± 0.12	9.85 ± 0.11	9.75 ± 0.12
Mean cell volume (fL)	46.4 ± 0.2	46.0 ± 0.3	45.3 ± 0.3**	45.3 ± 0.3**	45.0 ± 0.2**	45.4 ± 0.3**
Mean cell hemoglobin (pg)	15.8 ± 0.1	15.8 ± 0.2	15.7 ± 0.2[b]	15.6 ± 0.1	15.5 ± 0.2	15.5 ± 0.1
Mean cell hemoglobin concentration (g/dL)	34.0 ± 0.3	34.2 ± 0.4	34.5 ± 0.5[b]	34.4 ± 0.3	34.6 ± 0.4	34.3 ± 0.4
Platelets (10^3/μL)	922.6 ± 32.1[b]	712.7 ± 54.2*	801.6 ± 69.9	920.7 ± 24.0	849.3 ± 64.9	779.0 ± 53.3
Reticulocytes (10^6/μL)	0.082 ± 0.016	0.127 ± 0.019	0.147 ± 0.027*	0.147 ± 0.019*	0.206 ± 0.035**	0.181 ± 0.0**[c]
Leukocytes (10^3/μL)	1.05 ± 0.20	1.03 ± 0.14	1.35 ± 0.14	1.24 ± 0.18	1.17 ± 0.14	1.26 ± 0.22
Segmented neutrophils (10^3/μL)	0.16 ± 0.06	0.16 ± 0.03	0.21 ± 0.03	0.15 ± 0.02	0.24 ± 0.04*	0.42 ± 0.15*
Lymphocytes (10^3/μL)	0.88 ± 0.15	0.88 ± 0.12	1.13 ± 0.13	1.09 ± 0.16	0.93 ± 0.12	0.84 ± 0.17
Eosinophils (10^3/μL)	0.01 ± 0.00	0.00 ± 0.00	0.01 ± 0.00	0.00 ± 0.00**	0.00 ± 0.00*	0.00 ± 0.00*
Clinical Chemistry						
n	10	10	10	10	8	7
Cholesterol (mg/dL)	95.21 ± 3.30	87.43 ± 2.60	86.20 ± 3.78	93.38 ± 4.00	89.24 ± 3.10	108.41 ± 7.32
Triglyceride (mg/dL)	72 ± 7	83 ± 7	63 ± 6	61 ± 6	56 ± 5	66 ± 3
Female						
Hematology						
n	10	10	8	9	8	8
Hematocrit (%)	44.92 ± 0.59	45.01 ± 0.73	45.06 ± 0.77	43.92 ± 0.53	42.96 ± 1.13	44.09 ± 1.04
Hemoglobin (g/dL)	15.3 ± 0.2	15.7 ± 0.2	15.5 ± 0.3	15.2 ± 0.2	14.8 ± 0.4	14.9 ± 0.3
Erythrocytes (10^6/μL)	9.68 ± 0.11	9.77 ± 0.14	9.80 ± 0.15	9.66 ± 0.08	9.53 ± 0.27	9.60 ± 0.22
Mean cell volume (fL)	46.3 ± 0.3	46.1 ± 0.4	46.0 ± 0.4	45.6 ± 0.2	45.1 ± 0.1**	46.0 ± 0.3
Mean cell hemoglobin (pg)	15.8 ± 0.1	16.1 ± 0.1	15.9 ± 0.1	15.7 ± 0.1	15.5 ± 0.2	15.6 ± 0.1
Mean cell hemoglobin concentration (g/dL)	34.1 ± 0.4	35.0 ± 0.3	34.5 ± 0.3	34.6 ± 0.2	34.4 ± 0.3	33.9 ± 0.4
Platelets (10^3/μL)	849.6 ± 39.7	787.6 ± 43.4	788.1 ± 70.2	788.4 ± 47.2	650.0 ± 67.6*	700.4 ± 36.1*
Reticulocytes (10^6/μL)	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.2 ± 0.0	0.1 ± 0.0	0.1 ± 0.0
Leukocytes (10^3/μL)	1.52 ± 0.17	1.30 ± 0.17	1.74 ± 0.13	1.37 ± 0.18	1.31 ± 0.23	1.20 ± 0.23
Segmented neutrophils (10^3/μL)	0.22 ± 0.04	0.18 ± 0.03	0.29 ± 0.04	0.20 ± 0.03	0.20 ± 0.05	0.12 ± 0.02
Lymphocytes (10^3/μL)	1.30 ± 0.16	1.11 ± 0.16	1.42 ± 0.11	1.17 ± 0.18	1.11 ± 0.23	1.08 ± 0.22
Eosinophils (10^3/μL)	0.00 ± 0.00	0.01 ± 0.00	0.02 ± 0.01	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Clinical Chemistry						
n	8	10	9	10	9	7
Cholesterol (mg/dL)	87.20 ± 5.83	79.73 ± 4.00	86.00 ± 6.46	88.82 ± 6.17	82.28 ± 4.09	90.80 ± 8.72
Triglyceride (mg/dL)	66 ± 6	54 ± 6	59 ± 6	60 ± 4[b]	59 ± 4	60 ± 8

* 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=9
[c] n=7

TABLE G4
Hematology and Clinical Chemistry Data for Mice at the 15-Month Interim Evaluation in the 2-Year Feed Study of Benzyl Acetate[a]

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Male				
n	10	10	10	10
Hematology				
Hematocrit (%)	47.4 ± 1.5	48.3 ± 0.9	49.2 ± 0.6	50.6 ± 0.9*
Hemoglobin (g/dL)	15.3 ± 0.5[b]	16.2 ± 0.3	16.5 ± 0.2*	17.0 ± 0.4**
Erythrocytes (10^6/μL)	9.80 ± 0.36	9.99 ± 0.14	10.22 ± 0.13	10.52 ± 0.17*
Mean cell volume (fL)	48.4 ± 0.4	48.3 ± 0.3	48.2 ± 0.3	48.2 ± 0.3
Mean cell hemoglobin (pg)	16.1 ± 0.2[b]	16.2 ± 0.2	16.1 ± 0.3	16.1 ± 0.2
Mean cell hemoglobin concentration (g/dL)	33.2 ± 0.2[b]	33.6 ± 0.2	33.5 ± 0.4	33.6 ± 0.5
Platelets (10^3/μL)	892.0 ± 53.1	904.6 ± 50.2	1,014.4 ± 55.2	986.8 ± 27.6[c]
Reticulocytes (10^6/μL)	0.1 ± 0.0[c]	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0
Leukocytes (10^3/μL)	2.15 ± 0.25	3.71 ± 0.58	3.35 ± 0.40	2.81 ± 0.24
Segmented neutrophils (10^3/μL)	0.70 ± 0.08	1.25 ± 0.20	0.94 ± 0.09	0.95 ± 0.16
Lymphocytes (10^3/μL)	1.42 ± 0.20	2.42 ± 0.40	2.34 ± 0.32	1.80 ± 0.14
Monocytes (10^3/μL)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Eosinophils (10^3/μL)	0.04 ± 0.01	0.05 ± 0.02	0.07 ± 0.02	0.05 ± 0.02
Clinical Chemistry				
Cholesterol (mg/dL)	108 ± 5	93 ± 3	103 ± 3	102 ± 4
Triglyceride (mg/dL)	104 ± 7	88 ± 6	90 ± 5	96 ± 9
Alkaline phosphatase (IU/L)	66 ± 2	69 ± 3	68 ± 2	67 ± 4
Creatine kinase (IU/L)	236 ± 34[d]	204 ± 25[d]	718 ± 378[e]	–[f]
Sorbitol dehydrogenase (IU/L)	31 ± 5	33 ± 3[c]	25 ± 3	34 ± 8[c]

TABLE G4
Hematology and Clinical Chemistry Data for Mice at the 15-Month Interim Evaluation in the 2-Year Feed Study of Benzyl Acetate (continued)

	0 ppm	330 ppm	1,000 ppm	3,000 ppm
Female				
Hematology				
n	9	10	10	10
Hematocrit (%)	49.7 ± 0.9	49.6 ± 0.9	48.2 ± 0.6	50.8 ± 0.9
Hemoglobin (g/dL)	16.5 ± 0.3	16.5 ± 0.3	16.2 ± 0.2	17.1 ± 0.3
Erythrocytes (10^6/μL)	10.22 ± 0.15	10.25 ± 0.16	9.95 ± 0.11	10.54 ± 0.17
Mean cell volume (fL)	48.7 ± 0.4	48.4 ± 0.3	48.6 ± 0.3	48.2 ± 0.3
Mean cell hemoglobin (pg)	16.2 ± 0.1	16.1 ± 0.1	16.3 ± 0.1	16.2 ± 0.3
Mean cell hemoglobin concentration (g/dL)	33.2 ± 0.2	33.2 ± 0.2	33.7 ± 0.3	33.6 ± 0.4
Platelets (10^3/μL)	892.0 ± 53.1	904.6 ± 50.2	1,014.4 ± 55.2	986.8 ± 27.6
Reticulocytes (10^6/μL)	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0
Leukocytes (10^3/μL)	3.54 ± 0.51	4.07 ± 0.51	3.45 ± 0.36	3.40 ± 0.50
Segmented neutrophils (10^3/μL)	1.00 ± 0.17	1.29 ± 0.22	1.05 ± 0.21	1.04 ± 0.21
Lymphocytes (10^3/μL)	2.52 ± 0.36	2.71 ± 0.32	2.36 ± 0.27	2.33 ± 0.34
Monocytes (10^3/μL)	0.00 ± 0.00[g]	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Eosinophils (10^3/μL)	0.02 ± 0.01	0.07 ± 0.04	0.04 ± 0.01	0.03 ± 0.02
Clinical Chemistry				
n	9	10	10	9
Cholesterol (mg/dL)	108 ± 3	96 ± 4	91 ± 4*	98 ± 5
Triglyceride (mg/dL)	109 ± 6	90 ± 7	85 ± 6*	94 ± 4
Alkaline phosphatase (IU/L)	144 ± 7	137 ± 7	128 ± 10	115 ± 6*[b]
Creatine kinase (IU/L)	306 ± 121[h]	239 ± 61[d]	225 ± 30[e]	–[f]
Sorbitol dehydrogenase (IU/L)	21 ± 3	21 ± 2	21 ± 3[c]	27 ± 3*

* 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=8
c n=9
d n=5
e n=3
f No measurements taken due to 100% mortality.
g n=10
h n=4

APPENDIX H
PANCREATIC ENZYME LEVELS

TABLE H1
Pancreatic Enzyme Levels for Rats in the 13-Week Feed Study of Benzyl Acetate[a]

	0 ppm	3,130 ppm	6,250 ppm	12,500 ppm	25,000 ppm
Male					
n	9	9	9	9	9
Amylase (IU/mg protein)	25.50 ± 1.22	27.34 ± 2.04	27.94 ± 1.51	30.86 ± 1.18*	30.33 ± 1.28*
Lipase (IU/mg protein)	47.93 ± 6.94	23.76 ± 6.74*	49.07 ± 3.75	32.41 ± 4.56	22.72 ± 7.07*
Carboxypeptidase A (IU/mg protein)	1.54 ± 0.09	1.86 ± 0.14	1.67 ± 0.07	1.80 ± 0.11	1.96 ± 0.13*
Chymotrypsin (IU/mg protein)	0.32 ± 0.05	0.27 ± 0.03	0.27 ± 0.01	0.22 ± 0.01**	0.23 ± 0.03*
Ribonuclease (IU/mg protein)	32.66 ± 2.72	30.42 ± 3.62	34.41 ± 2.11	31.19 ± 1.76	33.17 ± 2.91
Female					
n	9	9	9	8	9
Amylase (IU/mg protein)	22.82 ± 0.59	21.57 ± 1.99	25.67 ± 0.86*	27.06 ± 1.60*	24.42 ± 1.45
Lipase (IU/mg protein)	29.91 ± 6.23	12.14 ± 3.96	25.08 ± 6.35	21.89 ± 5.87	37.33 ± 4.48
Carboxypeptidase A (IU/mg protein)	1.77 ± 0.11	2.06 ± 0.12	1.87 ± 0.11	2.03 ± 0.16	1.54 ± 0.11
Chymotrypsin (IU/mg protein)	0.49 ± 0.17	0.40 ± 0.07	0.38 ± 0.05	0.43 ± 0.08	0.38 ± 0.05
Ribonuclease (IU/mg protein)	40.11 ± 2.51	35.98 ± 4.85	42.30 ± 4.50	50.24 ± 5.57	38.86 ± 2.44

* 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; no measurements taken for males or females receiving 50,000 ppm because of high mortality in these groups

TABLE H2
Pancreatic Enzyme Levels for Male Rats at the 15-Month Interim Evaluation in the 2-Year Feed Study of Benzyl Acetate[a]

	0 ppm	3,000 ppm	6,000 ppm	12,000 ppm
n	10	10	10	10
Amylase (IU/mg protein)	60.02 ± 3.88	67.66 ± 3.50	64.12 ± 3.46	56.77 ± 6.18
Carboxypeptidase A (IU/mg protein)	0.50 ± 0.08	0.61 ± 0.12	0.49 ± 0.12	0.44 ± 0.08
Lipase (IU/mg protein)	57.81 ± 8.38	64.52 ± 10.57	60.03 ± 5.68	73.57 ± 7.47

[a] Mean ± standard error

TABLE H3
Pancreatic Enzyme Levels for Mice in the 13-Week Feed Study of Benzyl Acetate[a]

	0 ppm	3,130 ppm	6,250 ppm	12,500 ppm	25,000 ppm	50,000 ppm
Male						
n	10	10	10	10	10	9
Amylase (IU/mg protein)	10.71 ± 1.00	8.29 ± 0.39	10.35 ± 0.96	9.29 ± 0.62	8.84 ± 0.53	11.21 ± 0.62
Lipase (IU/mg protein)	21.40 ± 3.55	22.48 ± 2.55	29.52 ± 2.87	27.27 ± 3.32	28.61 ± 2.04	33.53 ± 4.11*
Carboxypeptidase A (IU/mg protein)	0.75 ± 0.08	0.55 ± 0.03	0.72 ± 0.06	0.61 ± 0.05	0.55 ± 0.03	0.68 ± 0.04
Chymotrypsin (IU/mg protein)	0.74 ± 0.08	0.83 ± 0.10	0.63 ± 0.04	0.79 ± 0.18	0.53 ± 0.04	0.78 ± 0.10
Ribonuclease (IU/mg protein)	23.89 ± 1.79	23.05 ± 2.61	24.97 ± 2.41	25.39 ± 2.40	22.67 ± 1.47	20.56 ± 1.56
Female						
n	10	10	10	10	10	9
Amylase (IU/mg protein)	12.96 ± 0.96	9.46 ± 0.79*	9.03 ± 0.82**	10.15 ± 1.41*	9.81 ± 0.82*	11.02 ± 2.06*
Lipase (IU/mg protein)	29.89 ± 4.05	24.93 ± 3.59	25.27 ± 3.73	28.26 ± 4.12	22.56 ± 2.13	31.19 ± 5.89
Carboxypeptidase A (IU/mg protein)	0.85 ± 0.08	0.58 ± 0.06*	0.55 ± 0.06**	0.56 ± 0.07**	0.59 ± 0.05*	0.67 ± 0.13*
Chymotrypsin (IU/mg protein)	0.58 ± 0.03	0.68 ± 0.12	0.67 ± 0.07	0.68 ± 0.06	0.86 ± 0.09**	0.80 ± 0.09*
Ribonuclease (IU/mg protein)	27.25 ± 1.97	21.42 ± 2.41*	20.17 ± 2.12*	22.21 ± 2.28	17.70 ± 1.46**	21.83 ± 2.78*

* 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

APPENDIX I
CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

PROCUREMENT AND CHARACTERIZATION OF BENZYL ACETATE

Benzyl acetate was obtained from Givaudan Corporation (Clifton, NJ) in two lots. Lot 8743-84 was used throughout the 13-week studies and during the 2-year studies until depleted; lot 845585 was used during the remainder of the 2-year studies. Identity, purity, and stability analyses were conducted by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO). The reports on analyses performed in support of the benzyl acetate studies are on file at the National Institute of Environmental Health Sciences.

Both lots of the chemical, a clear, colorless liquid, were identified as benzyl acetate by infrared, ultraviolet/visible, and nuclear magnetic resonance (NMR) spectroscopy. All spectra were consistent with those expected for the structure and with the literature spectra (*Sadtler Standard Spectra*) of benzyl acetate (Figures I1 and I2).

The purity of benzyl acetate was determined by elemental analyses, Karl Fischer water analysis, titrations for free acid and ester, thin-layer chromatography (TLC), and gas chromatography. Titration for free acid was performed by dissolving samples in deionized water:2-propanol (1:1) (lot 8743-84) or ethanol (lot 845585) and titrating the samples with 0.01N aqueous sodium hydroxide. The titration was monitored colorimetrically with a phenolphthalein indicator. Titration for ester was performed by reacting for 2 hours with 1N aqueous potassium hydroxide and back-titrating with 1N sulfuric acid to the phenolphthalein endpoint (lot 8743-84) or by reacting for 2 hours with 0.5N alcoholic potassium hydroxide and back-titrating with 0.5N hydrochloric acid, with potentiometric monitoring using a combination mV/pH electrode filled with 3M potassium chloride (lot 845585). TLC was performed on Silica Gel 60 F-254 plates with two solvent systems: A) toluene:1,4-dioxane (85:15) and B) methylene chloride. Visualization was accomplished with ultraviolet (254 nm) light and with iodine vapors. Gas chromatography with flame ionization detection (FID) for lot 8743-84 was performed using two systems: A) 10% Carbowax 20 M-TPA on 80/100 Chromosorb W(AW) column and a nitrogen carrier gas at 70 mL/minute, and with two oven temperature programs: 1) 170° C, isothermal, and 2) 60° C for 5 minutes, then 60° to 200° C at 10° C/minute and B) 3% SP-2250 on 100/120 Supelcoport column and a nitrogen carrier gas at 70 mL/minute, with two oven temperature programs: 1) 120° C, isothermal, and 2) 50° C for 5 minutes, then 50° to 250° C at 10° C/minute. Gas Chromatography for lot 845585 was performed using two systems: C) 10% Carbowax 20 M-TPA on 80/100 Chromosorb W(AW) column and a nitrogen carrier gas at 70 mL/minute, with an oven temperature program of 60° C for 5 minutes, then 60° to 200° C at 10° C/minute and D) DB-5 Megabore and a helium carrier gas at 10 mL/minute, with two oven temperature programs: 1) 120° C, isothermal, and 2) 40° C for 5 minutes, then 40° to 200° C at 10° C/minute.

For lot 8743-84, elemental analyses for carbon and hydrogen were in agreement with the theoretical values for benzyl acetate. Karl Fischer analysis indicated 0.05% ± 0.01% water. Titration for free acid indicated less than 0.001 ± 0.000 mEq acid/g sample. Titration for ester indicated a purity of 101.1% ± 0.9%. TLC analysis indicated a major spot only by both systems. Gas chromatography indicated a major peak and one impurity with a relative area of approximately 0.4% of the major peak by both systems. An overall purity of 99% was determined for lot 8743-84.

For lot 845585, elemental analyses for carbon and hydrogen were in agreement with the theoretical values for benzyl acetate. Karl Fischer analysis indicated 0.13% ± 0.01% water. Titration for free acid indicated 0.0149 ± 0.0004 mEq acid/g sample. Titration for ester indicated a purity of 98.4% ± 0.9%. TLC analysis indicated a major spot only by both systems; visualization with visible and ultraviolet (366 nm) light also detected no impurities by either system. Gas chromatography indicated a major

peak and one impurity with a relative area of 0.21% of the major peak using each system. Concomitant analysis of lots 8743-84 and 845585 with gas chromatography using systems C and D indicated a purity of 100.5% ± 1.0% for lot 845585 relative to lot 8743-84. An overall purity of 98% was determined for lot 845585.

Stability studies were performed by the analytical chemistry laboratory. Gas chromatography was performed with an FID and 3% OV-225 on 80/100 mesh Supelcoport column and a nitrogen carrier gas at 60 mL/minute with an oven temperature of 130° C. These studies indicated that benzyl acetate was stable as a bulk chemical for 2 weeks at temperatures up to 60° C. The stability of the bulk chemical was monitored periodically at the study laboratory with infrared and ultraviolet spectroscopy and gas chromatography with an FID and 10% Carbowax 20M-TPA on 80/100 mesh Chromasorb W(AW) column and a nitrogen carrier gas at 35 mL/minute with an oven temperature of 150° C. No degradation of the bulk chemical was observed.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

The dose formulations were prepared weekly by mixing benzyl acetate with feed in a Patterson-Kelly twin-shell blender (Table I1). The formulations were stored in sealed, double plastic bags for no longer than 13 days.

Homogeneity and stability studies of the (330 ppm) dose formulations were conducted by the analytical chemistry laboratory. The 10 g samples of the dose formulations were extracted with 50 mL methanol and centrifuged, and 20 mL aliquots of the extracts were then mixed with a 2 mL solution of valerophenone (0.66 mg/mL in methanol) and diluted to 25 mL with methanol. The solutions were analyzed with gas chromatography with an FID and 10% SP-2330 on 100/120 Supelcoport and a nitrogen carrier gas at a flow rate of 30 mL/minute with an oven temperature program of 120° C for 20 minutes, then 120° to 200° C at 10° C/minute, with a 6-minute hold at 200° C. Homogeneity was confirmed; stability (with losses of approximately 4%) was established for at least 3 weeks when the dose formulations were stored in the dark at −20° C. Dose formulations stored open to air and light showed significant losses of benzyl acetate (approximately 11%); based on these observations, the dosed feed was stored in the dark at −20° C and was replaced daily in animal feeders during the 2-year studies.

Based on the appearance of another peak during the gas chromatographic analysis of the dose formulations for the stability studies, the dose formulations were analyzed for benzyl alcohol. Benzyl alcohol was identified in the dose formulations by full mass scan gas chromatography/mass spectroscopy. A 10 g sample of the dose formulations was extracted with 50 mL methanol and analyzed with a gas chromatographic system similar to that used in the homogeneity study, but with a helium carrier gas and an oven temperature program of 40° C for 3 minutes, then 40° to 225° C at 10° C/minute. For quantification of benzyl alcohol, dose formulations were extracted with methanol, 0.06 mg/mL valerophenone in methanol was added, and the extracts were diluted further with methanol prior to gas chromatographic analysis. The system was the same as that used for the homogeneity studies, but the oven temperature was 110° C. These analyses indicated concentrations of benzyl alcohol ranging from 0.9% to 2.0% relative to the benzyl acetate concentrations after 3 days storage under simulated animal cage conditions.

Dose formulations of benzyl acetate were analyzed by the study laboratory using gas chromatography with the system described for the homogeneity study but with an oven temperature program of 125° C for 5 minutes, then 125° to 140° C at 5° C/minute, with a 10-minute hold at 140° C. Dose formulations were analyzed four times during the 13-week studies and approximately every 6 to 8 weeks during the 2-year studies. All dose formulations for rats and mice during the 13-week and 2-year studies were equal to or within 10% of the target concentrations (Tables I2 and I3). Results of periodic referee analysis performed by the analytical chemistry laboratory indicated good agreement with the results obtained by the study laboratory for the 13-week and the 2-year dose formulations (Table I4).

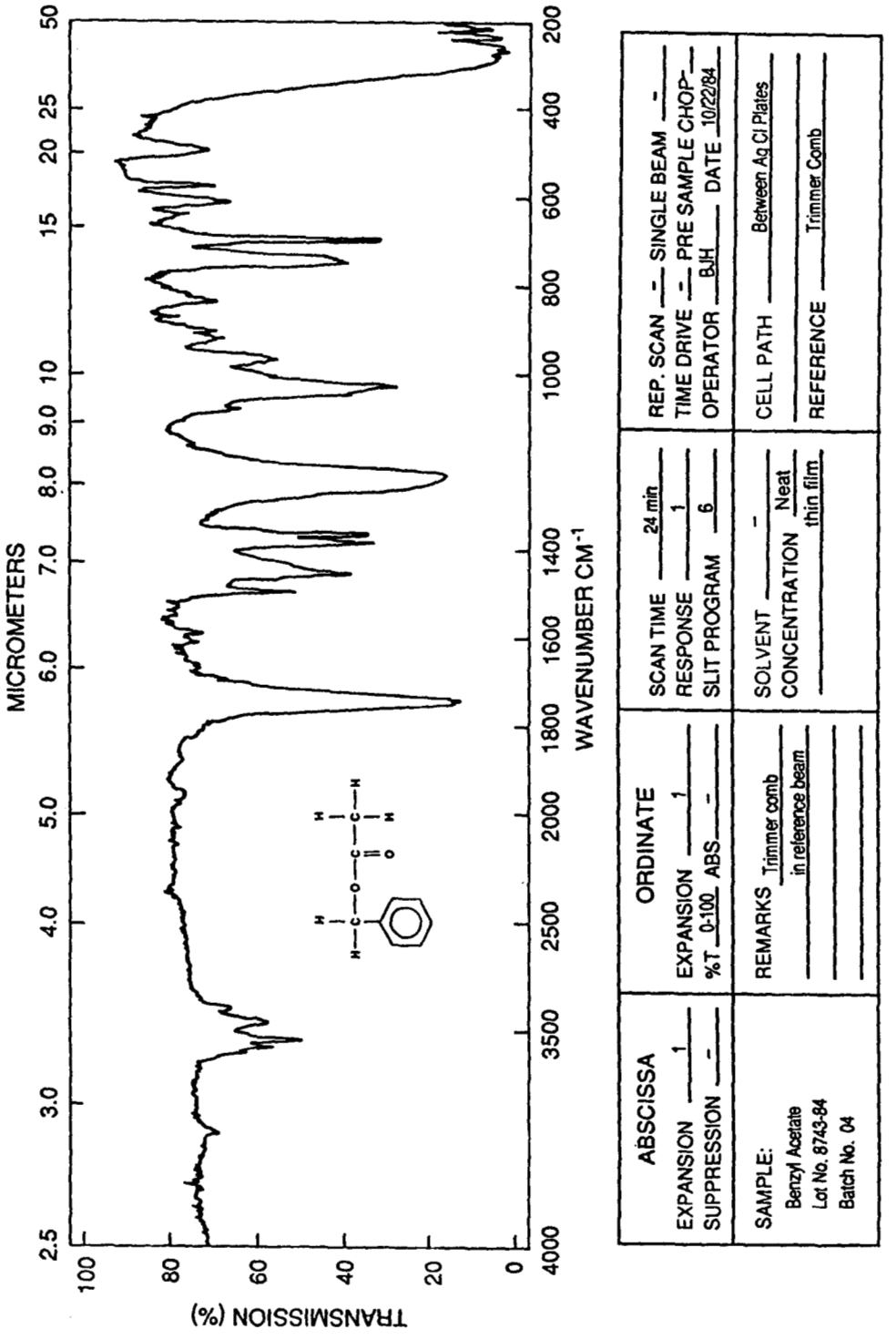

FIGURE I1
Infrared Absorption Spectrum of Benzyl Acetate

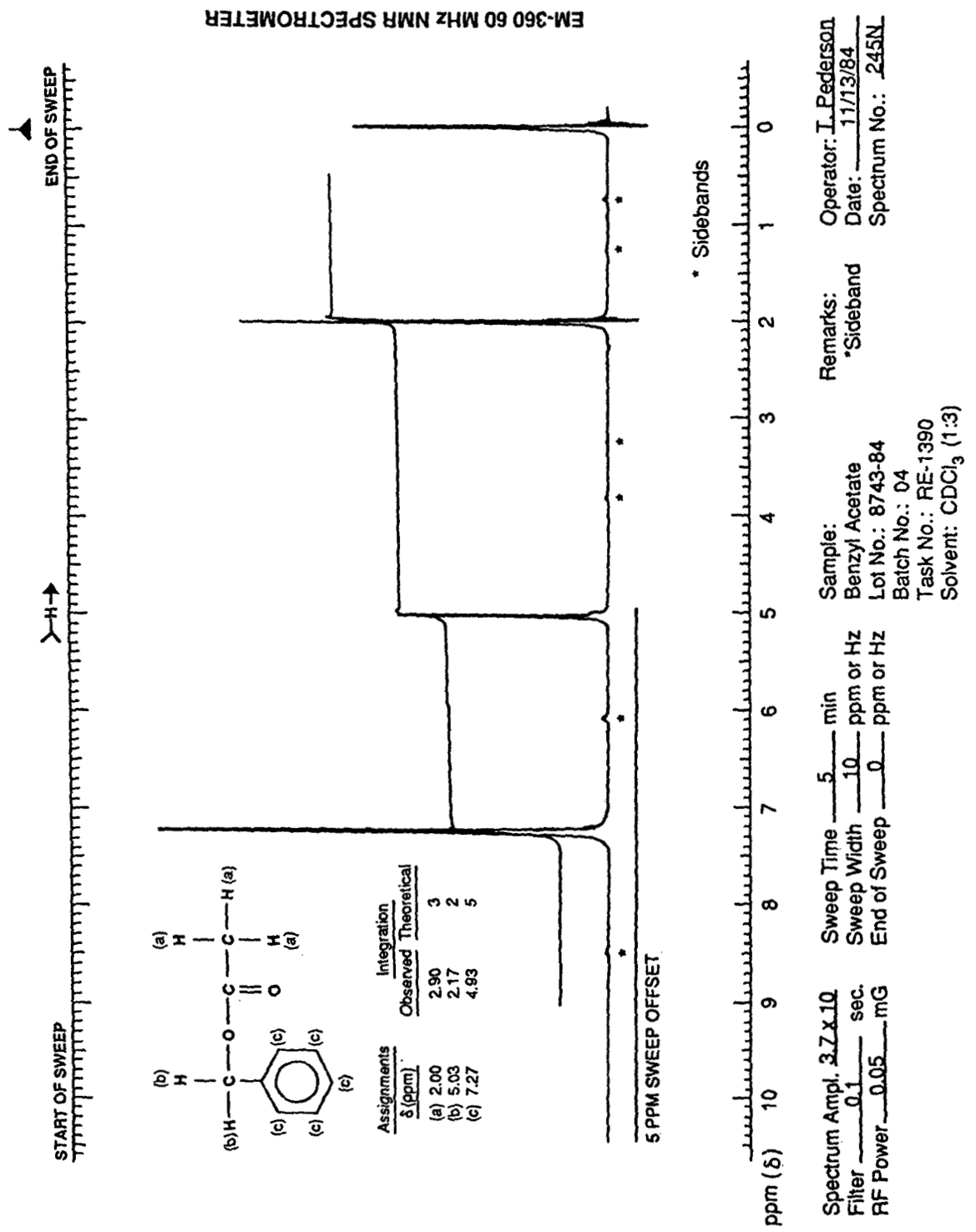

FIGURE I2
Nuclear Magnetic Resonance Spectrum of Benzyl Acetate

TABLE I1
Preparation and Storage of Dose Formulations in the Feed Studies of Benzyl Acetate

13-Week Studies	2-Year Studies
Preparation A premix of feed and benzyl acetate was prepared, then remaining feed was blended into the premix in a Patterson-Kelly twin-shell blender with the intensifier bar on for 5 minutes and off for 10 minutes. Doses were prepared weekly.	Same as 13-week studies
Chemical Lot Number 8743-84	8743-84 and 845585
Maximum Storage Time 13 days	13 days
Storage Conditions In sealed, double plastic bags in Bain Marie containers in the dark at –20° C	Same as 13-week studies
Study Laboratory Southern Research Institute, Birmingham, AL	Same as 13-week studies
Referee Laboratory Midwest Research Institute, Kansas City, MO	Same as 13-week studies

TABLE I2
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 13-Week Feed Studies of Benzyl Acetate

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration[a] (ppm)	Difference from Target (%)
17 April 1985	19 April 1985	3,130[b]	2,940	–6
		3,130[c]	2,960	–5
		3,130[d]	2,880	–8
		50,000[b]	48,200	–4
		50,000[c]	47,800	–4
		50,000[d]	47,400	–5
24 April 1985	24, 25 April 1985	3,130	2,910	–7
		3,130	2,920	–7
		6,250	6,000	–4
		6,250	6,060	–3
		12,500	12,400	–1
		12,500	12,400	–1
		25,000	24,600	–2
		25,000	24,600	–2
		50,000	49,400	–1
		50,000	49,000	–2
5 June 1985	6, 7 June 1985	3,130	3,200	+2
		3,130	3,340	+7
		6,250	6,340	+1
		6,250	6,320	+1
		12,500	12,300	–2
		12,500	12,000	–4
		25,000	24,100	–4
		25,000	24,100	–4
		50,000	48,900	–2
		50,000	48,800	–2
24 July 1985	24, 25 July 1985	3,130	2,940	–6
		3,130	2,900	–7
		6,250	5,900	–6
		6,250	6,060	–3
		12,500	12,200	–2
		12,500	12,200	–2
		25,000	24,600	–2
		25,000	24,600	–2
		50,000	49,600	–1
		50,000	49,200	–2

[a] Results of duplicate analyses
[b] Sample selection from top left of twin-shell blender
[c] Sample selection from top right of twin-shell blender
[d] Sample selection from bottom of twin-shell blender

TABLE I3
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 2-Year Feed Studies of Benzyl Acetate

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration[a] (ppm)	Difference from Target (%)
Rats				
29 August 1986	2 September 1986	3,000	2,940	-2
		3,000	2,960	-1
		6,000	5,800	-3
		6,000	5,840	-3
		12,000	11,600	-3
		12,000	11,800	-2
17, 20 October 1986	20-22 October 1986	3,000	2,960	-1
		3,000	3,000	0
		6,000	5,840	-3
		6,000	5,910	-2
		12,000	11,800	-2
		12,000	11,800	-2
5, 8 December 1986	8-10 December 1986	3,000	2,980	-1
		3,000	2,940	-2
		6,000	5,700	-5
		6,000	5,680	-5
		12,000	11,900	-1
		12,000	11,700	-2
16, 19 January 1987	19-21 January 1987	3,000	2,940	-2
		3,000	2,880	-4
		6,000	5,750	-4
		6,000	5,760	-4
		12,000	11,600	-3
		12,000	11,800	-2
27 February and 2 March 1987	2-4 March 1987	3,000	2,760	-8
		3,000	2,840	-5
		6,000	5,760	-4
		6,000	5,840	-3
		12,000	11,800	-2
		12,000	11,700	-2
27, 28 April 1987	27-29 April 1987	3,000	2,990	0
		3,000	3,000	0
		6,000	5,870	-2
		6,000	5,860	-2
		12,000	12,300	+2
		12,000	11,900	-1

TABLE I3
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 2-Year Feed Studies of Benzyl Acetate (continued)

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration (ppm)	Difference from Target (%)
Rats (continued)				
26, 29 June 1987	29 June - 1 July 1987	3,000	2,910	–3
		3,000	2,860	–5
		6,000	5,850	–2
		6,000	5,900	–2
		12,000	11,800	–2
		12,000	11,800	–2
21, 24 August 1987	24-26 August 1987	3,000	2,980	–1
		3,000	3,000	0
		6,000	6,020	0
		6,000	6,060	+1
		12,000	12,000	0
		12,000	12,000	0
26 October 1987	26-28 October 1987	3,000	3,080	+3
		3,000	3,060	+2
		6,000	6,060	+1
		6,000	6,110	+2
		12,000	12,000	0
		12,000	12,000	0
7, 8 December 1987	7-9 December 1987	3,000	2,940	–2
		3,000	2,930	–2
		6,000	5,980	0
		6,000	5,980	0
		12,000	11,700	–2
		12,000	11,800	–2
15, 18 January 1988	18-20 January 1988	3,000	2,970	–1
		3,000	2,990	0
		6,000	5,920	–1
		6,000	5,910	–2
		12,000	11,800	–2
		12,000	11,900	–1
18, 21 March 1988	21-23 March 1988	3,000	2,920	–3
		3,000	2,900	–3
		6,000	5,880	–2
		6,000	5,920	–1
		12,000	11,900	–1
		12,000	12,000	0
9 May 1988	9-11 May 1988	3,000	2,960	–1
		3,000	2,930	–2
		6,000	5,940	–1
		6,000	6,000	0
		12,000	11,800	–2
		12,000	11,900	–1

TABLE I3
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 2-Year Feed Studies of Benzyl Acetate (continued)

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration (ppm)	Difference from Target (%)
Rats (continued)				
24, 27 June 1988	27-29 June 1988	3,000	2,960	-1
		3,000	2,940	-2
		6,000	5,840	-3
		6,000	5,830	-3
		12,000	12,000	0
		12,000	11,900	-1
5, 8 August 1988	8-10 August 1988	3,000	2,980	-1
		3,000	3,040	+1
		6,000	6,020	0
		6,000	5,980	0
		12,000	12,000	0
		12,000	12,000	0
Mice				
15 August 1986	18 August 1986	330	324	-2
		330	331	0
		1,000	956	-4
		1,000	954	-5
		3,000	2,870	-4
		3,000	2,860	-5
17 October 1986	20-22 October 1986	330	310	-6
		330	310	-6
		1,000	963	-4
		1,000	962	-4
		3,000	2,960	-1
		3,000	3,000	0
5 December 1986	8-10 December 1986	330	322	-2
		330	328	-1
		1,000	974	-3
		1,000	990	-1
		3,000	2,980	-1
		3,000	2,940	-2
16, 19 January 1987	19-21 January 1987	330	310	-6
		330	309	-6
		1,000	922	-8
		1,000	950	-5
		3,000	2,940	-2
		3,000	2,880	-4
27 February and 2 March 1987	2-4 March 1987	330	298	-10
		330	304	-8
		1,000	922	-8
		1,000	928	-7
		3,000	2,760	-8
		3,000	2,840	-5

TABLE I3
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 2-Year Feed Studies of Benzyl Acetate (continued)

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration (ppm)	Difference from Target (%)
Mice (continued)				
27 April 1987	27-29 April 1987	330	338	+2
		330	322	-2
		1,000	994	-1
		1,000	991	-1
		3,000	2,990	0
		3,000	3,000	0
26 June 1987	29 June - 1 July 1987	330	316	-4
		330	319	-3
		1,000	940	-6
		1,000	960	-4
		3,000	2,910	-3
		3,000	2,860	-5
21 August 1987	24-26 August 1987	330	324	-2
		330	324	-2
		1,000	988	-1
		1,000	998	0
		3,000	2,980	-1
		3,000	3,000	0
23, 26 October 1987	26-28 October 1987	330	310	-6
		330	306	-7
		1,000	1,040	+4
		1,000	990	-1
		3,000	3,080	+3
		3,000	3,060	+2
7 December 1987	7-9 December 1987	330	325	-2
		330	328	-1
		1,000	979	-2
		1,000	949	-5
		3,000	2,940	-2
		3,000	2,950	-2
15, 18 January 1988	18-20 January 1988	330	340	+3
		330	322	-2
		1,000	982	-2
		1,000	972	-3
		3,000	2,970	-1
		3,000	2,990	0
18 March 1988	21-23 March 1988	330	334	+1
		330	336	+2
		1,000	976	-2
		1,000	984	-2
		3,000	2,920	-3
		3,000	2,900	-3

TABLE I3
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 2-Year Feed Studies of Benzyl Acetate (continued)

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration (ppm)	Difference from Target (%)
Mice (continued)				
6, 9 May 1988	9-11 May 1988	330	346	+5
		330	346	+5
		1,000	984	–2
		1,000	996	0
		3,000	2,960	–1
		3,000	2,930	–2
24 June 1988	27-29 June 1988	330	332	+1
		330	338	+2
		1,000	961	–4
		1,000	966	–3
		3,000	2,960	–1
		3,000	2,940	–2
5 August 1988	8-10 August 1988	330	332	+1
		330	328	–1
		1,000	968	–3
		1,000	1,040	+4
		3,000	2,980	–1
		3,000	3,040	+1

[a] Results of duplicate analyses

TABLE I4
Results of Referee Analysis of Dose Formulations in the 13-Week and 2-Year Feed Studies of Benzyl Acetate

Date Prepared	Target Concentration (ppm)	Determined Concentration (ppm)	
		Study Laboratory[a]	Referee Laboratory[b]
13-Week Studies			
24 April 1985	6,250	6,060	5,630 ± 120
24 July 1985	25,000	24,600	23,400 ± 100
2-Year Studies			
Rats			
17 October 1986	3,000	2,960	2,690 ± 50
28 April 1987	12,000	12,300	11,800 ± 100
9 May 1988	6,000	5,940	5,750 ± 40
Mice			
15 August 1986	1,000	956	881 ± 19[c]
17 October 1986	3,000	2,960	2,690 ± 50
23 October 1987	330	310	289 ± 5

[a] Results of duplicate analyses
[b] Results of triplicate analyses ± standard deviation
[c] Test was repeated with the same results

APPENDIX J
FEED AND COMPOUND CONSUMPTION IN THE 2-YEAR FEED STUDIES

TABLE J1
Feed and Compound Consumption by Male Rats in the 2-Year Feed Study of Benzyl Acetate

Week	0 ppm		3,000 ppm			6,000 ppm			12,000 ppm		
	Feed (g/day)[a]	Body Weight (g)	Feed (g/day)	Body Weight (g)	Dose/ Day[b] (mg/kg/day)	Feed (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)	Feed (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)
2	15.4	147	15.1	144	314	15.0	141	641	14.7	135	1,314
6	17.4	250	16.1	244	198	16.0	242	397	16.2	231	839
10	15.9	297	16.0	290	165	15.5	288	324	15.6	274	684
13	15.6	324	16.0	319	150	15.5	313	298	14.9	301	596
17	15.8	350	16.0	342	140	15.5	338	275	14.4	324	533
21	16.3	367	15.9	362	131	15.9	358	266	15.2	342	534
25	17.6	379	17.7	373	142	18.2	372	294	17.5	359	584
29	17.3	398	16.8	386	131	17.0	385	264	15.9	368	518
33	17.0	407	16.6	399	125	16.4	396	249	16.0	380	506
37	16.6	413	19.0	398	143	17.3	405	257	14.2	391	437
41	16.8	423	17.3	412	126	16.2	414	235	16.2	397	489
45	16.6	421	16.7	409	122	16.4	412	238	16.3	397	493
49	16.3	431	16.5	420	118	16.5	414	240	15.1	402	452
53	18.0	434	16.1	426	114	17.4	423	247	16.6	412	484
57	16.5	442	15.2	428	107	15.6	428	218	14.3	416	411
61	15.8	442	14.6	435	101	14.7	431	205	13.9	414	403
65	15.9	439	15.4	431	107	15.4	434	213	15.2	418	437
69	16.2	443	16.8	430	117	16.9	432	235	15.9	419	454
73	14.5	448	13.6	432	95	13.6	442	184	13.5	425	381
77	16.3	443	15.5	433	108	16.5	435	228	15.1	419	432
81	14.9	449	14.6	431	102	14.7	436	202	13.3	418	383
85	14.8	449	14.1	432	98	14.2	437	195	14.0	421	400
89	15.5	443	14.3	426	101	13.9	432	193	14.8	410	433
93	15.0	440	14.9	427	105	14.7	434	203	14.9	418	428
97	15.9	443	15.5	426	109	14.8	430	207	14.9	415	430
101	15.2	432	15.0	425	106	16.1	422	228	15.2	411	444
Mean for weeks											
1-13	16.1	255	15.8	250	207	15.5	246	415	15.4	235	858
14-52	16.7	399	16.9	389	131	16.6	388	257	15.7	373	505
53-101	15.7	442	15.1	429	105	15.3	432	212	14.7	417	425

[a] Grams of feed consumed per animal per day
[b] Milligrams of benzyl acetate consumed per kilogram body weight per day

TABLE J2
Feed and Compound Consumption by Female Rats in the 2-Year Feed Study of Benzyl Acetate

Week	0 ppm		3,000 ppm			6,000 ppm			12,000 ppm		
	Feed (g/day)[a]	Body Weight (g)	Feed (g/day)	Body Weight (g)	Dose/ Day[b] (mg/kg/day)	Feed (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)	Feed (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)
2	11.2	119	11.3	117	290	11.3	113	600	11.2	117	1,149
6	10.2	148	10.9	157	209	11.2	156	431	11.1	156	852
10	10.3	176	10.5	172	183	10.7	173	369	10.5	173	731
13	10.5	187	9.7	181	161	10.0	182	329	9.9	183	653
17	9.6	195	9.7	190	153	9.8	191	309	9.6	193	595
21	9.9	199	9.9	195	152	10.0	194	310	9.7	196	596
25	10.3	209	10.3	202	153	11.2	202	332	11.1	200	666
29	11.0	214	10.7	207	155	10.8	208	312	10.6	205	623
33	9.9	222	10.1	214	142	10.3	212	291	10.0	213	565
37	11.3	225	11.2	216	156	10.2	217	282	10.8	214	606
41	10.5	233	11.1	225	148	10.4	221	282	10.4	223	560
45	10.4	236	10.5	225	140	10.3	224	276	10.2	224	544
49	10.8	246	10.6	231	138	10.6	230	275	10.2	229	532
53	11.6	254	11.0	241	137	11.6	239	291	10.7	235	544
57	11.8	260	10.6	249	128	10.7	248	259	10.1	242	501
61	10.5	272	10.4	256	122	10.6	254	249	10.0	250	480
65	12.3	277	11.3	262	130	11.4	260	264	11.5	254	545
69	12.7	287	12.7	271	141	12.6	270	281	12.3	266	553
73	11.8	302	10.5	285	111	11.1	282	238	11.1	275	486
77	12.3	310	11.8	282	126	12.1	282	258	12.2	278	527
81	11.9	314	12.0	295	122	11.5	294	235	10.7	293	438
85	11.4	315	11.4	300	114	11.9	304	236	11.7	298	471
89	12.6	315	11.6	298	117	12.9	301	257	12.0	299	483
93	11.9	316	12.2	297	123	11.9	307	233	11.9	306	466
97	12.7	321	13.1	306	128	12.4	312	238	12.6	314	479
101	12.8	320	12.4	306	121	12.6	313	241	13.0	313	497
Mean for weeks											
1-13	10.5	157	10.6	157	211	10.8	156	432	10.7	157	846
14-52	10.4	220	10.4	212	148	10.4	211	297	10.3	211	587
52-101	12.0	297	11.6	281	125	11.8	282	252	11.5	279	498

[a] Grams of feed consumed per animal per day
[b] Milligrams of benzyl acetate consumed per kilogram body weight per day

TABLE J3
Feed and Compound Consumption by Male Mice in the 2-Year Feed Study of Benzyl Acetate

Week	0 ppm		330 ppm			1,000 ppm			3,000 ppm		
	Feed (g/day)[a]	Body Weight (g)	Feed (g/day)	Body Weight (g)	Dose/ Day[b] (mg/kg/day)	Feed (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)	Feed (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)
1	4.7	20.8	4.4	20.6	70	3.3	20.4	162	2.8	20.4	414
5	4.1	25.6	4.3	25.1	56	4.3	23.3	183	4.3	23.2	558
9	3.6	28.0	3.8	28.2	45	3.7	26.1	140	3.6	26.2	417
13	3.6	31.0	3.5	30.1	39	3.6	28.5	128	3.6	28.5	380
29	4.0	39.3	4.0	38.9	34	3.8	37.3	101	4.2	36.9	340
33	3.9	41.0	4.1	40.2	33	3.9	38.0	102	4.1	37.5	330
37	4.2	41.6	4.2	40.5	34	4.0	38.7	105	4.0	38.3	315
41	4.2	42.4	4.3	41.9	34	4.1	39.8	104	3.7	39.3	286
45	4.7	42.2	4.7	41.8	37	4.6	39.7	115	4.7	38.9	361
49	4.6	41.0	4.5	41.1	36	4.4	39.6	111	4.3	38.2	336
53	4.6	40.8	4.2	40.8	34	4.1	38.9	104	4.1	38.0	327
57	4.5	42.9	4.5	42.5	35	4.5	40.6	111	4.7	39.3	359
61	4.4	43.5	4.4	42.5	34	4.2	40.4	105	4.3	39.4	326
65	4.7	44.3	4.2	43.0	32	3.7	40.8	91	4.2	40.1	313
69	4.4	45.2	4.5	44.6	33	4.2	42.0	100	4.2	40.8	306
73	4.7	44.5	4.5	44.4	33	4.4	42.5	105	4.6	41.2	334
77	4.3	46.0	4.8	45.2	35	4.2	42.7	98	4.3	41.3	312
81	4.9	45.9	4.7	44.8	34	4.7	42.2	112	4.6	41.1	334
85	4.6	45.5	4.8	43.5	37	4.3	41.8	104	4.4	40.2	330
89	4.9	42.7	4.8	43.6	37	4.7	41.1	114	4.8	39.7	364
93	4.7	44.2	4.6	43.0	35	4.3	40.5	107	4.3	39.1	328
97	4.9	44.0	4.9	42.3	38	4.6	39.8	115	4.5	38.3	351
101	4.5	43.9	4.6	42.2	36	4.4	39.7	111	4.5	38.1	352
Mean for weeks											
1-13	4.0	26	4.0	26	53	3.7	25	153	3.6	25	442
14-52	4.3	41	4.3	41	35	4.1	39	106	4.2	38	328
53-101	4.6	44	4.6	43	35	4.3	41	106	4.4	40	334

[a] Grams of feed consumed per animal per day
[b] Milligrams of benzyl acetate consumed per kilogram body weight per day

TABLE J4
Feed and Compound Consumption by Female Mice in the 2-Year Feed Study of Benzyl Acetate

Week	0 ppm		330 ppm			1,000 ppm			3,000 ppm		
	Feed (g/day)[a]	Body Weight (g)	Feed (g/day)	Body Weight (g)	Dose/ Day[b] (mg/kg/day)	Feed (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)	Feed (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)
2	3.3	19.1	3.4	18.6	59	3.4	18.0	188	3.6	17.5	614
6	3.8	23.5	3.6	22.7	52	3.4	21.2	161	3.2	20.0	487
10	3.5	26.0	3.5	25.0	47	3.4	23.8	142	3.2	22.5	421
30	4.1	36.0	3.7	34.9	35	3.6	32.9	109	3.5	32.0	328
34	4.6	37.7	4.3	36.4	39	4.0	33.8	119	3.7	33.0	340
38	4.6	37.4	4.3	36.4	39	4.5	33.4	133	4.1	32.8	371
42	4.8	38.3	4.6	37.8	40	4.1	34.7	117	4.0	34.1	350
46	5.1	38.8	4.9	38.1	42	4.5	35.0	128	4.1	33.9	362
50	4.9	37.5	4.8	37.1	43	4.7	34.1	139	4.2	33.5	373
54	3.4	35.8	3.5	35.6	32	3.9	33.3	118	3.2	31.3	307
58	5.0	39.8	5.0	38.9	42	4.6	35.8	128	4.5	35.1	381
62	4.9	40.8	4.8	39.6	40	4.8	36.5	131	4.4	35.7	367
66	5.5	43.0	5.2	42.6	40	5.1	38.5	131	4.9	36.9	396
70	5.0	44.1	5.3	43.5	40	4.8	38.8	124	4.5	37.2	365
74	4.8	43.5	5.0	43.9	37	4.9	39.5	123	4.4	37.7	348
78	4.5	45.1	4.6	45.1	33	4.6	40.5	114	4.2	38.8	326
82	5.3	44.0	5.7	44.4	42	5.1	39.8	128	4.7	38.6	364
86	5.1	43.5	5.6	44.3	42	5.0	39.6	125	5.0	39.2	383
90	5.1	42.3	5.0	42.0	39	4.8	37.8	127	4.7	38.1	368
94	5.0	41.4	5.0	42.2	39	4.7	37.2	127	4.6	37.5	367
98	5.6	42.1	5.0	42.6	39	4.8	37.0	131	4.7	37.2	376
Mean for weeks											
1-13	3.5	23	3.5	22	53	3.4	21	164	3.3	20	507
14-52	4.7	38	4.5	37	40	4.2	34	124	3.9	33	354
52-98	5.0	42	5.0	42	39	4.8	38	126	4.5	37	362

[a] Grams of feed consumed per animal per day
[b] Milligrams of benzyl acetate consumed per kilogram body weight per day

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

TABLE K1
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 K2
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 K3
Nutrient Composition of NIH-07 Rat and Mouse Ration

Nutrient	Mean ± Standard Deviation	Range	Number of Samples
Protein (% by weight)	22.68 ± 0.79	21.30 - 24.10	24
Crude fat (% by weight)	5.49 ± 0.31	4.80 - 5.90	24
Crude fiber (% by weight)	3.54 ± 0.33	2.80 - 4.40	24
Ash (% by weight)	6.62 ± 0.95	2.40 - 7.30	24
Amino Acids (% of total diet)			
Arginine	1.308 ± 0.060	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)	6,216 ± 1,013	4,500 - 8,240	24
Vitamin D (IU/kg)	4,450 ± 1,382	3,000 - 6,300	4
α-Tocopherol (ppm)	37.95 ± 9.406	22.50 - 48.90	8
Thiamine (ppm)	19.67 ± 2.66	15.0 - 25.0	24
Riboflavin (ppm)	7.92 ± 0.87	6.10 - 9.00	8
Niacin (ppm)	103.38 ± 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 B_{12} (ppb)	38.45 ± 22.01	10.6 - 65.0	8
Choline (ppm)	3,089 ± 328	2,400 - 3,430	8
Minerals			
Calcium (%)	1.24 ± 0.12	0.96 - 1.45	24
Phosphorus (%)	0.96 ± 0.06	0.85 - 1.10	24
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)	360.54 ± 100	255.0 - 523.0	8
Manganese (ppm)	91.97 ± 6.01	81.70 - 99.40	8
Zinc (ppm)	54.72 ± 5.67	46.10 - 64.50	8
Copper (ppm)	11.06 ± 2.50	8.09 - 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 K4
Contaminant Levels in NIH-07 Rat and Mouse Ration

	Mean ± Standard Deviation[a]	Range	Number of Samples
Contaminants			
Arsenic (ppm)	0.32 ± 0.20	0.05 - 0.77	24
Cadmium (ppm)	<0.10		24
Lead (ppm)	0.25 ± 0.16	0.05 - 0.60	24
Mercury (ppm)[b]	0.05 ± 0.01	0.05 - 0.08	24
Selenium (ppm)	0.34 ± 0.10	0.20 - 0.60	24
Aflatoxins (ppb)	<5.0		24
Nitrate nitrogen (ppm)[c]	22.70 ± 8.44	10.00 - 37.0	24
Nitrite nitrogen (ppm)[c]	0.20 ± 0.22	<0.10 - 0.90	24
BHA (ppm)[d]	3.88 ± 5.69	<0.10 - 22.0	24
BHT (ppm)[d]	1.00 ± 0.28	<0.10 - 2.00	24
Aerobic plate count (CFU/g)[e]	303,417 ± 317,324	37,000 - 1,200,000	24
Coliform (MPN/g)[f]	187 ± 236	<3.00 - 1100	24
E. coli (MPN/g)[g]	3.13 ± 0.38	<3.00 - 4.00	24
Total nitrosoamines (ppb)[h]	9.68 ± 3.72	3.90 - 19.40	24
N-Nitrosodimethylamine (ppb)[h]	7.83 ± 3.12	2.90 - 14.00	24
N-Nitrosopyrrolidine (ppb)[h]	1.84 ± 1.47	1.00 - 5.40	24
Pesticides			
α-BHC[i]	<0.01		24
β-BHC	<0.02		24
γ-BHC	<0.01		24
δ-BHC	<0.01		24
Heptachlor	<0.01		24
Aldrin	<0.01		24
Heptachlor epoxide	<0.01		24
DDE	<0.01		24
DDD	<0.01		24
DDT	<0.01		24
HCB	<0.01		24
Mirex	<0.01		24
Methoxychlor	<0.05		24
Dieldrin	<0.01		24
Endrin	<0.01		24
Telodrin	<0.01		24
Chlordane	<0.05		24
Toxaphene	<0.1		24
Estimated PCBs	<0.2		24
Ronnel	<0.01		24
Ethion	<0.02		24
Trithion	<0.05		24
Diazinon	<0.1		24
Methyl parathion	<0.02		24
Ethyl parathion	<0.02		24
Malathion[j]	0.18 ± 0.20	0.05 - 0.85	24
Endosulfan I	<0.01		24
Endosulfan 2	<0.01		24
Endosulfan sulfate	<0.03		24

TABLE K4
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] Lots milled 6 August 1986 and 4 December 1986 contained 0.06 ppm and 0.08 ppm respectively; all other lots contained <0.05 ppm.
[c] Sources of contamination: alfalfa, grains, and fish meal
[d] Sources of contamination: soy oil and fish meal
[e] CFU = colony forming units
[f] MPN = most probable number
[g] Four lots contained more than 3.0 MPN/g.
[h] All values were corrected for percent recovery.
[i] BHC is hexachlorocyclohexane or benzene hexachloride.
[j] Fifteen lots contained more than 0.05 ppm.

APPENDIX L
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 F344/N rats of each sex from the control group. These samples were processed appropriately and were submitted to Microbiological Associates, Inc. (Bethesda, MD) for viral titer screening. The following tests were performed:

Method of Analysis	Time of Analysis
ELISA	
Mycoplasma arthritidis	Study termination
Mycoplasma pulmonis	Study termination
PVM (pneumonia virus of mice)	Study termination
RCV/SDA (rat coronavirus/sialodacryoadenitis virus)	Study termination
Sendai	Study termination
Hemagglutination Inhibition	
H-1 (Toolan's H-1 virus)	Study termination
KRV (Kilham rat virus)	Study termination

During the 2-year study, 15 male and 15 female F344/N rats were selected at the time of randomization and allocation of the animals to the various study groups. At 6, 12, and 18 months into the study, blood was drawn from five rats of each sex. Additional samples for viral screening at 24 months were collected from five male and five female control animals of each sex. Blood collected from each animal was allowed to clot, and the serum was separated. The serum was cooled on ice and shipped to Microbiological Associates for determination of the virus antibody titers. The following tests were performed:

Method of Analysis	Time of Analysis
ELISA	
CARB (cilia-associated respiratory bacillus)	12 months
M. arthritidis	24 months
M. pulmonis	24 months
PVM	6, 12, 18, and 24 months
RCV/SDA	6, 12, 18, and 24 months
Sendai	6, 12, 18, and 24 months
Hemagglutination Inhibition	
H-1	6, 12, 18, and 24 months
KRV	6, 12, 18, and 24 months

Mice

For the 13-week study, samples for viral screening were collected from five B6C3F$_1$ mice of each sex at terminal sacrifice. These samples were processed appropriately and were submitted to Microbiological Associates for viral titer screening. The following tests were performed:

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

During the 2-year study, 15 male and 15 female B6C3F$_1$ mice were selected at the time of randomization and allocation of the animals to the various study groups. At 6, 12, and 18 months into the study, blood was drawn from five rats of each sex. Additional samples for viral screening at 24 months were collected from five mice of each sex. Blood collected from each animal was allowed to clot, and the serum was separated. The serum was cooled on ice and shipped to Microbiological Associates for determination of the virus antibody titers. The following tests were performed:

Method of Analysis	Time of Analysis
ELISA	
Ectromelia virus	6, 12, 18, and 24 months
CARB	12 months
GDVII	6, 12, 18, and 24 months
LCM (lymphocytic choriomeningitis virus)	6, 12, and 18 months
M. arthritidis	24 months
M. pulmonis	24 months
MHV	6, 12, 18, and 24 months
Mouse adenoma virus	6, 12, 18, and 24 months
MVM	12, 18, and 24 months
PVM	6, 12, 18, and 24 months
Reovirus 3	6, 12, and 18 months
Sendai	6, 12, 18, and 24 months

Method of Analysis (continued)	Time of Analysis (continued)
Hemagglutination Inhibition	
K	6, 12, 18, and 24 months
MVM	6 months
Polyoma virus	6, 12, 18, and 24 months
Immunofluorescent Assay	
EDIM	6, 12, 18, and 24 months
LCM	24 months
Reo3	24 months

The serology results for sentinel animals are presented in Table L1.

TABLE L1
Murine Virus Antibody Determinations for Rats and Mice in the 13-Week and 2-Year Feed Studies of Benzyl Acetate

Interval	Incidence of Antibody in Sentinel Animals	Positive Serologic Reaction for
13-Week Studies		
Rats		
Study termination	0/10	None positive
Mice		
Study termination	0/10	None positive
2-Year Studies		
Rats		
6 months	0/10	None positive
12 months	0/10	None positive
18 months	0/10	None positive
24 months	0/10	None positive
Mice		
6 months	0/10	None positive
12 months	0/10	None positive
18 months	0/13	None positive
24 months	4/10	*M. arthritidis*

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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
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
401	2,4-Diaminophenol Dihydrochloride
402	Furan
403	Resorcinol
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
427	Turmeric Oleoresin
434	1,3-Butadiene
443	Oxazepam

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Public Health Service
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P.O. Box 12233, MD A0-01
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