NATIONAL TOXICOLOGY PROGRAM
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No. 309

TOXICOLOGY AND CARCINOGENESIS STUDIES OF DECABROMODIPHENYL OXIDE

(CAS NO. 1163-19-5)

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

NATIONAL TOXICOLOGY PROGRAM

The National Toxicology Program (NTP), established in 1978, develops and evaluates scientific information about potentially toxic and hazardous chemicals. This knowledge can be used for protecting the health of the American people and for the primary prevention of disease. By bringing together the relevant programs, staff, and resources from the U.S. Public Health Service, DHHS, the National Toxicology Program has centralized and strengthened activities relating to toxicology research, testing and test development/validation efforts, and the dissemination of toxicological information to the public and scientific communities and to the research and regulatory agencies.

The NTP is made up of four charter DHHS agencies: 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.

NTP TECHNICAL REPORT

ON THE

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NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 27709

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

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

Five categories of interpretative conclusions were adopted for use in June 1983 in the Technical Reports series to specifically emphasize consistency and the concept of actual evidence of carcinogenicity. For each definitive study result (male rats, female rats, male mice, female mice), one of the following quintet will be selected to describe the findings. These categories refer to the strength of the experimental evidence and not to either potency or mechanism.

- **Clear Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing a chemically related increased incidence of malignant neoplasms, studies that exhibit a substantially increased incidence of benign neoplasms, or studies that exhibit an increased incidence of a combination of malignant and benign neoplasms where each increases with dose.
- **Some Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing a chemically related increased incidence of benign neoplasms, studies that exhibit marginal increases in neoplasms of several organs/tissues, or studies that exhibit a slight increase in uncommon malignant or benign neoplasms.
- **Equivocal Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing a chemically related marginal increase of neoplasms.
- **No Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing no chemically related increases in malignant or benign neoplasms.
- **Inadequate Study of Carcinogenicity** demonstrates that because of major qualitative or quantitative limitations, the studies cannot be interpreted as valid for showing either the presence or absence of a carcinogenic effect.

Additionally, the following concepts (as patterned from the International Agency for Research on Cancer Monographs) have been adopted by the NTP to give further clarification of these issues:

> The term *chemical carcinogenesis* generally means the induction by chemicals of neoplasms not usually observed, the earlier induction by chemicals of neoplasms that are commonly observed, or the induction by chemicals of more neoplasms than are generally found. Different mechanisms may be involved in these situations. Etymologically, the term *carcinogenesis* means induction of cancer, that is, of malignant neoplasms; however, the commonly accepted meaning is the induction of various types of neoplasms or of a combination of malignant and benign neoplasms. In the Technical Reports, the words *tumor* and *neoplasm* are used interchangeably.

This study was initiated by the National Cancer Institute's Carcinogenesis Bioassay Program, now part of the National Institute of Environmental Health Sciences, National Toxicology Program. The studies described in this Technical Report have been conducted in compliance with NTP chemical health and safety requirements and must meet or exceed all applicable Federal, state, and local health and safety regulations. All NTP toxicology and carcinogenesis studies are subjected to a data audit before being presented for peer review.

Although every effort is made to prepare the Technical Reports as accurately as possible, mistakes may occur. Readers are requested to identify any mistakes so that corrective action may be taken. Further, anyone who is aware of related ongoing or published studies not mentioned in this report is encouraged to make this information known to the NTP. Comments and questions about the National Toxicology Program Technical Reports on Toxicology and Carcinogenesis Studies should be directed to Dr. J.E. Huff, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709 (919-541-3780).

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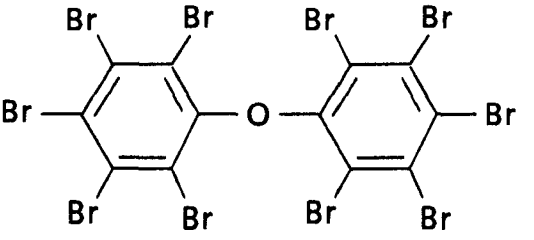

DECABROMODIPHENYL OXIDE

CAS No. 1163-19-5

$C_{12}Br_{10}O$ Molecular weight 960

Synonyms: Decabromodiphenyl ether; Bis(pentabromophenyl)ether; DBDPO

ABSTRACT

Toxicology and carcinogenesis studies of decabromodiphenyl oxide, a flame retardant for plastics and other materials, were conducted by exposing groups of 50 male and 50 female F344/N rats and B6C3F$_1$ mice at 0, 25,000, and 50,000 ppm in the diet for 103 weeks. These concentrations were selected because no toxicity was observed at any dose in the 14-day or 13-week studies and 50,000 ppm chemical in the diet is considered to be the highest dose to which rats and mice can be exposed for extended periods of time without reducing the nutritional value of the diet. No compound-related gross or microscopic pathologic effects were observed in the 14-day or 13-week studies.

Body weights of dosed male and female rats and mice in the 2-year studies were comparable to those of the controls. Decreased survival of low dose male rats was not believed to be compound related. No other effects on survival were observed in the 2-year studies. Loss of control male mice (presumably due to fighting) was significant during the first part of the study.

In the 2-year studies, nonneoplastic lesions were observed at increased incidences in rats and mice of each sex. Thrombosis and degeneration of the liver, fibrosis of the spleen, and lymphoid hyperplasia were observed in high dose male rats. Degeneration of the eye was observed in low dose female rats. Nonneoplastic lesions observed in dosed mice were granulomas in the liver of low dose males and hypertrophy in the liver of low dose and high dose males. Follicular cell hyperplasia was observed in thyroid glands of dosed male mice (control, 2/50; low dose, 10/50; high dose, 19/50).

The incidences of neoplastic nodules in the liver of low and high dose male rats (1/50; 7/50; 15/49) and high dose female rats (1/50; 3/49; 9/50) were significantly greater than those in the controls. Mononuclear cell leukemia occurred in dosed male rats with a positive trend (30/50; 33/50; 35/50); this marginal increase was not considered biologically significant. Acinar cell adenomas were observed in the pancreas of four high dose male rats, and a sarcoma was observed in the spleen of one low dose and one high dose male rat. Hepatocellular adenomas or carcinomas (combined) occurred at marginally increased incidences in dosed male mice (8/50; 22/50; 18/50). The incidences of thyroid gland follicular cell adenomas or carcinomas (combined) were increased in dosed male mice (0/50; 4/50; 3/50).

A study of decabromodiphenyl oxide absorption from the gastrointestinal tract indicated that absorption was minimal, possibly less than 1%, at the doses administered in the 2-year studies. Additional chemical analysis indicated that the decabromodiphenyl oxide used in these studies contained several

less brominated diphenyl oxides. Therefore, since absorption and toxicity of minor impurities are unknown, effects observed in these studies must be attributed to the approximately 95% pure preparation used rather than to pure decabromodiphenyl oxide.

Decabromodiphenyl oxide was not mutagenic in strains TA1535, TA1537, TA98, or TA100 of *Salmonella typhimurium* in the presence or absence of Aroclor 1254-induced Sprague-Dawley male rat or Syrian male hamster liver S9 when tested according to the preincubation protocol. Decabromodiphenyl oxide was not mutagenic in the mouse lymphoma L5178Y/TK$^{+/-}$ assay in the presence or absence of Aroclor 1254-induced F344 male rat liver S9. Decabromodiphenyl oxide did not induce sister-chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells in vitro in the presence or absence of S9 prepared from livers of Aroclor 1254-induced male Sprague-Dawley rats.

An audit of experimental data was conducted for these 2-year studies on decabromodiphenyl oxide. No data discrepancies were found that influenced the final interpretations.

Under the conditions of these 2-year feed studies of decabromodiphenyl oxide, there was *some evidence of carcinogenicity** for male and female F344/N rats as shown by increased incidences of neoplastic nodules of the liver in low dose (25,000 ppm) males and high dose (50,000 ppm) groups of each sex. There was *equivocal evidence of carcinogenicity* for male B6C3F$_1$ mice as shown by increased incidences of hepatocellular adenomas or carcinomas (combined) in the low dose group and of thyroid gland follicular cell adenomas or carcinomas (combined) in both dosed groups. There was *no evidence of carcinogenicity* for female B6C3F$_1$ mice receiving 25,000 or 50,000 ppm in the diet. Several nonneoplastic lesions were observed at increased incidences, the most notable being thyroid gland follicular cell hyperplasia in male mice.

*Categories of evidence of carcinogenicity are defined in the Note to the Reader on page 2. The discussion and vote regarding the interpretative conclusions are summarized on pages 15-16.

CONTRIBUTORS

The NTP Technical Report on the Toxicology and Carcinogenesis Studies of Decabromodiphenyl Oxide is based on the 13-week studies that began in February 1979 and ended in May 1979 and on the 2-year studies that began in July 1980 and ended in September 1982 at Hazleton Laboratories America, Inc.

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PEER REVIEW PANEL

The members of the Peer Review Panel who evaluated the draft Technical Report on decabromodiphenyl oxide on August 14, 1985, are listed below. Panel members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, Panel members have five major responsibilities: (a) to ascertain that all relevant literature data have been adequately cited and interpreted, (b) to determine if the design and conditions of the NTP studies were appropriate, (c) to ensure that the Technical Report presents the experimental results and conclusions fully and clearly, (d) to judge the significance of the experimental results by scientific criteria, and (e) to assess the evaluation of the evidence of carcinogenicity and other observed toxic responses.

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SUMMARY OF PEER REVIEW COMMENTS ON THE TOXICOLOGY AND CARCINOGENESIS STUDIES OF DECABROMODIPHENYL OXIDE

On August 14, 1985, the draft Technical Report on the toxicology and carcinogenesis studies of decabromodiphenyl oxide received peer review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The review meeting began at 9:00 a.m. in the Conference Center, Building 101, South Campus, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.

Dr. H. Matthews, NTP, began the discussion with a summary of the study design, results, and conclusions. Dr. Mirer, a principal reviewer, considered the chemical disposition study to be a significant contribution to the Technical Report and suggested the description of the findings should be in the Results section rather than only in an appendix. The results could be important in interpretation of studies involving doses by other routes or biologic monitoring data. Further, Dr. Mirer said that statistical tests would be desirable where there are increased nontumor pathologic effects, whether or not the lesions are correlated with neoplasia.

As a second principal reviewer, Dr. Swenberg agreed with the conclusions. He said that the decreased survival in control male mice was very striking and could be highlighted in the Abstract as well as the text. A summary paragraph should be included that states the implications of the pharmacokinetic data with respect to the doses used in the studies. [See page 11.]

As a third principal reviewer, Dr. Turnbull also agreed with the conclusions. He noted that the increased incidence of leukemia in dosed male rats was not considered biologically significant due to a high incidence in the concurrent controls and lack of a significant increase in females. Yet, in the females, the incidence was almost significant. Dr. E. McConnell, NIEHS, stated that the reported incidences of leukemia in Fischer rats have been increasing over the last couple of years, primarily, he thought, because of better diagnosis, particularly in the early stages, rather than because of a true increase in the incidence. Thus, concurrent control rates would be more appropriate for comparisons than would historic rates.

As a fourth principal reviewer, Dr. Hooper agreed with the conclusions in female rats and male and female mice. He said that the conclusions in male rats should be upgraded to clear evidence of carcinogenicity, based on the substantial dose-related increases in benign liver tumors (neoplastic nodules). Dr. Matthews said that the conclusion reflected, in part, that there were no increases in hepatocellular carcinomas. Dr. Kociba contended that the categorization for rats was too strong in that only a small percentage of neoplastic nodules progress to malignant tumors. Rather, a category such as "some evidence of benign tumor induction" would be more appropriate. Dr. Perera said that until the guidelines are changed, the Panel should adhere to the wording as given in the Note to the Reader and on that basis she agreed with Dr. Hooper. Dr. Hooper commented that the design would have been improved if only a single lot of the 99% pure chemical had been used. The use of four lots of varying purity coupled with very low (2%) absorption might have affected the experimental outcome, particularly if the active agents were present as impurities in only one of the less pure batches. Dr. Matthews acknowledged the low absorption but said that it was confirmed that decabromodiphenyl oxide was absorbed. The absorption of impurities is not known. Further, only two lots were used in the long-term studies and they would be identified.

There was considerable discussion about the strength of evidence for carcinogenicity in male mice. Dr. Kociba stated that poor survival in concurrent controls pointed to use of historical rates as appropriate. Since the rates of hepatocellular adenomas or carcinomas (combined) for both low dose and high dose groups were within the historical control range, he felt that the correct conclusion was no evidence of carcinogenicity. Dr. J. Huff, NIEHS, noted that the low dose and high dose rates were

greater (36% and 44%) than the mean historical rate (30%); thus, equivocal evidence of carcinogenicity was proper. Dr. Perera commented that the stated genetic nonuniformity of the mice was another reason that concurrent controls should be used. Dr. Purchase said that he could not accept equivocal evidence of carcinogenicity as there was a lack of statistical significance with both liver and thyroid gland neoplasms. Dr. Huff reminded the Panel that there was a statistically significant increase in liver neoplasia for low dose male mice, and Dr. G. Boorman, NIEHS, said the conclusion was influenced by the high incidence of thyroid gland follicular cell hyperplasias. Dr. Swenberg was of the opinion that the conclusion was correct in that the liver and thyroid gland findings were neither clearly positive nor clearly negative. Dr. Tannenbaum asked for more consistency in deciding when to use historical controls. Dr. Swenberg commented that, for a variable tumor, historical control values are appropriate for comparison purposes.

Dr. Hooper moved that the conclusion of some evidence of carcinogenicity for female rats be accepted as written. Dr. Turnbull seconded the motion, and it was approved by 10 affirmative votes with 1 abstention (Dr. Kociba). Dr. Hooper moved that the conclusion of no evidence of carcinogenicity for female mice be accepted as written. Dr. Turnbull seconded the motion, and it was approved by 10 affirmative votes with 1 abstention (Dr. Kociba). Dr. Hooper moved that the conclusion for male mice, equivocal evidence of carcinogenicity, be accepted as written. Dr. Turnbull seconded the motion, and it was approved by six affirmative votes (Dr. Hooper, Dr. Kotelchuck, Dr. Mirer, Dr. Perera, Dr. Swenberg, and Dr. Turnbull) with three negative votes (Dr. Crowley, Dr. Purchase, and Dr. Tannenbaum) and one abstention (Dr. Kociba). Dr. Hooper moved that the conclusion for male rats be changed to clear evidence of carcinogenicity. Dr. Perera seconded the motion, and it was defeated by six negative votes (Dr. Jones, Dr. Kotelchuck, Dr. Purchase, Dr. Swenberg, Dr. Tannenbaum, and Dr. Turnbull) with four affirmative votes (Dr. Crowley, Dr. Hooper, Dr. Mirer, and Dr. Perera) and one abstention (Dr. Kociba). Dr. Hooper then moved that the conclusion for male rats, some evidence of carcinogenicity, be accepted as written. The motion was seconded, and it was approved by eight affirmative votes; there were two negative votes (Dr. Crowley and Dr. Mirer) and one abstention (Dr. Kociba).

I. INTRODUCTION

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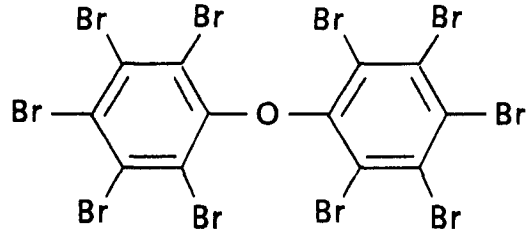

DECABROMODIPHENYL OXIDE

CAS No. 1163-19-5

$C_{12}Br_{10}O$ **Molecular weight 960**

Synonyms: Decabromodiphenyl ether; Bis(pentabromophenyl)ether; DBDPO

Decabromodiphenyl oxide is a completely brominated aromatic that is a white to off-white powder. This relatively inert chemical has found considerable use as a flame retardant because of its capacity to release bromine on incineration. Bromine suppresses combustion by reacting with free radicals. Some chemical and physical properties of this compound are listed in Table 1.

Use and Production

Decabromodiphenyl oxide is used as a flame retardant primarily in high-impact polystyrene but is also used in adhesives, epoxy resins, synthetic fibers, and plastics such as ABS (acrylonitrile/butadiene/styrene) polymers and polyethylene (AIHA, 1981; Webber, 1983). Production figures for decabromodiphenyl oxide are not current, but production is estimated to exceed 10 million pounds per year (Webber, 1983).

Environmental Occurrence and Human Exposure

No reports of environmental contamination by decabromodiphenyl oxide were found. Laboratory studies indicate that this compound does not accumulate in fish and that it is degraded by ultraviolet light in the wavelength range and intensity of sunlight (Norris et al., 1973). Human exposure to decabromodiphenyl oxide occurs in the course of manufacture and use. Surveys have determined employee time-weighted average exposures of 1-4 mg/m^3 in air with excursions up to 42 mg/m^3 during short tasks. More than 90% of the particles in air were smaller than 10 microns in diameter. Based on the nuisance nature of this material, the recommended workplace environmental exposure level in air is 5 mg/m^3 (8-hour time-weighted average for a 40-hour week) (AIHA, 1981). A health assessment of workers exposed to decabromodiphenyl oxide in the course of manufacture found a higher than normal prevalence of primary hypothyroidism and a significant reduction of calf sensory and fibula motor velocities but no other significant dermatologic or neurologic effects or other adverse health effects. However, the investigators could not be sure if the observed effects were due to exposure to decabromodiphenyl oxide or prior exposure to polybrominated biphenyls that were previously manufactured in this plant. Polybrominated biphenyls persisted in the serum of exposed employees, whereas decabromodiphenyl oxide was not detected (Bahn et al., 1980). Adverse effects have not been reported as a result of decabromodiphenyl oxide use, but no studies have been conducted to determine the effects of dermal or oral absorption of the chemical from treated cloth (Ulsamer et al., 1980). Repeated application of decabromodiphenyl oxide in petrolatum to human skin three times per week for 3 weeks did not produce any adverse effect (Norris et al., 1973, 1975a).

Absorption, Distribution, and Metabolism

Studies with ^{14}C-labeled decabromodiphenyl oxide administered orally to Sprague-Dawley rats indicate that more than 99% of the administered label was excreted in feces within 2 days

TABLE 1. PROPERTIES OF DECABROMODIPHENYL OXIDE (a)

Melting range	290°-306° C
Decomposition point	425° C
Specific gravity	3.0
Vapor pressure	5 mm Hg at 306° C
Solubility at 25° C	Water: 20-30 ppb Cottonseed oil: 600 ppm Acetone: 500 ppm Chlorobenzene: 6,000 ppm *o*-Xylene: 8,700 ppm
Technical product composition:	Decabromodiphenyl oxide, 77.4% Nonabromodiphenyl oxide, 21.8% Octabromodiphenyl oxide, 0.8%

(a) Norris et al., 1973; Kociba et al., 1975; AIHA, 1981

following administration (Norris et al., 1973, 1975a). An analysis of bromine in tissues following long-term exposure in diets that provided 0.1 mg/kg per day to rats indicated a slight increase in bromine content in liver and adipose tissue at 90 days but no significant increase following 12 months of exposure (Norris et al., 1975a). A significant increase in the bromine content of adipose, but no other tissues, was observed following a similar dose of decabromodiphenyl oxide for 2 years but not at lower doses (Kociba et al., 1975). There was no indication as to whether the failure of decabromodiphenyl oxide to accumulate in tissues was due to lack of absorption from the gastrointestinal tract or rapid metabolism and clearance.

Effects on Animals

Decabromodiphenyl oxide has low acute toxicity (Norris et al., 1973, 1975a,b; Kociba et al., 1975). Oral administration of doses up to 2,000 mg/kg as a 10% suspension in corn oil failed to produce any signs of toxicity in rats either directly after dosing or during a 14-day observation period. This chemical is not a dermal irritant to rats or rabbits and is only mildly irritating when placed in the eyes of rabbits. Repeated oral doses of up to 800 mg/kg per day produced no overt indication of toxicity during a 30-day study. Gross pathologic changes observed following repeated dosing were limited to dose-related liver enlargement. Histopathologic examination of organs and tissues from animals in the repeated-dose studies revealed lesions in the liver, kidney, and thyroid gland. Lesions observed were centrilobular cytoplasmic enlargement and vacuolation in liver, hyaline degenerative changes in the kidney, and hyperplasia of the thyroid gland. It was speculated that thyroid gland hyperplasia could have resulted from competition between bromine and iodine in the thyroid gland, but no evidence of this effect was presented. A dose of 8 mg/kg per day was established as a no-effect level and 80 mg/kg per day as a marginal-effect level (Norris et al., 1973). Carlson (1980) studied a series of diphenyl oxides for their capacity to induce hepatic enzymes and reported that decabromodiphenyl oxide increased liver weight but had no significant effect on hepatic enzymes. The same study reported penta- and octabromodiphenyl oxides to be potent inducers of hepatic enzymes. In a separate study of the porphyrinogenic action of fire retardants, decabromodiphenyl oxide was found to be nonporphyrinogenic in Japanese quail or chick embryo liver cells (Koster et al., 1980).

Teratogenicity and Reproductive Effects

Daily intubation of pregnant female rats on gestation days 6-15 with 0, 10, 100, or 1,000 mg decabromodiphenyl oxide/kg, suspended in corn oil, caused no teratogenic response (Norris et al., 1973, 1975a). Some fetal toxicity was observed in these studies in the form of subcutaneous edema and delayed ossification of normally developed bones of the fetal skull. These effects were observed at the high dose only.

Mutagenicity

Published information regarding decabromodiphenyl oxide mutagenicity is limited to a report that it does not cause cytogenetic aberrations in rat bone marrow cells (Norris et al., 1975a) and an unconfirmed report that it is not mutagenic in Salmonella (Ulsamer et al., 1980). NTP studies of decabromodiphenyl oxide mutagenicity indicate that it was not mutagenic in *Salmonella typhimurium* strains TA1535, TA1537, TA98, or TA100 in the presence or absence of Aroclor 1254-induced male Sprague-Dawley rat or male Syrian hamster liver S9 when tested according to the preincubation protocol (Appendix G). It was also not mutagenic in the mouse lymphoma L5178Y/TK$^{+/-}$ assay in the presence or absence of Aroclor 1254-induced male F344 rat liver S9. Tests for cytogenetic effects in Chinese hamster ovary cells indicated that this chemical does not cause chromosomal aberrations or sister-chromatid exchanges either in the presence or asence of S9 prepared from livers of Aroclor 1254-induced male Sprague-Dawley rats.

Carcinogenicity

A 2-year study of decabromodiphenyl oxide for chronic toxicity and carcinogenicity to male and female Sprague-Dawley rats (25 males and 25 females per dose) maintained on diets providing 0, 0.01, 0.1, or 1.0 mg/kg per day indicated no discernible alteration in appearance, behavior, body weight, feed consumption, hematologic analyses, urinalysis, clinical chemistry, organ weights, survival, or tumor incidence (Kociba et al., 1975). However, the doses and number of animals used in this study have been questioned as to their adequacy to determine carcinogenic potential (Ulsamer et al., 1980).

Study Rationale

Decabromodiphenyl oxide was chosen for study by the NTP as part of a class study of flame retardants. Since the low volatility and solubility of decabromodiphenyl oxide precluded inhalation, gavage, or drinking water exposure, the chemical was given in feed for systemic exposure.

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF DECABROMODIPHENYL OXIDE

PREPARATION AND CHARACTERIZATION OF FORMULATED DIETS

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

- Study Design
- Source and Specifications of Animals
- Animal Maintenance
- Clinical Examinations and Pathology
- Statistical Methods

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF DECABROMODIPHENYL OXIDE

Decabromodiphenyl oxide was obtained in four lots from Dow Chemical USA (Table 2). Purity and identity determinations were conducted on all lots (Appendix H). All four lots of the study material were identified as decabromodiphenyl oxide by infrared and ultraviolet/visible spectroscopy. All spectra were consistent with the structure of decabromodiphenyl oxide. The purity of all lots of study material was determined by elemental analysis, thin-layer chromatography, and high-performance liquid chromatography.

Results of elemental analyses of lot no. 08287-2 for carbon and bromine agreed with the theoretical values. This lot contained 0.04% water. Only a single spot was detected by thin-layer chromatography. Two incompletely resolved impurities with a combined area of 1.3% that of the major peak were detected by high-performance liquid chromatography. Cumulative data indicated that this lot was 99% pure.

Results of elemental analyses of lot no. D12478 for bromine agreed with the theoretical value; that for carbon was slightly low. This lot contained less than 0.05% water. Only a single spot was detected by thin-layer chromatography. Two impurities with a combined area of 2.8% that of the major peak were detected by high-performance liquid chromatography. Cumulative data indicated that this lot was approximately 97% pure.

Results of elemental analyses of lot no. MM04080-1 were low for both carbon and bromine. A trace impurity spot was detected by thin-layer chromatography. Four impurities with a combined area of 4.5% that of the major peak were detected by high-performance liquid chromatography. Cumulative data indicated that this lot was approximately 96% pure.

Results of elemental analyses of lot no. MM811102-3-1 for carbon and bromine agreed with the theoretical values. This lot contained 0.01% water. A minor impurity spot was detected by thin-layer chromatography. The initial high-performance liquid chromatographic analysis indicated three impurities with a combined area of 2.7% that of the major peak. A subsequent analysis performed by the analytical chemistry laboratory indicated the presence of three impurities with relative areas of 0.3%, 3.7%, and 1.7% that of the major peak. The two larger impurities were identified as unspecified isomers of nonabromodiphenyl oxide by mass spectroscopy. Cumulative data indicated that this lot was 94%-97% pure.

Decabromodiphenyl oxide was stable for 2 weeks at 60° C (Appendix H). Decabromodiphenyl oxide was stored frozen. Periodic characterization of decabromodiphenyl oxide by infrared spectroscopy and thin-layer or high-performance liquid chromatography detected no appreciable deterioration over the course of the studies.

TABLE 2. IDENTITY AND SOURCE OF LOTS USED IN THE FEED STUDIES OF DECABROMODIPHENYL OXIDE

	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
Lot Numbers	08287-2	08287-2, D12478	MM04080-1, MM81102-3-1
Date of Initial Use of Each Lot	10/17/78	2/27/79, 3/13/79	7/24/80, 3/25/82
Supplier	Dow Chemical USA (Midland, MI)	Same as 14-d studies	Same as 14-d studies

PREPARATION AND CHARACTERIZATION OF FORMULATED DIETS

Formulated diet mixtures were shown to be homogeneous (Appendix I). Decabromodiphenyl oxide was stable in feed when stored for 2 weeks at 25° C. Formulated diets were prepared by adding a dry premix (approximately equal amounts of feed and decabromodiphenyl oxide) to the feed (Table 3). The mixture then was blended for 15 minutes. In the 13-week studies, the formulated diets were stored frozen for no more than 1.5 weeks. In the 2-year studies, the formulated diets were stored at 14° C for no longer than 7 days.

Mixtures of decabromodiphenyl oxide in feed were analyzed to confirm that correct concentrations were prepared for administration to the animals (Appendix J). The study laboratory's periodic analysis during the 2-year studies indicated that 27/28 samples (96%) were within ± 10% of the target concentration (Table 4; Appendix K).

TABLE 3. PREPARATION AND STORAGE OF FORMULATED DIETS IN THE FEED STUDIES OF DECABROMODIPHENYL OXIDE

	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
Preparation	Decabromodiphenyl oxide mixed directly into feed and blended in a 5-kg Hobart mixer for approximately 15 min	Appropiate amount of decabromodiphenyl oxide and half of the feed premixed in Hobart mixing bowl for 5 min. The premix and 5 kg feed mixed for 12 min in a Patterson-Kelly® V-blender.	Decabromodiphenyl oxide was weighed and mixed with a small amount of feed for 2 min. Premix was transferred to a Hobart mixer with 5 kg of NIH 07 Rat and Mouse Ration and mixed for 1 min/kg of feed. This mixture was transferred to a Patterson-Kelly® twin-shell blender with the required amount of feed and mixed for 1 min/kg feed.
Maximum Storage Time	1.5 wk	1.5 wk	1 wk
Storage Conditions	Room temperature	Room temperature; 6 kg frozen, then thawed before use	14° C

TABLE 4. SUMMARY OF RESULTS OF ANALYSIS OF FORMULATED DIETS IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

	Target Concentration	
	25,000 ppm	50,000 ppm
Experimental mean	24,148	49,207
Standard deviation	1,403	2,206
Coefficent of variation (percent)	5.8	4.5
Range	22,270-26,450	46,050-53,600
Number of samples	14	14

II. MATERIALS AND METHODS

FOURTEEN-DAY STUDIES

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Charles River Breeding Laboratories and held for approximately 3 weeks before the studies began. Groups of five males and five females were fed diets containing 0, 5,000, 10,000, 20,000, 50,000, or 100,000 ppm decabromodiphenyl oxide for 14 days. Rats and mice were observed daily and were weighed on days 1, 7, and 14. A necropsy was performed on all animals. Details of animal maintenance are presented in Table 5.

THIRTEEN-WEEK STUDIES

Thirteen-week studies were conducted to evaluate the cumulative toxic effects of repeated administration of decabromodiphenyl oxide and to determine the concentrations to be used in the 2-year studies.

Four-week-old male and female F344/N rats and 5-week-old B6C3F$_1$ mice were obtained from Charles River Breeding Laboratories, observed for 4 weeks, and then assigned to cages according to a table of random numbers. The cages were then assigned to dosed and control groups according to another set of random numbers. Diets containing 0, 3,100, 6,200, 12,500, 25,000, or 50,000 ppm decabromodiphenyl oxide were fed to groups of 10 rats and 10 mice of each sex. Animals were housed five per cage. Formulated or control diets and water were available ad libitum.

Animals were checked twice daily; moribund animals were killed. Feed consumption was measured weekly by cage. Animal weights were recorded weekly. At the end of the 13-week studies, survivors were killed. A necropsy was performed on all animals except those excessively autolyzed or cannibalized. Tissues and groups examined are listed in Table 5.

TWO-YEAR STUDIES

Study Design

Diets containing 0, 25,000, or 50,000 ppm decabromodiphenyl oxide were fed to groups of 50 male and 50 female rats and 50 male and 50 female mice for 103 weeks.

Source and Specifications of Animals

The male and female F344/N rats and B6C3F$_1$ (C57BL/6N, female, × C3H/HeN, MTV$^-$, male) mice used in this study were produced under strict barrier conditions at Charles River Breeding Laboratories under a contract to the Carcinogenesis Program. Breeding stock for the foundation colonies at the production facility originated at the National Institutes of Health Repository. Animals shipped for study were progeny of defined microflora-associated parents that were transferred from isolators to barrier-maintained rooms. Animals were shipped to the study laboratory at 5-6 weeks of age. The animals were quarantined at the study laboratory for 14 days (rats) or 16 days (mice). Thereafter, a complete necropsy was performed on five animals of each sex and species to assess their health status. The rats were 7-8 weeks old and the mice were 9 weeks old when placed on study. The health of the animals was monitored during the course of the study according to the protocols of the NTP Sentinel Animal Program (Appendix L).

A quality control skin grafting program has been in effect since early 1978 to monitor the genetic integrity of the inbred mice used to produce the hybrid B6C3F$_1$ study animal. In mid-1981, data were obtained that showed incompatibility between the NIH C3H reference colony and the C3H colony from a Program supplier. In August 1981, inbred parental lines of mice were further tested for genetic integrity via isozyme and protein electrophoresis profiles that demonstrate phenotype expressions of known genetic loci.

The C57BL/6 mice were homogeneous at all loci tested. Eighty-five percent of the C3H mice monitored were variant at one to three loci, indicating some heterogeneity in the C3H line from this supplier. Nevertheless, the genome of this line is more homogeneous than that of randomly bred stocks.

TABLE 5. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE FEED STUDIES OF DECABROMODIPHENYL OXIDE

	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
EXPERIMENTAL DESIGN			
Size of Study Groups	5 males and 5 females of each species	10 males and 10 females of each species	50 males and 50 females of each species
Doses	0, 5,000, 10,000, 20,000, 50,000, or 100,000 ppm decabromodiphenyl oxide in the diet	0, 3,100, 6,200, 12,500, 25,000, or 50,000 ppm decabromodiphenyl oxide in the diet	0, 25,000, or 50,000 ppm decabromodiphenyl oxide in the diet
Date of First Dose	Rats--10/17/78; mice--10/18/78	2/27/79	Rats--9/23/80; mice--7/25/80
Date of Last Dose	Rats--10/31/78; mice--11/1/78	5/29/79	Not available
Duration of Dosing	14 consecutive days	13 wk	103 wk
Type and Frequency of Observation	Weighed on d 1, 7, and 14; observed daily	Observed 2 × d; body weights, feed consumption, clinical signs, and behavior recorded 1 × wk	Observed 2 × d; weighed initially, 1 × wk for 12 wk, monthly thereafter until wk 100 or 101, then every 2 wk
Necropsy and Histologic Examination	Necropsy performed on all animals; tissues examined: gross lesions, skin, mandibular lymph nodes, mammary glands, salivary glands, thigh muscle, sciatic nerve, sternebrae, femur, or vertebrae including marrow, costochondral junction (rib), thymus, larynx, trachea, lungs and bronchi, heart, thyroid gland, parathyroids, esophagus, stomach, duodenum, jejunum, tissue masses, ileum, colon, cecum, rectum, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenal glands, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, nasal cavity, brain, pituitary gland, spinal cord, and eyes	Necropsy performed on all animals; the following tissues examined histologically for control and high dose groups: gross lesions and tissue masses, mandibular or mesenteric lymph nodes, salivary gland, sternebrae, femur, or vertebrae including marrow, thyroid gland, parathyroids, small intestine, colon, liver, gallbladder (mice), prostate/testes or ovaries/uterus, lung and mainstem bronchi, heart, esophagus, stomach, brain, thymus, trachea, pancreas, spleen, kidneys, adrenal glands, urinary bladder, pituitary gland, spinal cord (if neurologic signs present), eyes (if grossly abnormal), and mammary gland	Necropsy and histologic examination performed on all animals; the following tissues were examined: gross lesions, skin, mandibular lymph nodes, mammary glands, salivary glands, sternum (including bone marrow), thymus, trachea, lungs and bronchi, heart, thyroid gland, parathyroids, esophagus, stomach, pancreas, gallbladder (mice), small intestine, colon, mesenteric lymph nodes, liver, spleen, kidneys, adrenal glands, urinary bladder, prostate/testes or ovaries/uterus, brain, pituitary gland, tissue masses, and regional lymph nodes
ANIMALS AND ANIMAL MAINTENANCE			
Strain and Species	F344/N rats; B6C3F$_1$ mice	Same as 14-d studies	Same as 14-d studies
Animal Source	Charles River Breeding Laboratories (Portage, MI)	Same as 14-d studies	Rats--Charles River Breeding Laboratories (Stone Ridge, NY); mice--Charles River Breeding Laboratories (Portage, MI)

TABLE 5. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE FEED STUDIES OF DECABROMODIPHENYL OXIDE (Continued)

	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
ANIMALS AND ANIMAL MAINTENANCE			
Study Laboratory	Hazleton Laboratories America	Hazleton Laboratories America	Hazleton Laboratories America
Method of Animal Identification	Ear clipping	Ear tags	Ear tags
Time Held Before Study	3 wk	4 wk	Rats--14 d; mice--16 d
Age When Placed on Study	Rats--7 wk; mice--6 wk	Rats--8 wk; mice--9 wk	Rats--7-8 wk; mice--9 wk
Age When Killed	Rats--9 wk; mice--8 wk	Rats--22 wk; mice--23 wk	Rats--111-112 wk; mice--112-113 wk
Necropsy Dates	Rats--10/31/78; mice--11/1/78	Rats--5/31/79-6/1/79; mice--5/29/79-5/30/79	Rats--9/22/82-9/24/82; mice--7/26/82-8/2/82
Method of Animal Distribution	Assigned to groups such that cage weights were approximately equal	According to tables of random numbers	Randomized to groups by weight class and then to dose groups
Feed	Purina Rodent Laboratory Chow-5001 (Ralston Purina Co., St. Louis, MO)	Same as 14-d studies	NIH 07 Rat and Mouse Ration (Zeigler Bros., Gardners, PA); available ad libitum
Bedding	Heat-treated hardwood chips (Sani-chips, P.J. Murphy Forest Products, Monachie, NJ)	Same as 14-d studies	Same as 14-d studies
Water	Automatic watering system (Hazleton Systems, Aberdeen, MD); available ad libitum	Same as 14-d studies	Same as 14-d studies
Cages	Polycarbonate (Hazleton Systems, Inc., Aberdeen, MD)	Polycarbonate (Hazleton Systems, Inc., Aberdeen, MD)	Same as 13-wk studies
Cage Filters	Remay filter sheets (Dupont Co., Wilmington, DE)	Same as 14-d studies	Nonwoven fiber filters (National Paper Co., Baltimore, MD)
Animals per Cage	5	5	Rats and female mice--5; male mice--5 until month 8; then 1 for intermittent periods; 1 after 15 months
Other Chemicals on Study in the Same Room	None	None	None
Animal Room Environment	Temp--72° ± 2° F; humidity--45% ± 5%; 10-15 room air changes/h; light 12 h/d	Temp--70° ± 1° F; humidity--45% ± 5%; light 12 h/d	Temp--68°-80° F; humidity--15%-90%; fluorescent light 12 h/d; 10-12 room air changes/h

Male mice from the C3H colony and female mice from the C57BL/6 colony were used as parents for the hybrid B6C3F$_1$ mice used in these studies. The influence of the potential genetic nonuniformity in the hybrid mice on these results is not known, but results of the studies are not affected because concurrent controls were included.

Animal Maintenance

All animals were initially housed five per cage; after the 7th month of the study, male mice were housed individually for varying periods. After 15 months, all male mice were housed individually. Feed and water were available ad libitum. Further details of animal maintenance are given in Table 5.

Clinical Examinations and Pathology

All animals were observed twice daily, and clinical signs were recorded once per week. Body weights by cage were recorded once per week for the first 12 weeks of the study and once per month thereafter. Mean body weights were calculated for each group. Moribund animals were killed, as were animals that survived to the end of the study. A necropsy was performed on all animals, including those found dead unless they were excessively autolyzed or cannibalized. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study in each group.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Tissues examined microscopically are listed in Table 5.

When the pathology examination was completed, the slides, individual animal data records, and summary tables were sent to an independent quality assurance laboratory. Individual animal records and tables were compared for accuracy, slides and tissue counts were verified, and histotechnique was evaluated. All tumor diagnoses, all target tissues, and all tissues from a randomly selected 10% of the animals were evaluated by a quality assurance pathologist. Slides of all target tissues and those about which the original and quality assurance pathologists disagreed were submitted to the Chairperson of the Pathology Working Group (PWG) for evaluation. Representative coded slides selected by the Chairperson were reviewed by PWG pathologists, who reached a consensus and compared their findings with the original and quality assurance diagnoses. When diagnostic differences were found, the PWG sent the appropriate slides and comments to the original pathologist for review. This procedure has been described, in part, by Maronpot and Boorman (1982) and Boorman et al. (1985). The final diagnoses represent a consensus of contractor pathologists and the NTP Pathology Working Group. For subsequent evaluations, the diagnosed lesions for each tissue type are combined according to the guidelines of McConnell et al. (1986).

Nonneoplastic lesions are not examined routinely by the quality assurance pathologist or PWG. Certain nonneoplastic findings are reviewed by the quality assurance pathologist and PWG if they are considered part of the toxic response to a chemical or if they are deemed of special interest.

Statistical Methods

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

Survival Analyses: The probability of survival was estimated by the product-limit procedure of Kaplan and Meier (1958) and is presented in the form of graphs. Animals were censored from the survival analyses at the time they were found dead of other than natural causes or were found to be missing; animals dying from natural causes were not censored. Statistical analyses for a possible dose-related effect on survival used the method of Cox (1972) for testing two groups

for equality and Tarone's (1975) life table test for a dose-related trend. All reported P values for the survival analysis are two-sided.

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

Analysis of Tumor Incidence: Three statistical methods are used to analyze tumor incidence data. The two that adjust for intercurrent mortality employ the classical method for combining contingency tables developed by Mantel and Haenszel (1959). Tests of significance included pairwise comparisons of high dose and low dose groups with controls and tests for overall dose-response trends.

For studies in which compound administration has little effect on survival, the results of the three alternative analyses will generally be similar. When differing results are obtained by the three methods, the final interpretation of the data will depend on the extent to which the tumor under consideration is regarded as being the cause of death. All reported P values for tumor analyses are one-sided.

Life Table Analyses--The first method of analysis assumed that all tumors of a given type observed in animals dying before the end of the study were "fatal"; i.e., they either directly or indirectly caused the death of the animal. According to this approach, the proportions of tumor-bearing animals in the dosed and control groups were compared at each point in time at which an animal died with a tumor of interest. The denominators of these proportions were the total number of animals at risk in each group. These results, including the data from animals killed at the end of the study, were then combined by the Mantel-Haenszel method to obtain an overall P value. This method of adjusting for intercurrent mortality is the life table method of Cox (1972) and of Tarone (1975). The underlying variable considered by this analysis is time to death due to tumor. If the tumor is rapidly lethal, then time to death due to tumor closely aproximates time to tumor onset. In this case, the life table test also provides a comparison of the time-specific tumor incidences.

Incidental Tumor Analyses--The second method of analysis assumed that all tumors of a given type observed in animals that died before the end of the study were "incidental"; i.e., they were merely observed at necropsy in animals dying of an unrelated cause. According to this approach, the proportions of tumor-bearing animals in dosed and control groups were compared in each of five time intervals: weeks 0-52, weeks 53-78, weeks 79-92, week 93 to the week before the terminal-kill period, and the terminal-kill period. The denominators of these proportions were the number of animals actually examined for tumors during the time interval. The individual time interval comparisons were then combined by the previously described method to obtain a single overall result. (See Haseman, 1984, for the computational details of both methods.)

Unadjusted Analyses--Primarily, survival-adjusted methods are used to evaluate tumor incidence. In addition, the results of the Fisher exact test for pairwise comparisons and the Cochran-Armitage linear trend test (Armitage, 1971; Gart et al., 1979) are given in the appendix containing the analyses of primary tumor incidence. These two tests are based on the overall proportion of tumor-bearing animals and do not adjust for survival differences.

Historical Control Data: Although the concurrent control group is always the first and most appropriate control group used for evaluation, there are certain instances in which historical control data can be helpful in the overall assessment of tumor incidence. Consequently, control tumor incidences from the NTP historical control data base (Haseman et al., 1984) are included for those tumors appearing to show compound-related effects.

III. RESULTS

RATS

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

MICE

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

FOURTEEN-DAY STUDIES

All rats lived to the end of the studies (Table 6). Final mean body weights were not adversely affected by decabromodiphenyl oxide. No compound-related clinical signs or gross pathologic effects were observed.

THIRTEEN-WEEK STUDIES

All the rats survived to the end of the studies (Table 7). The final mean body weights were not adversely affected by decabromodiphenyl oxide. Feed consumption by dosed rats was generally comparable to that by the controls. No compound-related gross or microscopic pathologic effects were observed.

Dose Selection Rationale: Doses selected for rats for the 2-year studies were 25,000 and 50,000 ppm decabromodiphenyl oxide in feed. These concentrations are the highest recommended for use in NTP feed studies.

TABLE 6. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE FOURTEEN-DAY FEED STUDIES OF DECABROMODIPHENYL OXIDE

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	5/5	162	225	+ 63	--
5,000	5/5	157	224	+ 67	99.6
10,000	5/5	161	227	+ 66	100.9
20,000	5/5	163	227	+ 64	100.9
50,000	5/5	164	230	+ 66	102.2
100,000	5/5	162	224	+ 62	99.6
FEMALE					
0	5/5	111	141	+ 30	--
5,000	5/5	114	146	+ 32	103.5
10,000	5/5	115	149	+ 34	105.7
20,000	5/5	117	145	+ 28	102.8
50,000	5/5	114	149	+ 35	105.7
100,000	5/5	116	142	+ 26	100.7

(a) Number surviving/number initially in group
(b) Initial group mean body weight
(c) Mean body weight change of the group

TABLE 7. SURVIVAL, MEAN BODY WEIGHTS, AND FEED CONSUMPTION OF RATS IN THE THIRTEEN-WEEK FEED STUDIES OF DECABROMODIPHENYL OXIDE

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)	Feed Consumption (d) Week 4	Week 13
MALE							
0	10/10	215 ± 8	369 ± 6	+154 ± 8	--	23	24
3,100	10/10	216 ± 4	367 ± 10	+151 ± 12	99	23	25
6,300	10/10	229 ± 5	381 ± 8	+152 ± 7	103	23	24
12,500	10/10	214 ± 7	362 ± 8	+148 ± 7	98	22	23
25,000	10/10	212 ± 6	374 ± 10	+162 ± 7	101	22	25
50,000	10/10	224 ± 5	363 ± 18	+139 ± 16	98	24	30
FEMALE							
0	10/10	149 ± 3	211 ± 5	+ 62 ± 2	--	22	16
3,100	10/10	151 ± 3	213 ± 3	+ 62 ± 3	101	19	15
6,300	10/10	147 ± 2	203 ± 4	+ 56 ± 3	96	21	17
12,500	10/10	150 ± 3	212 ± 3	+ 62 ± 3	100	22	15
25,000	10/10	150 ± 2	208 ± 3	+ 58 ± 1	99	20	18
50,000	10/10	151 ± 3	204 ± 4	+ 53 ± 3	97	20	14

(a) Number surviving/number initially in group
(b) Initial group mean body weight ± standard error of the mean
(c) Mean body weight change ± standard error of the mean
(d) Grams of feed consumed per day per animal. Not corrected for scatter.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Mean body weights of dosed and control rats were comparable throughout most of the studies (Table 8 and Figure 1). The average daily feed consumption per rat by low dose and high dose rats was estimated to be 109% and 108% that of the controls for males and 104% and 109% for females (Appendix M, Tables M1 and M2). The average amount of decabromodiphenyl oxide consumed per day was estimated to be 1,120 mg/kg and 2,240 mg/kg for low dose and high dose male rats and 1,200 mg/kg and 2,550 mg/kg for low dose and high dose female rats.

TABLE 8. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

Weeks on Study	Control		25,000 ppm			50,000 ppm		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors
MALE								
0	171	50	173	101	50	172	101	50
1	208	50	209	100	50	207	100	50
2	236	50	236	100	50	238	101	50
3	259	50	260	100	50	259	100	50
4	276	49	281	102	50	279	101	50
5	291	49	295	101	50	294	101	50
6	305	49	308	101	50	307	101	50
7	317	49	320	101	50	317	100	50
8	329	49	331	101	50	328	100	50
9	339	49	344	101	50	339	100	50
10	347	49	352	101	50	348	100	50
11	354	49	359	101	50	353	100	50
12	361	49	372	103	50	361	100	50
17	389	49	400	103	50	392	101	49
21	412	49	416	101	50	413	100	50
25	424	49	431	102	50	422	100	50
29	431	49	440	102	50	429	100	50
33	438	49	450	103	50	441	101	50
37	447	49	447	100	50	438	98	50
41	435	49	438	101	50	426	98	50
45	447	49	449	100	50	441	99	50
49	444	49	443	100	50	441	99	50
53	452	49	456	101	50	448	99	50
57	449	49	451	100	50	444	99	49
61	452	49	453	100	50	445	98	48
65	456	49	449	98	50	452	99	48
69	449	49	440	98	48	443	99	48
73	452	49	449	99	46	448	99	48
77	449	48	449	100	44	451	100	47
81	449	46	442	98	41	441	98	47
85	445	46	440	99	38	434	98	46
89	436	45	436	100	36	429	98	42
93	423	45	430	102	34	419	99	39
97	413	41	412	100	33	408	99	32
101	413	37	400	97	27	395	96	30
103	404	36	396	98	24	395	98	26
104	402	35	397	99	23	389	97	25
FEMALE								
0	127	50	127	100	50	126	99	50
1	139	50	139	100	50	138	99	50
2	150	50	151	101	50	150	100	50
3	159	50	159	100	50	157	99	50
4	168	50	169	101	50	167	99	50
5	173	50	174	101	50	173	100	50
6	179	50	182	102	50	177	99	50
7	185	50	186	101	50	184	99	50
8	191	50	191	100	50	188	98	50
9	195	50	196	101	50	192	98	50
10	199	50	198	99	50	198	99	50
11	202	50	199	99	50	198	98	50
12	204	50	205	100	50	203	100	50
17	217	50	214	99	50	209	96	50
21	223	50	219	98	50	217	97	50
25	228	50	227	100	50	223	98	50
29	233	50	229	98	50	227	97	50
33	238	50	234	98	50	234	98	50
37	244	50	240	98	50	239	98	50
41	246	50	240	98	50	240	98	50
45	252	50	251	100	50	247	98	50
49	256	50	255	100	50	254	99	50
53	269	50	268	100	49	268	100	50
57	278	50	276	99	49	272	98	50
61	288	50	286	99	49	283	98	50
65	299	50	297	99	49	294	98	50
69	307	50	303	99	48	297	97	50
73	315	50	315	100	47	309	98	49
77	327	49	324	99	47	314	96	46
81	331	48	327	99	46	324	98	45
85	337	47	332	99	46	327	97	45
89	341	47	335	98	44	329	96	43
93	338	46	334	99	42	322	95	43
97	338	43	330	98	39	319	94	39
101	333	41	328	98	35	318	95	35
103	329	41	334	102	33	322	98	34
104	333	40	336	101	33	320	96	34

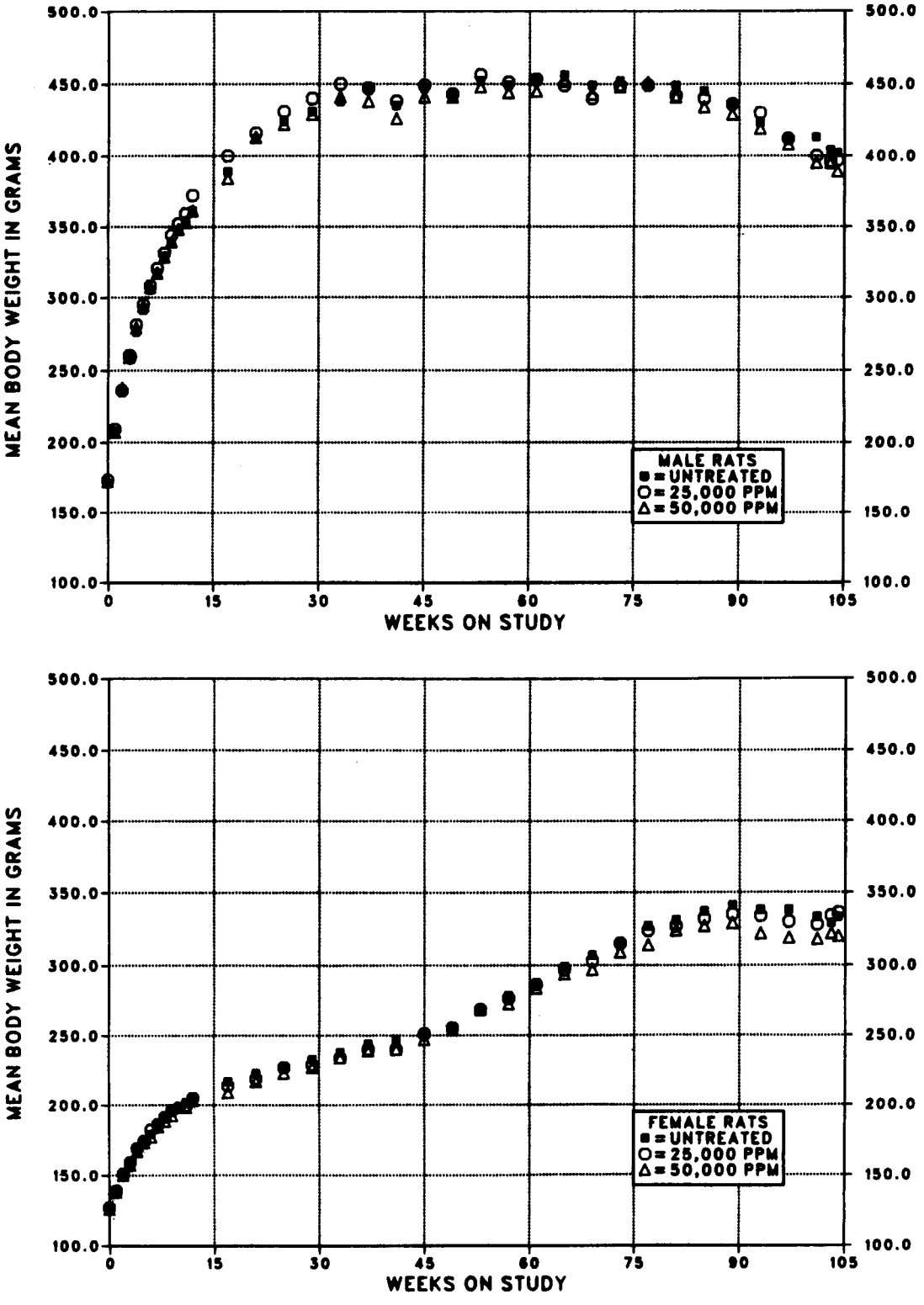

FIGURE 1. GROWTH CURVES FOR RATS FED DIETS CONTAINING DECABROMODIPHENYL OXIDE FOR TWO YEARS

Survival

Estimates of the probabilities of survival for male and female rats fed diets containing decabromodiphenyl oxide at the concentrations used in these studies and for the controls are shown in the Kaplan and Meier curves in Figure 2. The survival of the low dose group of male rats was significantly lower than that of the controls after week 102 (Table 9). No other significant differences in survival were observed between any groups of either sex.

Pathology and Statistical Analyses of Results

This section describes the significant or noteworthy changes in the incidences of rats with neoplastic or nonneoplastic lesions of the liver, hematopoietic system, spleen, mandibular lymph node, pancreas, eye, stomach, Zymbal gland, musculoskeletal system, and thyroid gland. Histopathologic findings on neoplasms in rats are summarized in Appendix A (Tables A1 and A2); Appendix A (Tables A3 and A4) also gives the survival and tumor status for individual male and female rats. Findings on nonneoplastic lesions are summarized in Appendix C (Tables C1 and C2). Appendix E (Tables E1 and E2) contains the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups. The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes). Historical incidences of tumors in control animals are listed in Appendix F.

TABLE 9. SURVIVAL OF RATS IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

	Control	25,000 ppm	50,000 ppm
MALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	15	26	24
Killed at termination	35	23	24
Died during termination period	0	1	2
Survival P values (c)	0.095	0.033	0.093
FEMALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	10	17	16
Killed at termination	40	33	34
Survival P values (c)	0.196	0.163	0.217

(a) Terminal kill period: week 104
(b) Includes animals killed in a moribund condition
(c) The result of the life table trend test is in the control column, and the results of the life table pairwise comparisons with the controls are in the dosed columns.

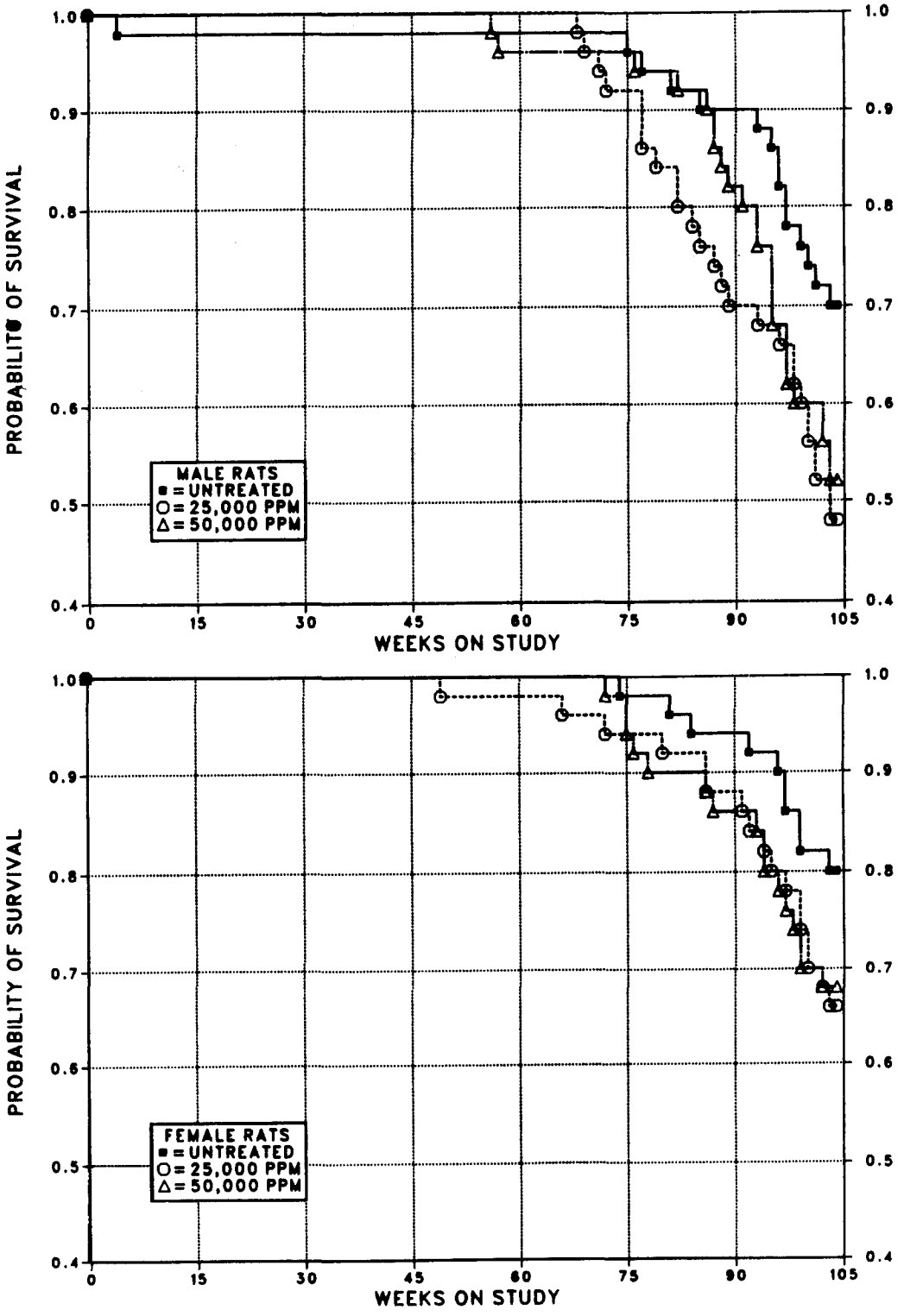

FIGURE 2. KAPLAN-MEIER SURVIVAL CURVES FOR RATS FED DIETS CONTAINING DECABROMODIPHENYL OXIDE FOR TWO YEARS

Liver: Thrombosis and degeneration were observed at increased incidences in high dose male rats (Table 10). The thrombosis was characterized by a near total occlusion of a major hepatic blood vessel by a dense fibrin coagulum. Peripheral infiltration of fibroblastic cells into the thrombus was evidence of antemortem occurrence. Neoplastic nodules in males and females occurred with significant positive trends (Table 11). The incidences of neoplastic nodules in dosed males and high dose females were significantly greater than those in the controls. Microscopically, the neoplastic nodules were generally spherical and occupied an area greater than one liver lobule. Demarcation from surrounding hepatic parenchyma was due either to compression of peripheral normal liver or by a discontinuity between the plates of the nodule and those of adjacent unaffected liver. Hepatocytes within the neoplastic nodules had variations in size, tinctorial characteristics, cytoplasmic vacuolization, and nuclear atypia.

TABLE 10. NUMBER OF RATS WITH LIVER LESIONS IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

Lesion	Male			Female		
	Control	25,000 ppm	50,000 ppm	Control	25,000 ppm	50,000 ppm
Number of animals examined	50	50	49	50	49	50
Degeneration	13	19	22	0	0	0
Pigmentation	4	4	10	16	8	5
Fatty metamorphosis	8	13	11	9	5	4
Thrombosis	1	0	9	0	0	0
Neoplastic nodule	1	7	15	1	3	9
Hepatocellular carcinoma	1	1	1	0	2	0

TABLE 11. ANALYSIS OF LIVER LESIONS IN RATS IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE (a)

	Control	25,000 ppm (b)	50,000 ppm (b)
MALE			
Neoplastic Nodule			
Overall Rates	1/50 (2%)	7/50 (14%)	15/49 (31%)
Adjusted Rates	2.9%	27.1%	52.7%
Terminal Rates	1/35 (3%)	6/24 (25%)	13/26 (50%)
Week of First Observation	104	89	87
Life Table Tests	P<0.001	P=0.008	P<0.001
Incidental Tumor Tests	P<0.001	P=0.014	P<0.001
Hepatocellular Carcinoma			
Overall Rates	1/50 (2%)	1/50 (2%)	1/49 (2%)
Neoplastic Nodule or Hepatocellular Carcinoma (c)			
Overall Rates	2/50 (4%)	8/50 (16%)	15/49 (31%)
Adjusted Rates	5.2%	31.1%	52.7%
Terminal Rates	1/35 (3%)	7/24 (29%)	13/26 (50%)
Week of First Observation	97	89	87
Life Table Tests	P<0.001	P=0.012	P<0.001
Incidental Tumor Tests	P<0.001	P=0.022	P<0.001
FEMALE			
Neoplastic Nodule			
Overall Rates	1/50 (2%)	3/49 (6%)	9/50 (18%)
Adjusted Rates	2.5%	9.1%	24.4%
Terminal Rates	1/40 (3%)	3/33 (9%)	7/34 (21%)
Week of First Observation	104	104	87
Life Table Tests	P=0.002	P=0.239	P=0.005
Incidental Tumor Tests	P=0.002	P=0.239	P=0.006
Hepatocellular Carcinoma			
Overall Rates	0/50 (0%)	2/49 (4%)	0/50 (0%)
Neoplastic Nodule or Hepatocellular Carcinoma (d)			
Overall Rates	1/50 (2%)	5/49 (10%)	9/50 (18%)
Adjusted Rates	2.5%	15.2%	24.4%
Terminal Rates	1/40 (3%)	5/33 (15%)	7/34 (21%)
Week of First Observation	104	104	87
Life Table Tests	P=0.003	P=0.064	P=0.005
Incidental Tumor Tests	P=0.003	P=0.064	P=0.006

(a) The statistical analyses used are discussed in Chapter II (statistical methods) and Appendix E (footnotes).
(b) The estimated dose in milligrams per kilogram body weight is given in Chapter III (body weights and clinical signs) and in Appendix M.
(c) Historical incidence in NTP studies (mean ± SD): 73/1,719 (4% ± 3%); range: 0/50-7/49
(d) Historical incidence in NTP studies (mean ± SD): 48/1,766 (3% ± 3%); range: 0/50-5/50

Hematopoietic System: Mononuclear cell leukemia in male rats occurred with a significant positive trend by the life table test, and the incidences in the dosed groups were significantly greater than that in the controls by the life table test (Table 12).

Spleen: Fibrosis was observed at an increased incidence in high dose male rats (control, 5/49; low dose, 8/50; high dose, 13/49). Hematopoiesis was observed at increased incidences in dosed female rats (control, 12/49; low dose, 24/48; high dose, 17/50). A sarcoma was observed in one low dose and one high dose male rat. The historical incidence of sarcomas of the spleen in NTP studies is 5/1,705 (0.3%).

Mandibular Lymph Node: Lymphoid hyperplasia was observed at an increased incidence in high dose male rats (control, 4/50; low dose, 6/50; high dose, 13/49).

Pancreas: Acinar cell adenomas in male rats occurred with a significant positive trend, and the incidence in the high dose group was significantly greater than that of the controls by the life table test (Table 13). Acinar cell hyperplasia was not diagnosed in any of the male rats. Acinar cell adenomas were observed in one low dose and one high dose female rat.

The Pathology Working Group (PWG) examined in a blind fashion the four acinar cell adenomas in the high dose male rats as well as other selected pancreatic lesions. Using current criteria on proliferative exocrine lesions (Boorman and Eustis, 1984), the PWG members agreed that the four lesions should be classified as one acinar cell adenoma, two acinar cell hyperplasias, and one mixed cell lesion. The latter lesion is uncommon in F344/N rats and consists of an admixture of islet and acinar cells. The PWG also diagnosed one acinar cell hyperplasia in a low dose male rat. The original pathologist reviewed the pancreatic lesions with the PWG comments and elected to retain his original diagnosis.

Eye: Retinal degeneration was observed at an increased incidence in low dose female rats (male: control, 5/50, 10%; low dose, 1/50, 2%; high dose, 2/50, 4%; female: control, 5/50, 10%; low dose, 15/50, 30%; high dose, 1/50, 2%).

Stomach: Acanthosis of the forestomach was observed at increased incidence in dosed male rats (male: control, 0/49; low dose, 2/50, 4%; high dose, 5/49, 10%; female: control, 2/49, 4%; low dose, 1/48, 2%; high dose, 1/50, 2%).

Zymbal Gland: Carcinomas were observed in 3/50 low dose female rats, 1/50 low dose male rats, and 1/50 high dose male rats. The historical incidence of Zymbal gland neoplasms in female rats is 6/1,772 (0.3% ± 1%) and in male rats is 11/1,772 (0.6% ± 1%). The greatest observed incidence in a female control group is 3/50 (6%).

Musculoskeletal System: Osteosarcomas were observed in three low dose males and one control female. The historical incidence of osteosarcomas in male rat controls in NTP studies is 8/1,727 (0.5% ± 1%), with the greatest incidence in any control group being 2/50 (4%).

Thyroid Gland: C-cell hyperplasia of the thyroid gland was observed at decreasing incidence in dosed male and female rats (male: control, 12/50, 24%; low dose, 6/49, 12%; high dose, 2/49%, 4%; female: control, 14/50, 28%; low dose, 7/49, 14%; high dose, 2/50, 4%).

TABLE 12. ANALYSIS OF MONONUCLEAR CELL LEUKEMIA IN RATS IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

	Control	25,000 ppm	50,000 ppm
MALE (a)			
Overall Rates	30/50 (60%)	33/50 (66%)	35/50 (70%)
Adjusted Rates	67.9%	81.9%	82.8%
Terminal Rates	21/35 (60%)	17/24 (71%)	19/26 (73%)
Week of First Observation	81	72	76
Life Table Tests	P=0.028	P=0.029	P=0.031
Incidental Tumor Tests	P=0.215	P=0.292	P=0.285
FEMALE			
Overall Rates	14/50 (28%)	21/50 (42%)	18/50 (36%)
Adjusted Rates	30.6%	53.5%	42.8%
Terminal Rates	9/40 (23%)	15/33 (45%)	11/34 (32%)
Week of First Observation	74	95	75
Life Table Tests	P=0.124	P=0.043	P=0.157
Incidental Tumor Tests	P=0.295	P=0.102	P=0.362

(a) Historical incidence of leukemia in NTP studies (mean ± SD): 458/1,727 (27% ± 9%); range: 5/50-23/50

TABLE 13. ANALYSIS OF PANCREATIC ACINAR CELL ADENOMAS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (a)

	Control	25,000 ppm	50,000 ppm
Overall Rates	0/49 (0%)	0/50 (0%)	4/49 (8%)
Adjusted Rates	0.0%	0.0%	13.7%
Terminal Rates	0/35 (0%)	0/24 (0%)	2/25 (8%)
Week of First Observation			97
Life Table Tests	P=0.010	(b)	P=0.037
Incidental Tumor Tests	P=0.017	(b)	P=0.067

(a) Historical incidence of acinar cell adenomas or carcinomas in NTP studies (mean ± SD): 3/1,677 (0.2% ± 0.6%); range: 0/88-1/47
(b) No P value is reported because no tumors were observed in the 25,000-ppm and control groups.

FOURTEEN-DAY STUDIES

All animals survived to the end of the studies (Table 14). Final mean body weights were not adversely affected by exposure to decabromodiphenyl oxide. No compound-related clinical signs or gross pathologic effects were observed.

THIRTEEN-WEEK STUDIES

No compound-related clinical signs; effects on survival, body weight, feed consumption; or gross or microscopic pathologic effects were observed (Table 15).

Dose Selection Rationale: Doses selected for mice for the 2-year studies were 25,000 and 50,000 ppm decabromodiphenyl oxide in feed. These concentrations are the highest recommended for use in NTP feed studies.

TABLE 14. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE FOURTEEN-DAY FEED STUDIES OF DECABROMODIPHENYL OXIDE

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	5/5	25.7	27.4	+1.7	--
5,000	5/5	26.4	29.1	+2.7	106.2
10,000	5/5	25.2	28.0	+2.8	102.2
20,000	5/5	26.2	27.5	+1.3	100.4
50,000	5/5	25.4	28.7	+3.3	104.7
100,000	5/5	25.9	28.4	+2.5	103.6
FEMALE					
0	5/5	19.9	22.0	+2.1	--
5,000	5/5	19.4	22.5	+3.1	102.3
10,000	5/5	19.5	22.5	+3.0	102.3
20,000	5/5	19.6	21.9	+2.3	99.5
50,000	5/5	19.8	22.5	+2.7	102.3
100,000	5/5	19.5	22.1	+2.6	100.5

(a) Number surviving/number initially in group
(b) Initial group mean body weight
(c) Mean body weight change

TABLE 15. SURVIVAL, MEAN BODY WEIGHTS, AND FEED CONSUMPTION OF MICE IN THE THIRTEEN-WEEK FEED STUDIES OF DECABROMODIPHENYL OXIDE

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)	Feed Consumption (d) Week 4	Week 13
MALE							
0	10/10	26.2 ± 0.4	34.5 ± 0.6	+ 8.3 ± 0.4	--	9	9
3,100	10/10	24.0 ± 0.8	32.5 ± 0.7	+ 8.5 ± 1.0	94.2	8	8
6,300	10/10	25.0 ± 0.6	34.6 ± 0.6	+ 9.6 ± 0.7	100.3	8	6
12,500	9/10	26.1 ± 0.8	35.0 ± 0.8	+ 8.9 ± 0.3	101.4	8	7
25,000	10/10	25.3 ± 0.5	33.9 ± 0.5	+ 8.6 ± 0.3	98.3	8	9
50,000	10/10	27.3 ± 0.5	34.5 ± 1.3	+ 7.2 ± 1.1	100.0	8	9
FEMALE							
0	10/10	19.4 ± 0.3	27.4 ± 0.7	+ 8.0 ± 0.6	--	10	9
3,100	10/10	19.9 ± 0.5	27.4 ± 0.7	+ 7.5 ± 0.6	100.0	9	9
6,300	10/10	19.6 ± 0.4	28.5 ± 1.1	+ 8.9 ± 0.8	104.0	9	10
12,500	9/10	19.5 ± 0.3	25.7 ± 0.8	+ 6.2 ± 0.8	93.8	9	9
25,000	10/10	19.7 ± 0.3	27.8 ± 0.7	+ 8.1 ± 0.6	101.5	9	8
50,000	10/10	19.4 ± 0.3	26.7 ± 0.4	+ 7.3 ± 0.3	97.4	10	8

(a) Number surviving/number initially in group. All deaths were judged accidental.
(b) Initial group body weight ± standard error of the mean. Subsequent calculations are based on those animals surviving to the end of the study.
(c) Mean body weight change of the survivors ± standard error of the mean
(d) Grams of feed consumed per animal per day. Not corrected for scatter.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

The mean body weights of dosed and control mice were comparable throughout most of the studies (Table 16 and Figure 3). The average daily feed consumption by low dose and high dose male mice was estimated to be 96% and 100% that of the controls and by low dose and high dose female mice, 94% and 96% that of the controls (Appendix M, Tables M3 and M4). The average amount of decabromodiphenyl oxide consumed per day was estimated to be 3,200 mg/kg and 6,650 mg/kg for low dose and high dose male mice and 3,760 mg/kg and 7,780 mg/kg for low dose and high dose female mice.

TABLE 16. MEAN BODY WEIGHTS AND SURVIVAL OF MICE IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

Weeks on Study	Control		25,000 ppm			50,000 ppm		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors
MALE								
0	28.3	50	28.2	100	50	28.4	100	50
1	29.4	50	27.9	95	50	29.3	100	50
2	30.6	50	29.7	97	49	29.7	97	49
3	30.9	50	30.2	98	49	30.6	99	49
4	32.0	50	31.6	99	49	32.1	100	49
5	31.8	50	31.5	99	49	31.5	99	49
6	33.2	50	32.3	97	48	31.6	95	49
7	34.0	50	33.3	98	48	33.4	98	49
8	34.8	50	33.6	97	48	34.1	98	49
9	34.7	49	35.1	101	47	34.0	98	48
10	35.4	49	34.1	96	46	34.2	97	46
11	35.2	49	34.5	98	46	34.7	99	46
12	35.6	48	35.2	99	46	35.1	99	46
16	36.5	47	36.5	100	46	35.9	98	46
20	36.9	47	36.4	99	45	35.9	97	46
24	37.0	45	36.4	98	45	36.2	98	45
28	38.5	40	38.4	100	45	37.3	97	45
32	39.9	39	40.1	101	45	39.0	98	45
36	39.0	36	41.0	105	43	40.0	103	44
40	40.4	34	41.1	102	43	39.6	98	44
44	40.2	33	41.7	104	43	40.8	101	44
48	41.0	33	43.0	105	43	42.0	102	44
52	39.6	33	41.1	104	43	41.1	104	44
54	41.2	32	41.3	100	43	39.8	97	43
56	40.0	32	41.4	104	43	40.4	101	43
58	40.1	31	41.5	103	43	41.5	103	43
60	40.7	31	42.1	103	43	41.2	101	41
62	40.1	30	41.3	103	43	41.1	102	40
64	40.9	28	41.6	102	42	41.1	100	39
66	40.0	27	39.0	98	41	40.0	100	39
68	40.0	26	39.7	99	40	39.6	99	39
70	39.0	26	39.0	100	40	39.0	100	39
72	38.6	26	39.9	103	40	38.8	101	38
74	39.3	26	39.7	101	39	39.3	100	36
76	38.3	26	39.5	103	38	38.9	102	35
80	40.0	26	39.0	98	38	39.0	98	35
84	39.0	22	39.0	100	36	38.0	97	32
88	39.1	22	38.8	99	35	39.5	101	32
92	40.0	22	40.0	100	30	39.0	98	29
96	40.0	20	39.0	98	26	38.0	95	27
100	38.0	19	38.0	100	25	37.0	97	26
102	37.0	19	38.0	103	25	37.0	100	24
103	37.0	19	38.0	103	25	38.0	103	24
FEMALE								
0	21.6	50	21.1	98	50	20.9	97	50
1	21.7	50	21.7	100	50	21.6	100	50
2	22.7	50	22.5	99	50	22.6	100	50
3	23.4	50	23.1	99	50	22.7	97	50
4	23.8	50	24.0	101	50	23.7	100	50
5	24.2	50	24.4	101	50	24.0	99	50
6	25.1	50	24.9	99	50	24.5	98	50
7	25.9	50	25.8	100	50	24.7	95	50
8	25.7	50	25.9	101	50	25.2	98	49
9	26.5	50	26.6	100	50	26.0	98	49
10	27.7	50	27.0	97	50	26.7	96	49
11	27.3	50	27.2	100	50	26.7	98	49
12	28.1	50	27.4	98	50	27.0	96	49
16	28.9	50	28.4	98	50	28.6	99	49
20	30.1	50	30.4	101	50	30.5	101	49
24	30.3	50	30.7	101	49	30.9	102	49
28	32.7	50	32.5	99	49	32.8	100	49
32	34.6	50	34.8	101	49	34.9	101	49
36	36.0	50	37.0	103	49	37.0	103	49
40	35.7	50	37.6	105	49	37.7	106	49
44	37.5	50	38.0	101	49	39.9	106	49
48	38.0	50	39.0	103	49	40.0	105	49
52	38.9	49	40.3	104	49	37.9	97	49
56	39.7	48	39.9	101	49	40.1	101	49
58	40.4	48	39.9	99	49	40.1	99	49
60	41.5	48	41.9	101	49	40.9	99	49
62	40.7	48	40.2	99	49	40.4	99	49
64	40.1	48	40.7	101	49	39.6	99	49
66	39.0	47	41.0	105	47	40.0	103	49
68	40.9	47	41.4	101	47	40.0	98	49
70	40.0	47	41.0	103	47	39.0	98	49
72	39.2	46	40.7	104	46	38.3	98	49
74	39.0	46	40.9	105	46	38.7	99	48
76	39.3	46	40.8	104	46	38.5	98	48
80	41.0	41	41.0	100	45	39.0	95	48
84	41.0	41	42.0	102	44	40.0	98	47
88	42.6	40	42.7	100	43	40.9	96	43
92	41.0	37	43.0	105	38	40.0	98	40
96	41.0	30	44.1	108	36	41.0	100	39
100	40.0	28	42.0	105	33	38.0	95	34
102	42.0	27	43.0	102	31	40.0	95	32
103	41.0	27	43.0	105	31	39.0	95	32

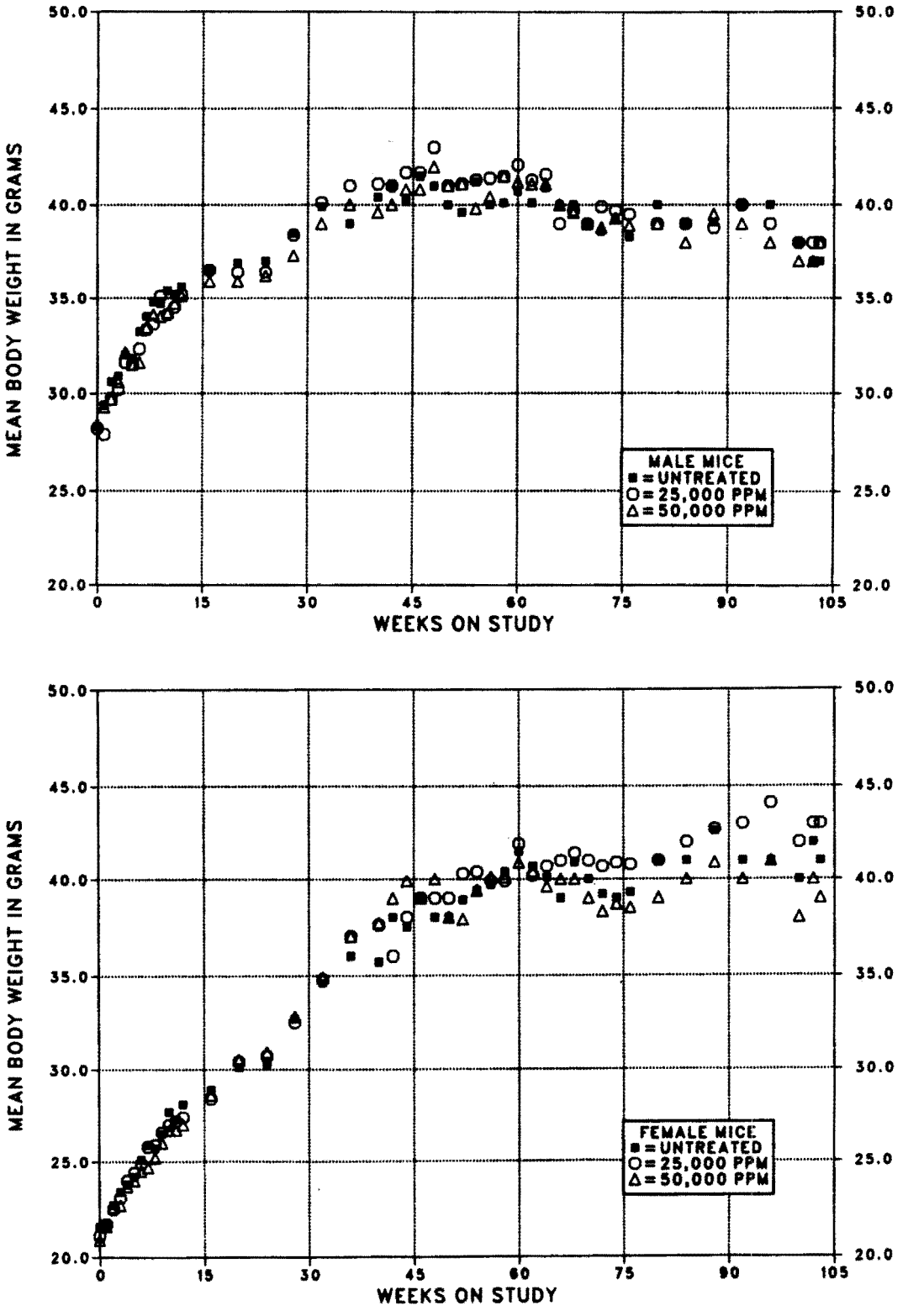

FIGURE 3. GROWTH CURVES FOR MICE FED DIETS CONTAINING DECABROMODIPHENYL OXIDE FOR TWO YEARS

Survival

Estimates of the probabilities of survival for male and female mice fed diets containing decabromodiphenyl oxide at the concentrations used in these studies and for the controls are shown in the Kaplan and Meier curves in Figure 4. Loss of control male mice (presumably due to fighting) was significant during the first part of the study. All male mice were caged individually after 15 months. Thereafter, the survival of control and dosed male mice was comparable. No significant differences in survival were observed between any groups of either sex (Table 17).

Pathology and Statistical Analyses of Results

This section describes the significant or noteworthy changes in the incidences of mice with neoplastic or nonneoplastic lesions of the liver, thyroid gland, testis, stomach, and multiple organs. Histopathologic findings on neoplasms in mice are summarized in Appendix B (Tables B1 and B2); Appendix B (Tables B3 and B4) also gives the survival and tumor status for individual male and female mice. Findings on nonneoplastic lesions are summarized in Appendix D (Tables D1 and D2). Appendix E (Tables E3 and E4) contains the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups. The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes). Historical incidences of tumors in control animals are listed in Appendix F.

TABLE 17. SURVIVAL OF MICE IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

	Control	25,000 ppm	50,000 ppm
MALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	31	25	26
Killed at termination	18	25	24
Died during termination period	1	0	0
Survival P values (c)	0.139	0.111	0.161
FEMALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	23	19	18
Killed at termination	26	31	32
Died during termination period	1	0	0
Survival P values (c)	0.276	0.504	0.305

(a) Terminal kill period: weeks 103-104
(b) Includes animals killed in a moribund condition
(c) The result of the life table trend test is in the control column, and the results of the life table pairwise comparisons with the controls are in the dosed columns.

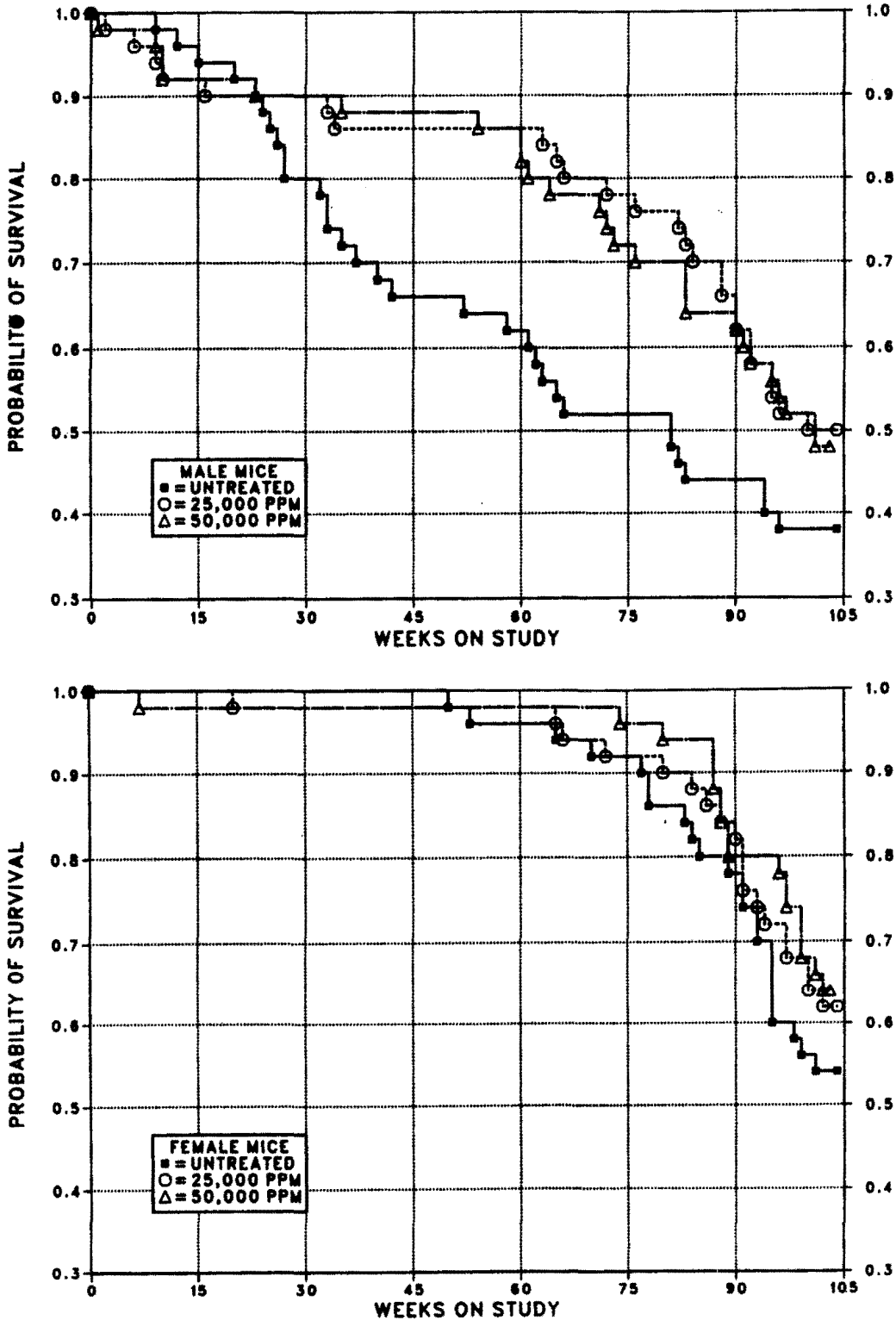

FIGURE 4. KAPLAN-MEIER SURVIVAL CURVES FOR MICE FED DIETS CONTAINING DECABROMODIPHENYL OXIDE FOR TWO YEARS

Liver: Granulomas were observed at an increased incidence in low dose male mice (male: control, 8/50, 16%; low dose, 22/50, 44%; high dose, 12/50, 24%; female: control, 23/50, 46%; low dose, 27/50, 54%; high dose, 24/50, 48%). Centrilobular hypertrophy was observed at increased incidence in dosed male mice (control, 0/50; low dose, 34/50, 68%; high dose, 32/50, 64%). This lesion consisted of enlarged hepatocytes with frothy vacuolated cytoplasm. The incidence of hepatocellular adenomas or carcinomas (combined) in low dose male mice was greater than that in the controls, and the incidence in the high dose male mice was marginally elevated relative to controls (Table 18). However, the significance of this effect may be decreased by the larger number of early deaths in control male mice. There was no significant compound-related effect on the incidences of hepatocellular adenomas or carcinomas (combined) in female mice (control, 8/50, 16%; low dose, 13/50, 26%; high dose, 13/50, 26%).

TABLE 18. ANALYSIS OF LIVER TUMORS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (a)

	Control	25,000 ppm (b)	50,000 ppm (b)
Hepatocellular Adenoma			
Overall Rates	4/50 (8%)	12/50 (24%)	12/50 (24%)
Adjusted Rates	19.0%	46.2%	39.0%
Terminal Rates	3/19 (16%)	11/25 (44%)	7/24 (29%)
Week of First Observation	81	100	60
Life Table Tests	P=0.078	P=0.081	P=0.095
Incidental Tumor Tests	P=0.084	P=0.088	P=0.099
Hepatocellular Carcinoma			
Overall Rates	5/50 (10%)	14/50 (28%)	8/50 (16%)
Adjusted Rates	20.7%	42.9%	26.8%
Terminal Rates	1/19 (5%)	8/25 (32%)	4/24 (17%)
Week of First Observation	81	72	76
Life Table Tests	P=0.494	P=0.118	P=0.486
Incidental Tumor Tests	P=0.523	P=0.139	P=0.542
Hepatocellular Adenoma or Carcinoma (c)			
Overall Rates	8/50 (16%)	22/50 (44%)	18/50 (36%)
Adjusted Rates	33.9%	67.7%	56.5%
Terminal Rates	4/19 (21%)	15/25 (60%)	11/24 (46%)
Week of First Observation	81	72	60
Life Table Tests	P=0.124	P=0.036	P=0.115
Incidental Tumor Tests	P=0.116	P=0.036	P=0.116

(a) The statistical analyses used are discussed in Chapter II (statistical methods) and Appendix E (footnotes).
(b) The estimated dose in milligrams per kilogram body weight is given in Chapter III (body weights and clinical signs) and in Appendix M.
(c) Historical incidence in NTP studies (mean ± SD): 540/1,784 (30% ± 8%); range: 7/50-29/50

Thyroid Gland: Follicular cell hyperplasia was observed at increased incidence in dosed mice (male: control, 2/50, 4%; low dose, 10/50, 20%; high dose, 19/50, 38%; female: control, 4/50, 8%; low dose, 9/50, 18%; high dose, 7/49, 14%). Microscopically, all these lesions were focal or multifocal and most were small, involving one to four follicles. The involved epithelium was cuboidal to tall, columnar, hyperchromatic, and, in some animals, multilayered. In some animals, the hyperplastic epithelium produced papillary projections into the lumen of the follicle.

The incidences of follicular cell adenomas or carcinomas (combined) in dosed male mice were greater (but not statistically greater) than that in the controls (male: control, 0/50; low dose, 4/50, 8%; high dose, 3/50, 6%; female: control, 1/50, 2%; low dose, 3/50, 6%; high dose, 3/50, 6%). The historical incidence of follicular cell neoplasms in untreated male mice in NTP studies is 28/1,680 (2% ± 2%). The highest incidence observed in a control group is 3/42 (Appendix F, Table F9).

Testis: Interstitial cell tumors were observed in 2/48 high dose male mice but in 0/50 controls and 0/50 low dose mice. The historical incidence in NTP studies is 5/1,768 (0.3% ± 0.7%). The highest incidence observed in a control group is 1/48.

Stomach: Ulcers were observed at an increased incidence in high dose female mice (male: control, 5/49, 10%; low dose, 3/50, 6%; high dose, 5/50, 10%; female: control, 1/50, 2%; low dose, 1/50, 2%; high dose, 8/50, 16%).

Multiple Organs: Suppurative inflammation or abscesses of the ovary, uterus, or peritoneum were observed in 12 control, 8 low dose, and 16 high female mice.

IV. DISCUSSION AND CONCLUSIONS

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Fourteen-day and 13-week studies of decabromodiphenyl oxide were conducted in F344/N rats and B6C3F$_1$ mice to determine toxicity and affected organs and to aid in the selection of doses for the 2-year toxicity and carcinogenicity studies. In 14-day studies, groups of five animals of each sex and species were exposed to decabromodiphenyl oxide at 0, 5,000, 20,000, 50,000, or 100,000 ppm in their diet. No effects on health, survival, or body weights were observed, and no compound-related clinical signs or gross pathologic effects were reported. In the 13-week studies, groups of 10 animals of each sex and species were exposed to decabromodiphenyl oxide at 0, 3,100, 6,300, 12,500, 25,000, or 50,000 ppm in their diet. No compound-related clinical signs or effects on survival, body weight, or feed consumption were observed. No gross or microscopic pathologic effects were reported.

Based on results of 14-day and 13-week studies, the 2-year studies were designed to expose groups of 50 animals of each sex and species to decabromodiphenyl oxide at 25,000 or 50,000 ppm in the diet. Feed consumption was slightly, but not significantly, elevated for both male and female rats in the dosed groups. The average daily consumption of decabromodiphenyl oxide was estimated to be 1,120 and 2,240 mg/kg for low dose and high dose male rats and 1,200 and 2,550 mg/kg for low dose and high dose female rats. No clinical signs of toxicity were reported for either sex of rats. No significant differences in survival were observed between any groups of either sex except low dose male rats. Survival of low dose male rats was significantly lower than that of the controls after week 102 (see Table 9). However, the late point in the study at which survival was decreased, lack of a dose effect, and lack of a similar effect in female rats or mice of either sex suggest that decreased survival in low dose male rats may not have been compound related.

In mice, mean body weights and feed consumption of dosed and control animals were comparable throughout most of the 2-year studies. The average amount of decabromodiphenyl oxide consumed per day was estimated to be 3,200 and 6,650 mg/kg for low dose and high dose male mice and 3,760 and 7,780 mg/kg for low dose and high dose female mice. No compound-related clinical signs of toxicity were reported. No significant differences in survival were observed between any groups of either sex (see Table 17). Overall survival of both sexes of both species was considered adequate for evaluation of tumor incidences.

At the end of the 2-year studies, neoplastic nodules in livers of male and female rats were observed with significant positive trends, and the incidences of neoplastic nodules in dosed male and high dose female rats were significantly greater than those in the controls (see Table 11). The incidences of neoplastic nodules in rats increased with dose in both males and females and appeared to be compound related. The incidence of hepatocellular carcinomas was low in all groups and was apparently not compound related. Therefore, the increased incidences of neoplastic nodules were considered as some evidence of decabromodiphenyl oxide carcinogenicity in rats.

Mononuclear cell leukemia was observed in dosed male rats with a significant positive trend by the life table test (see Table 12) but not by the incidental tumor test. Although leukemia is generally regarded as a life-threatening neoplasm, the incidence of this lesion in dosed male rats killed at the end of the study exceeded that observed in animals dying during the study, suggesting that the tumor may have been incidental rather than lethal in these particular groups. Moreover, control male rats in this study had the highest incidence of leukemia ever reported in untreated controls in NTP feed studies (30/50, 60%); the overall historical incidence is 458/1,727 (26.5%) (see Table 12; Appendix F, Table F1). The incidence of mononuclear cell leukemia in male rats increased slightly with dose, but because of the exceptionally high incidence in control rats, the marginal nature of the increase, and the lack of a significant increase in female rats, the increase over controls in male rats was not considered biologically significant. A sarcoma was observed in the spleen of one low dose and one high dose male rat. The historical incidence of splenic sarcomas in control NTP studies is 5/1,705 (0.3%).

Acinar cell adenomas of the pancreas occurred in high dose male rats with a significant positive

trend, and the incidence was marginally greater than that of the controls (see Table 13). Although the incidence in high dose males (4/50) appears quite high compared with that in historical controls (3/1,677), a review by the Pathology Working Group revealed that the criteria for acinar cell adenoma in this study included both acinar cell adenoma and acinar cell hyperplasia as diagnosed for other NTP studies. Thus, the historical controls are not an appropriate comparison. The incidence of proliferative exocrine pancreatic lesions depends both on the criteria used as well as on the amount of pancreatic tissue examined. When the entire pancreas in untreated male rats is embedded and a single section is made, the incidence of proliferative exocrine lesions approaches 25% (Boorman et al., 1985). Thus, the occurrence of exocrine pancreatic lesions in high dose male rats is not considered a compound-related effect. Acinar cell adenomas were also observed in one low dose and one high dose female rat. However, they were not significantly increased in either sex. Other tumors observed in dosed rats but at a less than significant incidence were Zymbal gland carcinomas in low dose female rats and osteosarcomas in low dose males.

Several nonneoplastic lesions were observed in dosed rats. Thrombosis and degeneration were observed at increased incidences in the liver of high dose male rats (see Table 10). Fibrosis of the spleen and lymphoid hyperplasia of the mandibular lymph nodes were observed at increased incidences in high dose male rats. The incidences of hematopoiesis in spleens of dosed female rats and acanthosis of the forestomach in dosed male rats were slightly increased. The incidence of degeneration of the eyes was increased in low dose female rats, but this lesion could have resulted from greater exposure to fluorescent light. This study was conducted before the NTP instituted cage rotation as part of the experimental protocol. One nonneoplastic lesion, C-cell hyperplasia of the thyroid gland, decreased in a dose-dependent fashion in male rats (control, 12/50; low dose, 6/49; high dose, 2/49) and female rats (control, 14/50; low dose, 7/49; high dose, 2/50) (Appendix C).

Neoplasia that occurred at significantly increased incidences in mice was limited to the livers of male mice. Hepatocellular adenomas or carcinomas (combined) were observed in low dose male mice at a significantly greater incidence than in the controls (control, 8/50; low dose, 22/50; high dose, 18/50) (see Table 18). Thyroid gland follicular cell adenomas or carcinomas (combined) in male mice were observed at marginally increased incidences (control, 0/50; low dose, 4/50; high dose, 3/50). The significance of this lesion was supported by an increased incidence of follicular cell hyperplasia in male mice. The evidence of carcinogenicity in male mice is weakened by the early loss of control animals and the lack of a statistically significant effect at the high dose. Therefore, the increased incidence of hepatocellular neoplasms in low dose animals and the less than significant increase in thyroid gland tumors are considered equivocal evidence of carcinogenicity of decabromodiphenyl oxide in male mice.

Nonneoplastic lesions were observed at increased incidences in several tissues of dosed mice. Granulomas were increased in the liver of low dose male mice, and centrilobular hypertrophy occurred at increased incidences in the liver of both low and high dose male mice. Follicular cell hyperplasia of the thyroid gland was increased in male mice (control, 4/50; low dose, 10/50; high dose, 19/50). This observation is consistent with the observation of thyroid gland hyperplasia in a repeated-dose study of decabromodiphenyl oxide in rats (Norris et al., 1973). These investigators speculated that thyroid gland hyperplasia could have resulted from competition between bromine and iodine in the thyroid gland. However, in the present study, a dose-dependent decrease in thyroid gland C-cell hyperplasia was observed in rats of each sex (Appendix C). An increased incidence of ulcers of the stomach was observed in high dose female mice.

Decabromodiphenyl oxide was not mutagenic in strains TA1535, TA1537, TA98, or TA100 of *Salmonella typhimurium* in the presence or absence of Aroclor 1254-induced male Sprague-Dawley rat or male Syrian hamster liver S9 when tested according to the preincubation protocol (Appendix G). Decabromodiphenyl oxide was not mutagenic in the mouse lymphoma L5178Y/TK$^{+/-}$ assay in the presence or absence

of Aroclor 1254-induced male F344 rat liver S9. Decabromodiphenyl oxide did not induce sister-chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells in vitro in the presence or absence of S9 prepared from livers of Aroclor 1254-induced male Sprague-Dawley rats.

Aromatic molecules such as diphenyl oxide become decreasingly soluble in both water and organic solvents as the degree of halogenation increases (see Table 1). Chemicals that are not in solution are absorbed from the gastrointestinal tract very sparingly. As a supplement to the carcinogenesis studies, additional experiments were conducted to quantitate decabromodiphenyl oxide absorption from the gastrointestinal tract of male rats and to determine the effect of dose on absorption (Appendix O). These studies were limited to male rats because gastrointestinal absorption is thought to be similar in each sex of both species. In these experiments, radiolabeled ^{14}C-decabromodiphenyl oxide (97.9%-99.2% pure) was diluted with unlabeled decabromodiphenyl oxide to yield the desired concentrations. Decabromodiphenyl oxide was mixed in the diet at approximate concentrations of 250, 500, 2,500, 5,000, 25,000 or 50,000 ppm or was administered by intravenous injection (1 mg/kg). Animals were preconditioned by being fed diets containing the respective dose of unlabeled decabromodiphenyl oxide for 7 days before being fed diets containing radiolabeled decabromodiphenyl oxide for 1 day and then being returned to diets containing unlabeled material for the remainder of the holding period.

Results of these studies indicate that, after exposure at all doses in the diet, greater than 99% of the radioactivity recovered was excreted in the feces within 72 hours. Excretion in urine accounted for approximately 0.01% or less of the dose. After a dose was administered intravenously, 61% of the recovered radioactivity was excreted in feces in 72 hours and approximately 0.1% was excreted in urine. Analysis of all major organs and tissues following oral dosing indicated trace levels of radioactivity in most tissues. The highest concentrations were found in gastrointestinal tissues, liver, kidney, lung, skin, and adipose tissue. The high ^{14}C-decabromodiphenyl oxide content of gastrointestinal tissues was attributed to intimate contact with the formulated diet; therefore, these tissues were not used to estimate absorption. Concentrations of decabromodiphenyl oxide in other tissues were near the limits of accurate detection and thereby contributed to the variability of estimates of absorption.

Estimates of decabromodiphenyl oxide absorption from the gastrointestinal tract were calculated by comparing tissue levels after oral exposure versus intravenous administration (Appendix O). For data obtained at similar time points,

$$\text{percent absorption} = \frac{\text{oral sample}}{\text{intravenous sample}} \times 100$$

Estimates of absorption obtained from a comparison of average tissue concentrations after intravenous dosing (Appendix O, Table O6) versus oral dosing (Table O4, Group III) indicate that 0.33% ± 0.19% of the 50,000-ppm dose was absorbed. In the 2-year studies, animals consuming 50,000 ppm decabromodiphenyl oxide in the diet were estimated to have consumed 2,240 mg/kg per day. However, based on estimated absorption, the animals absorbed only 7.4 ± 4.2 mg/kg per day. Data for the 25,000-ppm dose group (Table O2) indicate that the percent of dose absorbed was not significantly different from the high dose; therefore, these animals absorbed approximately 3.7 ± 2.1 mg/kg per day. It is not known if this represents a significant difference in dose for animals exposed at the high or low dose in these studies and may explain the lack of dose response in some instances.

Radioactivity present in the liver following exposure in the diet was confirmed as decabromodiphenyl oxide by extraction, purification, and reanalysis (Appendix O). However, the minimal absorption of decabromodiphenyl oxide from the gastrointestinal tract, and presumably from other potential routes of exposure as well, offers a partial explanation of the low short-term and long-term toxicity of the compound.

Additional significance of the absorption data is seen when one considers that the material used

in these studies is not 100% pure. Four lots of decabromodiphenyl oxide were used in the present studies. Analysis indicated purities of 94%-99% (Appendix H). Since decabromodiphenyl oxide is very poorly absorbed from the gastrointestinal tract and absorption of other components of the batches used is unknown, it is possible that another component might be absorbed in greater quantity and account for more of the observed toxicity than decabromodiphenyl oxide. Therefore, toxicity observed in this study could be attributed to the technical grade used rather than pure decabromodiphenyl oxide.

A dose-dependent increase in liver weight (approximately 40% greater than the controls) was observed in rats exposed to decabromodiphenyl oxide at 25,000 and 50,000 ppm in the diet for 11 days (Appendix O; Figure 14). Liver weights of animals exposed at the two lowest doses were unaffected; liver weights of animals exposed at 2,500 or 5,000 ppm were increased by 30%-40%. This observation confirms and quantitates earlier reports (Norris et al., 1973, 1975a,b; Kociba et al., 1975; Carlson, 1980). Liver weights were not recorded in the 14-day and 13-week portions of these studies. No other effects were observed in these repeated-dose studies.

Previous studies of highly halogenated aromatics such as decabromodiphenyl oxide indicate that these compounds are poorly metabolized, if at all (Matthews et al., 1977; Matthews and Tuey, 1980). However, results of the supplementary study presented in Appendix O indicate that much of the absorbed decabromodiphenyl oxide is metabolized and excreted in bile. From this cursory study of decabromodiphenyl oxide tissue distribution and clearance, this compound does not appear to have the same potential for bioaccumulation as polychlorinated or polybrominated biphenyls with which it shares structural and chemical similarities. This observation offers additional explanation of the low long-term toxicity of this compound.

The experimental and tabulated data for the NTP Technical Report on decabromodiphenyl oxide were examined for accuracy, consistency, and compliance with Good Laboratory Practice requirements. As summarized in Appendix P, the audit revealed no major problems with the conduct of the studies or with collection and documentation of the experimental data. No discrepancies were found that influenced the final interpretation of the results of these studies.

Conclusions: Under the conditions of these 2-year feed studies of decabromodiphenyl oxide, there was *some evidence of carcinogenicity** for male and female F344/N rats as shown by increased incidences of neoplastic nodules of the liver in low dose (25,000 ppm) males and high dose (50,000 ppm) groups of each sex. There was *equivocal evidence of carcinogenicity* for male $B6C3F_1$ mice as shown by increased incidences of hepatocellular adenomas or carcinomas (combined) in the low dose group and of thyroid gland follicular cell adenomas or carcinomas (combined) in both dosed groups. There was *no evidence of carcinogenicity* for female $B6C3F_1$ mice receiving 25,000 or 50,000 ppm in the diet. Several nonneoplastic lesions were observed at increased incidences, the most notable being thyroid gland follicular cell hyperplasia in male mice.

*Categories of evidence of carcinogenicity are defined in the Note to the Reader on page 2. The discussion and vote regarding the interpretative conclusions are summarized on pages 15-16.

V. REFERENCES

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APPENDIX A

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*Skin	(50)	(50)	(50)
Squamous cell papilloma	1 (2%)		
Squamous cell carcinoma	1 (2%)		1 (2%)
Basal cell carcinoma	1 (2%)		1 (2%)
Keratoacanthoma	2 (4%)	3 (6%)	1 (2%)
Neurofibrosarcoma	1 (2%)		
*Subcutaneous tissue	(50)	(50)	(50)
Fibroma	3 (6%)	4 (8%)	3 (6%)
Fibrosarcoma	4 (8%)		1 (2%)
Neurofibroma	2 (4%)	2 (4%)	1 (2%)
Neurofibrosarcoma	2 (4%)	2 (4%)	
RESPIRATORY SYSTEM			
#Lung	(50)	(50)	(49)
Alveolar/bronchiolar adenoma	1 (2%)	1 (2%)	3 (6%)
Paraganglioma, metastatic		1 (2%)	
Sarcoma, NOS, metastatic			1 (2%)
Osteosarcoma, metastatic		2 (4%)	
HEMATOPOIETIC SYSTEM			
*Multiple organs	(50)	(50)	(50)
Leukemia, mononuclear cell	30 (60%)	33 (66%)	35 (70%)
#Spleen	(49)	(50)	(49)
Sarcoma, NOS		1 (2%)	1 (2%)
#Mandibular lymph node	(50)	(50)	(49)
Squamous cell carcinoma, metastatic	1 (2%)		
CIRCULATORY SYSTEM			
#Heart	(50)	(50)	(49)
Osteosarcoma, metastatic		1 (2%)	
DIGESTIVE SYSTEM			
#Salivary gland	(49)	(50)	(48)
Sarcoma, NOS	1 (2%)		2 (4%)
Fibrosarcoma			1 (2%)
#Liver	(50)	(50)	(49)
Neoplastic nodule	1 (2%)	7 (14%)	15 (31%)
Hepatocellular carcinoma	1 (2%)	1 (2%)	1 (2%)
Osteosarcoma, metastatic		2 (4%)	
#Pancreas	(49)	(50)	(49)
Acinar cell adenoma			4 (8%)
#Jejunum	(49)	(50)	(48)
Carcinoma, NOS	1 (2%)		
Leiomyoma			1 (2%)
URINARY SYSTEM			
#Perirenal tissue	(48)	(50)	(49)
Pheochromocytoma, metastatic			1 (2%)
#Kidney/tubule	(48)	(50)	(49)
Cystadenoma, NOS			1 (2%)

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#Anterior pituitary	(50)	(50)	(50)
Carcinoma, NOS		1 (2%)	
Adenoma, NOS	10 (20%)	10 (20%)	9 (18%)
#Adrenal	(49)	(50)	(49)
Cortical adenoma	4 (8%)	1 (2%)	1 (2%)
#Adrenal medulla	(49)	(50)	(49)
Pheochromocytoma	31 (63%)	18 (36%)	18 (37%)
Pheochromocytoma, malignant	4 (8%)	1 (2%)	5 (10%)
#Thyroid	(50)	(49)	(49)
C-cell adenoma	6 (12%)	5 (10%)	1 (2%)
C-cell carcinoma	2 (4%)	2 (4%)	2 (4%)
#Parathyroid	(49)	(48)	(47)
Adenoma, NOS			1 (2%)
#Pancreatic islets	(49)	(50)	(49)
Islet cell adenoma	4 (8%)	1 (2%)	1 (2%)
REPRODUCTIVE SYSTEM			
*Mammary gland	(50)	(50)	(50)
Adenocarcinoma, NOS	1 (2%)		
Fibroadenoma		3 (6%)	
*Preputial gland	(50)	(50)	(50)
Carcinoma, NOS	4 (8%)	4 (8%)	2 (4%)
Adenoma, NOS		1 (2%)	2 (4%)
#Prostate	(47)	(49)	(49)
Adenoma, NOS	3 (6%)		3 (6%)
#Testis	(47)	(50)	(49)
Interstitial cell tumor	44 (94%)	47 (94%)	47 (96%)
*Epididymis	(50)	(50)	(50)
Mesothelioma, invasive			1 (2%)
NERVOUS SYSTEM			
#Cerebrum	(50)	(50)	(50)
Astrocytoma	2 (4%)	1 (2%)	
#Brain	(50)	(50)	(50)
Osteosarcoma, invasive		1 (2%)	
#Cerebellum	(50)	(50)	(50)
Granular cell tumor, NOS		1 (2%)	
SPECIAL SENSE ORGANS			
*Zymbal gland	(50)	(50)	(50)
Carcinoma, NOS		1 (2%)	1 (2%)
MUSCULOSKELETAL SYSTEM			
*Skull	(50)	(50)	(50)
Osteosarcoma		1 (2%)	
*Vertebra	(50)	(50)	(50)
Osteosarcoma		1 (2%)	
*Skeletal muscle	(50)	(50)	(50)
Osteosarcoma		1 (2%)	
BODY CAVITIES			
*Mediastinum	(50)	(50)	(50)
Sarcoma, NOS, invasive			1 (2%)
*Abdominal cavity	(50)	(50)	(50)
Paraganglioma, malignant		1 (2%)	

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
BODY CAVITIES (Continued)			
*Mesentery	(50)	(50)	(50)
Sarcoma, NOS, invasive			1 (2%)
Osteosarcoma, metastatic		1 (2%)	
*Tunica vaginalis	(50)	(50)	(50)
Mesothelioma, NOS		1 (2%)	1 (2%)
Mesothelioma, malignant	1 (2%)		1 (2%)
ALL OTHER SYSTEMS			
*Multiple organs	(50)	(50)	(50)
Mesothelioma, invasive	1 (2%)		
Adipose tissue			
Pheochromocytoma, invasive			1
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Natural death	12	18	19
Moribund sacrifice	3	9	7
Terminal sacrifice	35	23	24
TUMOR SUMMARY			
Total animals with primary tumors**	49	50	49
Total primary tumors	168	156	167
Total animals with benign tumors	48	49	48
Total benign tumors	111	96	97
Total animals with malignant tumors	41	37	43
Total malignant tumors	56	51	54
Total animals with secondary tumors##	2	4	4
Total secondary tumors	2	8	6
Total animals with tumors uncertain-- benign or malignant	1	9	16
Total uncertain tumors	1	9	16

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
# Number of animals examined microscopically at this site
Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*Skin	(50)	(50)	(50)
Squamous cell papilloma			2 (4%)
Basal cell tumor			1 (2%)
Basal cell carcinoma		1 (2%)	
*Subcutaneous tissue	(50)	(50)	(50)
Carcinoma, NOS, invasive		1 (2%)	
Sarcoma, NOS	1 (2%)		
Fibrosarcoma	2 (4%)	1 (2%)	1 (2%)
Fibrosarcoma, invasive			1 (2%)
Myxosarcoma			1 (2%)
Lipoma	1 (2%)		
RESPIRATORY SYSTEM			
#Lung	(50)	(49)	(50)
Alveolar/bronchiolar adenoma			1 (2%)
Fibrosarcoma, metastatic	1 (2%)		1 (2%)
Liposarcoma, metastatic		2 (4%)	
HEMATOPOIETIC SYSTEM			
*Multiple organs	(50)	(50)	(50)
Leukemia, mononuclear cell	14 (28%)	21 (42%)	18 (36%)
CIRCULATORY SYSTEM			
#Myocardium	(50)	(49)	(50)
Fibrosarcoma, metastatic	1 (2%)		
Neurofibrosarcoma			1 (2%)
Neurilemoma			1 (2%)
DIGESTIVE SYSTEM			
#Liver	(50)	(49)	(50)
Neoplastic nodule	1 (2%)	3 (6%)	9 (18%)
Hepatocellular carcinoma		2 (4%)	
#Pancreas	(49)	(48)	(49)
Acinar cell adenoma		1 (2%)	1 (2%)
#Gastric serosa	(49)	(48)	(50)
Sarcoma, NOS, metastatic	1 (2%)		
#Ileum	(49)	(47)	(50)
Leiomyosarcoma	1 (2%)		
URINARY SYSTEM			
None			
ENDOCRINE SYSTEM			
#Anterior pituitary	(50)	(50)	(50)
Carcinoma, NOS	1 (2%)	2 (4%)	1 (2%)
Adenoma, NOS	24 (48%)	22 (44%)	24 (48%)

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM (Continued)			
#Adrenal	(50)	(48)	(50)
Cortical adenoma	4 (8%)		2 (4%)
#Adrenal medulla	(50)	(48)	(50)
Pheochromocytoma	3 (6%)	4 (8%)	2 (4%)
Pheochromocytoma, malignant	1 (2%)		
#Thyroid	(50)	(49)	(50)
Follicular cell adenoma	1 (2%)		
Follicular cell carcinoma			1 (2%)
C-cell adenoma	9 (18%)	6 (12%)	5 (10%)
C-cell carcinoma	2 (4%)	4 (8%)	3 (6%)
REPRODUCTIVE SYSTEM			
*Mammary gland	(50)	(50)	(50)
Adenoma, NOS		1 (2%)	2 (4%)
Adenocarcinoma, NOS	1 (2%)		2 (4%)
Papillary cystadenocarcinoma NOS	1 (2%)		
Fibroadenoma	24 (48%)	18 (36%)	21 (42%)
*Clitoral gland	(50)	(50)	(50)
Carcinoma, NOS	4 (8%)	3 (6%)	3 (6%)
Adenoma, NOS		1 (2%)	1 (2%)
*Vagina	(50)	(50)	(50)
Papilloma, NOS			1 (2%)
Fibrosarcoma			1 (2%)
#Uterus	(49)	(49)	(50)
Endometrial stromal polyp	9 (18%)	10 (20%)	11 (22%)
Endometrial stromal sarcoma	1 (2%)		1 (2%)
#Cervix uteri	(49)	(49)	(50)
Squamous cell carcinoma	1 (2%)	1 (2%)	
#Ovary	(48)	(48)	(50)
Granulosa cell tumor	1 (2%)		
NERVOUS SYSTEM			
#Cerebrum	(49)	(50)	(49)
Carcinoma, NOS, invasive		1 (2%)	
Astrocytoma	1 (2%)	1 (2%)	
#Brain	(49)	(50)	(49)
Carcinoma, NOS, invasive	1 (2%)		1 (2%)
SPECIAL SENSE ORGANS			
*Zymbal gland	(50)	(50)	(50)
Carcinoma, NOS		3 (6%)	
MUSCULOSKELETAL SYSTEM			
*Vertebra	(50)	(50)	(50)
Osteosarcoma	1 (2%)		
BODY CAVITIES			
*Mesentery	(50)	(50)	(50)
Endometrial stromal sarcoma, invasive			1 (2%)
ALL OTHER SYSTEMS			
*Multiple organs	(50)	(50)	(50)
Mesothelioma, NOS			1 (2%)

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Natural death	7	12	9
Moribund sacrifice	3	5	7
Terminal sacrifice	40	33	34
TUMOR SUMMARY			
Total animals with primary tumors**	49	49	50
Total primary tumors	109	105	118
Total animals with benign tumors	41	35	41
Total benign tumors	75	63	75
Total animals with malignant tumors	28	34	26
Total malignant tumors	32	39	33
Total animals with secondary tumors##	3	4	3
Total secondary tumors	4	4	4
Total animals with tumors uncertain--benign or malignant	2	3	10
Total uncertain tumors	2	3	10

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
# Number of animals examined microscopically at this site
Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE: UNTREATED CONTROL

ANIMAL NUMBER	0001	0027	0029	0038	0030	0044	0047	0020	0050	0004	0008	0023	0014	0043	0042	0002	0003	0005	0006	0007	0009	0110	0111	0112	0113
WEEKS ON STUDY	0004	0755	0777	0881	0885	0993	0955	0966	0966	0971	0997	0999	1000	1001	1003	1004	1004	1004	1004	1004	1004	1004	1004	1004	1004
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																X									
Squamous cell carcinoma																			X						
Basal cell carcinoma																									
Keratoacanthoma									X																
Neurofibrosarcoma																					X				
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																		X							
Fibrosarcoma		X						X																	
Neurofibroma																									
Neurofibrosarcoma																							X		
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																				X					
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																			X						
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	–
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																						X			
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma										X															
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Large intestine	+	+	+	+	+	–	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	–	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS					X		X					X			X										
Adrenal	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma									X																
Pheochromocytoma							X						X	X	X	X	X	X	X		X	X	X	X	X
Pheochromocytoma, malignant																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell adenoma															X							X	X		X	X
C-cell carcinoma																									
Parathyroid	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																						X			
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Testis	+	+	+	+	+	–	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor		X	X	X			X	X	X	X	X		X		X	X	X	X	X	X	X	X	X	X	X
Prostate	+	+	+	+	+	–	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																	X								
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																X	X								
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma			X																						
BODY CAVITIES																									
Tunica vaginalis	+	+	+	+	+	N	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, malignant										X															
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, invasive										X															
Leukemia, mononuclear cell				X	X	X	X		X		X		X	X	X			X	X	X	X	X	X	X	X

+ : Tissue Examined Microscopically
– : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: No Tissue Information Submitted
C : Necropsy, No Histology Due To Protocol
A : Autolysis
M : Animal Missing
B : No Necropsy Performed

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	015	016	017	018	019	021	022	024	025	026	028	031	032	033	034	035	036	037	039	040	041	045	046	048	049	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Squamous cell papilloma																										1
Squamous cell carcinoma																										1
Basal cell carcinoma																				X						1
Keratoacanthoma										X																2
Neurofibrosarcoma																										1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroma									X				X													3
Fibrosarcoma			X									X														4
Neurofibroma											X								X							2
Neurofibrosarcoma																						X				2
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, metastatic																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	47
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sarcoma, NOS																										1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplastic nodule																					X					1
Hepatocellular carcinoma																										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, NOS																							X			1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma, NOS	X												X	X			X		X	X						10
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cortical adenoma			X																X				X			4
Pheochromocytoma	X	X	X	X	X		X	X	X	X	X		X		X		X		X	X	X		X	X		31
Pheochromocytoma, malignant	X														X								X		X	4
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell adenoma													X													6
C-cell carcinoma							X															X				2
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islet cell adenoma	X						X													X						4
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenocarcinoma, NOS																							X			1
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Interstitial cell tumor	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	44
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma, NOS														X				X								3
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																		X		X						4
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Astrocytoma										X																2
BODY CAVITIES																										
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Mesothelioma, malignant																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, invasive																										1
Leukemia, mononuclear cell	X	X	X	X		X			X							X		X	X	X			X	X	X	30

* Animals Necropsied

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE: LOW DOSE

ANIMAL NUMBER	144	127	107	101	119	145	147	150	118	129	133	139	115	122	140	105	124	111	120	117	128	142	108	125	136
WEEKS ON STUDY	068	069	071	072	077	077	077	079	082	082	084	085	087	088	089	093	096	098	098	099	100	100	101	101	103
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma					X					X															
Neurofibroma																		X							
Neurofibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Paraganglioma, metastatic	X																								
Osteosarcoma, metastatic			X															X							
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	−	+	+	+	+	+	+	−	+	−	−	−	+	−	+	+	+	−	+	−	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic			X																						
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule															X										
Hepatocellular carcinoma																									
Osteosarcoma, metastatic			X															X							
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS		X							X											X	X				
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma															X										
Pheochromocytoma												X					X		X			X	X	
Pheochromocytoma, malignant													X												
Thyroid	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell adenoma																		X							
C-cell carcinoma																									
Parathyroid	+	+	−	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma								X																	
REPRODUCTIVE SYSTEM																									
Mammary gland	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	N	+	+	+
Fibroadenoma																									
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor	X		X	X	X	X		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Prostate	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS				X										X											
Adenoma, NOS																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, invasive									X																
Granular cell tumor, NOS																									
Astrocytoma															X										
SPECIAL SENSE ORGANS																									
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N
Carcinoma, NOS																							X		
MUSCULOSKELETAL SYSTEM																									
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Osteosarcoma										X								X							
Muscle	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Osteosarcoma			X																						
BODY CAVITIES																									
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Paraganglioma, malignant	X																								
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, NOS					X																				
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Osteosarcoma, metastatic			X																						
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leukemia, mononuclear cell				X	X		X				X	X	X	X	X	X	X		X			X	X	X	X

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: LOW DOSE (Continued)

ANIMAL NUMBER	13 7	10 2	10 3	10 4	10 6	10 9	11 0	11 2	11 3	11 4	11 6	12 1	12 3	12 6	13 0	13 1	13 2	13 4	13 5	13 8	14 1	14 3	14 6	14 8	14 9	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	10 3	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Keratoacanthoma																	X	X						X		3
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroma		X					X																			4
Neurofibroma																				X						2
Neurofibrosarcoma													X						X							2
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma															X											1
Paraganglioma, metastatic																										1
Osteosarcoma, metastatic																										2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, NOS																					X					1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	40
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma, metastatic																										1
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplastic nodule						X		X	X	X	X			X					X							7
Hepatocellular carcinoma							X																			1
Osteosarcoma, metastatic																										2
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS												X														1
Adenoma, NOS				X							X						X	X		X				X		10
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cortical adenoma																										1
Pheochromocytoma	X	X	X	X	X		X	X									X	X	X	X			X		X	18
Pheochromocytoma, malignant																										1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
C-cell adenoma										X					X									X	X	5
C-cell carcinoma										X		X														2
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islet cell adenoma																										1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroadenoma								X							X			X								3
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Interstitial cell tumor	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	47
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS													X	X												4
Adenoma, NOS			X																							1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma, invasive																										1
Granular cell tumor, NOS																								X		1
Astrocytoma																										1
SPECIAL SENSE ORGANS																										
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																										1
MUSCULOSKELETAL SYSTEM																										
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Osteosarcoma																										2
Muscle	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Osteosarcoma																										1
BODY CAVITIES																										
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Paraganglioma, malignant																										1
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Mesothelioma, NOS																										1
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Osteosarcoma, metastatic																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leukemia, mononuclear cell	X	X		X	X	X	X	X		X		X	X	X				X	X		X	X	X	X	X	33

* Animals Necropsied

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE: HIGH DOSE

ANIMAL NUMBER	250	243	249	206	231	202	248	203	244	230	216	235	201	213	236	246	214	222	228	204	233	247	217	232	205
WEEKS ON STUDY	056	057	076	082	086	087	087	088	089	091	093	093	095	095	095	095	097	097	097	098	102	102	103	103	104
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma				X																					
Basal cell carcinoma																									
Keratoacanthoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma					X					X											X				
Fibrosarcoma							X																		
Neurofibroma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma												X											X		
Sarcoma, NOS, metastatic																			X						
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS															X										
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Thymus	+	+	–	+	+	+	+	+	–	–	+	+	–	+	–	+	–	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+
Sarcoma, NOS																			X						
Fibrosarcoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Neoplastic nodule							X														X				
Hepatocellular carcinoma																					X				
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																			X		X				
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Leiomyoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma, NOS																									
Pheochromocytoma, metastatic												X													
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS											X							X	X			X			
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma						X		X	X	X		X						X				X			
Pheochromocytoma, malignant							X						X												X
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
C-cell adenoma																									X
C-cell carcinoma			X																						
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	N	+	+	+	N	+	+
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																							X		
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
Adenoma, NOS																									
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, invasive																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
BODY CAVITIES																									
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Sarcoma, NOS, invasive																			X						
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, NOS															X										
Mesothelioma, malignant																									
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Sarcoma, NOS, invasive															X										
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leukemia, mononuclear cell			X		X	X	X	X	X	X		X		X		X	X			X	X	X	X	X	X
Adipose tissue																									
Pheochromocytoma, invasive													X												

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: HIGH DOSE (Continued)

ANIMAL NUMBER	207	208	209	210	211	212	215	218	219	220	221	223	224	225	226	227	229	234	237	238	239	240	241	242	245	TOTAL:
WEEKS ON STUDY	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Squamous cell carcinoma																										1
Basal cell carcinoma					X																					1
Keratoacanthoma																X										1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroma																										3
Fibrosarcoma																										1
Neurofibroma															X											1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma																		X								3
Sarcoma, NOS, metastatic																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sarcoma, NOS																										1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Sarcoma, NOS				X																						2
Fibrosarcoma													X													1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Neoplastic nodule	X				X	X	X	X			X		X	X	X	X	X				X		X			15
Hepatocellular carcinoma																										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Acinar cell adenoma											X	X														4
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Leiomyoma																						X				1
Large intestine	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
Kidney	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cystadenoma, NOS								X																		1
Pheochromocytoma, metastatic																										1
Urinary bladder	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma, NOS					X	X				X				X											X	9
Adrenal	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cortical adenoma																			X							1
Pheochromocytoma	X		X		X	X			X	X			X	X						X	X				X	18
Pheochromocytoma, malignant				X								X														5
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
C-cell adenoma																										1
C-cell carcinoma																									X	2
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	47
Adenoma, NOS					X																					1
Pancreatic islets	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islet cell adenoma												X														1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Testis	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Interstitial cell tumor	X		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	47
Prostate	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma, NOS	X													X												3
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS	X					X																				2
Adenoma, NOS																				X					X	2
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, invasive											X															1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	*50
Carcinoma, NOS																			X							1
BODY CAVITIES																										
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Sarcoma, NOS, invasive																										1
Tunica vaginalis	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Mesothelioma, NOS																										1
Mesothelioma, malignant											X															1
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Sarcoma, NOS, invasive																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leukemia, mononuclear cell	X	X	X	X				X	X	X		X		X	X	X	X		X	X	X	X	X		X	35
Adipose tissue																										
Pheochromocytoma, invasive																										1

*Animals Necropsied

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE: UNTREATED CONTROL

ANIMAL NUMBER	055	094	064	093	061	082	095	053	097	071	051	052	054	056	057	058	059	060	062	063	065	066	067	068	069
WEEKS ON STUDY	074	081	084	092	096	097	097	099	099	103	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104
INTEGUMENTARY SYSTEM																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS		X																							
Fibrosarcoma																									
Lipoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	–	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma, metastatic																									
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS, metastatic																									
Small intestine	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS			X																						
Adenoma, NOS						X						X	X	X		X	X		X	X		X	X		
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																	X			X					X
Pheochromocytoma	X												X												
Pheochromocytoma, malignant																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma													X												
C-cell adenoma																X			X		X			X	
C-cell carcinoma																		X					X		
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS														X											
Papillary cystadenocarcinoma, NOS												X													
Fibroadenoma	X		X				X	X						X		X		X	X	X					
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS												X							X			X			
Uterus	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Endometrial stromal polyp																					X			X	X
Endometrial stromal sarcoma									X																
Ovary	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor																							X		
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive			X																						
Astrocytoma																									
MUSCULOSKELETAL SYSTEM																									
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Osteosarcoma						X																			
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leukemia, mononuclear cell	X			X	X		X			X		X			X				X	X				

+ : Tissue Examined Microscopically
– : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: : No Tissue Information Submitted
C : Necropsy, No Histology Due To Protocol
A : Autolysis
M : Animal Missing
B : No Necropsy Performed

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	070	072	073	074	075	076	077	078	079	080	081	083	084	085	086	087	088	089	090	091	092	096	098	099	100	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	
INTEGUMENTARY SYSTEM																										
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	*50
Sarcoma, NOS																										1
Fibrosarcoma																			X			X				2
Lipoma													X													1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma, metastatic																						X				1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	–	+	+	+	+	+	+	–	–	+	+	+	–	+	+	+	+	–	+	+	+	+	42
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma, metastatic																						X				1
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplastic nodule								X																		1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sarcoma, NOS, metastatic			X																							1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leiomyosarcoma						X																				1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS																										1
Adenoma, NOS	X	X		X		X	X					X	X	X		X	X		X	X			X		X	24
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cortical adenoma															X											4
Pheochromocytoma					X																					3
Pheochromocytoma, malignant											X															1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell adenoma																										1
C-cell adenoma					X						X	X				X	X									9
C-cell carcinoma																										2
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	49
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenocarcinoma, NOS																										1
Papillary cystadenocarcinoma, NOS																										1
Fibroadenoma		X	X	X		X			X			X	X			X	X	X	X	X			X	X	X	24
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																							X			4
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Squamous cell carcinoma			X																							1
Endometrial stromal polyp								X		X		X			X				X		X					9
Endometrial stromal sarcoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	48
Granulosa cell tumor																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	49
Carcinoma, NOS, invasive																										1
Astrocytoma																X										1
MUSCULOSKELETAL SYSTEM																										
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Osteosarcoma																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leukemia, mononuclear cell			X	X								X							X	X						14

* Animals Necropsied

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE: LOW DOSE

ANIMAL NUMBER	184	166	164	189	151	173	198	163	165	160	176	172	186	188	199	187	156	152	153	154	155	157	158	159	161
WEEKS ON STUDY	049	066	072	080	086	086	091	092	094	095	097	099	099	100	100	102	103	104	104	104	104	104	104	104	104
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive											X														
Fibrosarcoma		X																							
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liposarcoma, metastatic																				X					
Trachea	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	–	+	+	–	+	–	+	–	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Esophagus	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	–	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS															X								X		
Adenoma, NOS					X	X	X		X					X			X	X		X	X			X	
Adrenal	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Pheochromocytoma							X													X					
Thyroid	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell adenoma																			X						
C-cell carcinoma																X									X
Parathyroid	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																					X				
Fibroadenoma						X	X	X	X			X						X		X	X	X		X	
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS	X								X																
Adenoma, NOS																									
Uterus	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Endometrial stromal polyp						X		X				X												X	
Ovary	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive															X										
Astrocytoma										X															
SPECIAL SENSE ORGANS																									
Zymbal gland	N	N	+	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS			X								X														
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leukemia, mononuclear cell										X	X	X	X	X		X		X		X		X		X	X

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: LOW DOSE (Continued)

ANIMAL NUMBER	162	167	168	169	170	171	174	175	177	178	179	180	181	182	183	185	190	191	192	193	194	195	196	197	200	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Basal cell carcinoma													X													1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Carcinoma, NOS, invasive																										1
Fibrosarcoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liposarcoma, metastatic																		X								2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thymus	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	42
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Neoplastic nodule						X								X		X										3
Hepatocellular carcinoma																	X							X		2
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Acinar cell adenoma														X												1
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS																										2
Adenoma, NOS			X		X	X		X	X	X	X	X		X					X		X		X			22
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pheochromocytoma																					X			X		4
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
C-cell adenoma		X					X			X					X						X					6
C-cell carcinoma												X												X		4
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenoma, NOS																										1
Fibroadenoma		X		X				X				X			X			X		X			X			18
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																									X	3
Adenoma, NOS																		X								1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Squamous cell carcinoma																				X						1
Endometrial stromal polyp	X						X			X	X		X									X				10
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS, invasive																										1
Astrocytoma																										1
SPECIAL SENSE ORGANS																										
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	*50
Carcinoma, NOS																					X					3
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leukemia, mononuclear cell		X			X	X				X	X		X		X	X			X				X			21

* Animals Necropsied

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE: HIGH DOSE

ANIMAL NUMBER	253	291	297	282	254	268	290	266	275	289	284	273	251	278	279	260	252	255	256	257	258	259	261	262	263
WEEKS ON STUDY	072	075	075	076	078	086	087	093	094	094	096	097	098	099	099	102	104	104	104	104	104	104	104	104	104
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Basal cell tumor																					X				
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Fibrosarcoma, invasive	X																								
Myxosarcoma								X																	
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Fibrosarcoma, metastatic	X																								
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	–	+	–	–	+	–	–	–	–	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neurofibrosarcoma																									
Neurilemoma																									
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule							X						X							X		X			
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																		X							
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS					X																				
Adenoma, NOS				X								X				X	X			X			X		X
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																			X						
Pheochromocytoma											X														
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma																									
C-cell adenoma													X	X											
C-cell carcinoma																		X	X						
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS														X											
Adenocarcinoma, NOS																									
Fibroadenoma						X			X		X				X	X		X	X	X					X
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																				X					
Adenoma, NOS																									
Vagina	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Papilloma, NOS																									
Fibrosarcoma	X																								
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrial stromal polyp	X			X										X									X		
Endometrial stromal sarcoma											X														
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	
Carcinoma, NOS, invasive					X																				
BODY CAVITIES																									
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Endometrial stromal sarcoma, invasive											X														
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, NOS			X																						
Leukemia, mononuclear cell		X		X			X		X	X		X		X					X	X			X	

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: HIGH DOSE (Continued)

ANIMAL NUMBER	264	265	267	269	270	271	272	274	276	277	280	281	283	285	286	287	288	292	293	294	295	296	298	299	300	TOTAL:
WEEKS ON STUDY	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Squamous cell papilloma						X																			X	2
Basal cell tumor																										1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibrosarcoma																	X									1
Fibrosarcoma, invasive																										1
Myxosarcoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma			X																							1
Fibrosarcoma, metastatic																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	–	–	+	+	+	+	+	38
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neurofibrosarcoma															X											1
Neurilemoma												X														1
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplastic nodule	X								X			X				X									X	9
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Acinar cell adenoma																										1
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Large intestine	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS																										1
Adenoma, NOS	X		X	X	X		X		X	X		X		X	X		X	X		X	X	X	X	X		24
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cortical adenoma																						X				2
Pheochromocytoma									X																	2
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell carcinoma																									X	1
C-cell adenoma										X										X					X	5
C-cell carcinoma											X															3
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	–	+	–	+	+	–	+	+	+	+	+	+	+	+	47
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenoma, NOS				X																						2
Adenocarcinoma, NOS																	X	X								2
Fibroadenoma	X		X		X			X	X		X		X		X			X					X	X		21
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS		X																X								3
Adenoma, NOS																	X									1
Vagina	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Papilloma, NOS					X																					1
Fibrosarcoma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endometrial stromal polyp			X		X								X					X		X	X			X		11
Endometrial stromal sarcoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, NOS, invasive																										1
BODY CAVITIES																										
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Endometrial stromal sarcoma, invasive																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, NOS																										1
Leukemia, mononuclear cell			X				X	X			X				X					X	X		X			18

*Animals Necropsied

APPENDIX B

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*Skin	(50)	(50)	(50)
Sarcoma, NOS		1 (2%)	
Fibrosarcoma	1 (2%)		
*Subcutaneous tissue	(50)	(50)	(50)
Fibroma		3 (6%)	
Fibrosarcoma	6 (12%)	8 (16%)	10 (20%)
RESPIRATORY SYSTEM			
#Lung	(50)	(50)	(50)
Hepatocellular carcinoma, metastatic	2 (4%)	1 (2%)	1 (2%)
Alveolar/bronchiolar adenoma	4 (8%)	1 (2%)	4 (8%)
Alveolar/bronchiolar carcinoma	2 (4%)	4 (8%)	1 (2%)
Fibrosarcoma, metastatic	1 (2%)	2 (4%)	1 (2%)
Rhabdomyosarcoma, metastatic			1 (2%)
HEMATOPOIETIC SYSTEM			
*Multiple organs	(50)	(50)	(50)
Malignant lymphoma, undiffer type		1 (2%)	
Malignant lymphoma, lymphocytic type	1 (2%)	2 (4%)	1 (2%)
Malignant lymphoma, histiocytic type			2 (4%)
Malignant lymphoma, mixed type	1 (2%)	1 (2%)	1 (2%)
Granulocytic leukemia			2 (4%)
#Spleen	(49)	(50)	(50)
Malignant lymphoma, undiffer type		1 (2%)	
Malignant lymphoma, mixed type		1 (2%)	
#Axillary lymph node	(50)	(49)	(49)
Fibrosarcoma, metastatic		1 (2%)	
#Brachial lymph node	(50)	(49)	(49)
Fibrosarcoma, metastatic	1 (2%)		
#Liver	(50)	(50)	(50)
Kupffer cell sarcoma			1 (2%)
#Jejunum	(47)	(50)	(49)
Malignant lymphoma, mixed type		1 (2%)	
CIRCULATORY SYSTEM			
*Subcutaneous tissue	(50)	(50)	(50)
Hemangioma		1 (2%)	
#Spleen	(49)	(50)	(50)
Hemangiosarcoma	1 (2%)	1 (2%)	
#Mesenteric l. node	(50)	(49)	(49)
Hemangioma		1 (2%)	
#Liver	(50)	(50)	(50)
Hemangioma		2 (4%)	
Hemangiosarcoma	1 (2%)	1 (2%)	2 (4%)
DIGESTIVE SYSTEM			
#Liver	(50)	(50)	(50)
Hepatocellular adenoma	4 (8%)	12 (24%)	12 (24%)
Hepatocellular carcinoma	5 (10%)	14 (28%)	8 (16%)
#Glandular stomach	(49)	(50)	(50)
Adenomatous polyp, NOS			1 (2%)

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#Forestomach	(49)	(50)	(50)
Squamous cell papilloma			1 (2%)
#Duodenum	(47)	(50)	(49)
Adenomatous polyp, NOS		1 (2%)	
URINARY SYSTEM			
None			
ENDOCRINE SYSTEM			
#Adrenal	(49)	(50)	(50)
Cortical adenoma	1 (2%)	2 (4%)	1 (2%)
#Adrenal/capsule	(49)	(50)	(50)
Adenoma, NOS			2 (4%)
#Adrenal medulla	(49)	(50)	(50)
Pheochromocytoma	1 (2%)	2 (4%)	1 (2%)
Pheochromocytoma, malignant			1 (2%)
#Thyroid	(50)	(50)	(50)
Follicular cell adenoma		3 (6%)	3 (6%)
Follicular cell carcinoma		1 (2%)	
#Pancreatic islets	(48)	(48)	(47)
Islet cell carcinoma		1 (2%)	
REPRODUCTIVE SYSTEM			
*Preputial gland	(50)	(50)	(50)
Carcinoma, NOS			1 (2%)
#Testis	(50)	(50)	(48)
Interstitial cell tumor			2 (4%)
NERVOUS SYSTEM			
None			
SPECIAL SENSE ORGANS			
*Harderian gland	(50)	(50)	(50)
Adenocarcinoma, NOS	1 (2%)		
Papillary adenocarcinoma		3 (6%)	
MUSCULOSKELETAL SYSTEM			
*Muscle of back	(50)	(50)	(50)
Rhabdomyosarcoma			1 (2%)
*Muscle of leg	(50)	(50)	(50)
Rhabdomyosarcoma			1 (2%)
BODY CAVITIES			
*Mediastinum	(50)	(50)	(50)
Fibrosarcoma, metastatic			1 (2%)
ALL OTHER SYSTEMS			
*Multiple organs	(50)	(50)	(50)
Hepatocellular carcinoma, metastatic			1 (2%)
Fibrosarcoma, metastatic	1 (2%)		1 (2%)
Base of tail			
Fibroma	1		
Fibrosarcoma		1	

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Natural death	29	14	19
Moribund sacrifice	3	11	7
Terminal sacrifice	18	25	24
TUMOR SUMMARY			
Total animals with primary tumors**	21	37	36
Total primary tumors	30	70	59
Total animals with benign tumors	8	20	18
Total benign tumors	11	28	27
Total animals with malignant tumors	17	31	28
Total malignant tumors	19	42	32
Total animals with secondary tumors##	4	3	5
Total secondary tumors	5	4	6

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
# Number of animals examined microscopically at this site
Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*Subcutaneous tissue	(50)	(50)	(50)
Fibrosarcoma		2 (4%)	1 (2%)
Rhabdomyosarcoma	1 (2%)		
Neurofibrosarcoma	1 (2%)	1 (2%)	
RESPIRATORY SYSTEM			
#Lung	(50)	(50)	(50)
Adenocarcinoma, NOS, metastatic	1 (2%)		2 (4%)
Hepatocellular carcinoma, metastatic	1 (2%)		
Alveolar/bronchiolar adenoma	4 (8%)	2 (4%)	2 (4%)
Alveolar/bronchiolar carcinoma	2 (4%)	2 (4%)	2 (4%)
Papillary adenocarcinoma, metastatic	1 (2%)		
Granulosa cell carcinoma, metastatic	1 (2%)		
Pheochromocytoma, metastatic	1 (2%)		
Osteosarcoma, metastatic			1 (2%)
HEMATOPOIETIC SYSTEM			
*Multiple organs	(50)	(50)	(50)
Malignant lymphoma, NOS		1 (2%)	
Malignant lymphoma, undiffer type	3 (6%)	1 (2%)	
Malignant lymphoma, lymphocytic type	5 (10%)	4 (8%)	1 (2%)
Malignant lymphoma, histiocytic type	2 (4%)	2 (4%)	5 (10%)
Malignant lymphoma, mixed type	6 (12%)	5 (10%)	11 (22%)
Granulocytic leukemia		1 (2%)	
#Spleen	(50)	(50)	(50)
Malignant lymphoma, undiffer type	1 (2%)		
#Kidney	(50)	(50)	(50)
Malignant lymphoma, undiffer type		1 (2%)	
CIRCULATORY SYSTEM			
#Liver	(50)	(50)	(50)
Hemangioma		1 (2%)	
#Uterus	(50)	(50)	(50)
Hemangioma	1 (2%)		
DIGESTIVE SYSTEM			
#Liver	(50)	(50)	(50)
Hepatocellular adenoma	5 (10%)	10 (20%)	7 (14%)
Hepatocellular carcinoma	3 (6%)	4 (8%)	7 (14%)
Osteosarcoma, metastatic			1 (2%)
#Pancreas	(50)	(48)	(49)
Acinar cell carcinoma			1 (2%)
#Esophagus	(50)	(50)	(50)
Squamous cell papilloma	1 (2%)		
#Forestomach	(50)	(50)	(50)
Squamous cell papilloma		1 (2%)	1 (2%)
URINARY SYSTEM			
#Kidney	(50)	(50)	(50)
Osteosarcoma			1 (2%)

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#Anterior pituitary	(40)	(45)	(49)
Adenoma, NOS	8 (20%)	6 (13%)	6 (12%)
#Adrenal/capsule	(48)	(49)	(50)
Neoplasm, NOS			1 (2%)
#Adrenal medulla	(48)	(49)	(50)
Pheochromocytoma		1 (2%)	1 (2%)
Pheochromocytoma, malignant	1 (2%)		
#Periadrenal tissue	(48)	(49)	(50)
Adenocarcinoma, NOS, metastatic			1 (2%)
#Thyroid	(50)	(50)	(49)
Follicular cell adenoma	1 (2%)	3 (6%)	2 (4%)
Follicular cell carcinoma			1 (2%)
C-cell carcinoma	1 (2%)		
#Parathyroid	(41)	(28)	(47)
Adenoma, NOS			1 (2%)
#Pancreatic islets	(50)	(48)	(49)
Islet cell adenoma		1 (2%)	
Islet cell carcinoma			1 (2%)
REPRODUCTIVE SYSTEM			
*Mammary gland	(50)	(50)	(50)
Adenocarcinoma, NOS	2 (4%)	1 (2%)	1 (2%)
#Uterus	(50)	(50)	(50)
Adenocarcinoma, NOS			1 (2%)
Papillary adenoma			1 (2%)
Fibroma	1 (2%)		
Endometrial stromal polyp		3 (6%)	1 (2%)
#Ovary	(49)	(50)	(49)
Papillary adenocarcinoma			1 (2%)
Granulosa cell carcinoma	1 (2%)		
Teratoma, NOS		1 (2%)	
NERVOUS SYSTEM			
None			
SPECIAL SENSE ORGANS			
*Harderian gland	(50)	(50)	(50)
Carcinoma, NOS			1 (2%)
Adenoma, NOS	1 (2%)		
Adenocarcinoma, NOS			1 (2%)
Papillary adenoma	1 (2%)		
Papillary adenocarcinoma	2 (4%)		1 (2%)
MUSCULOSKELETAL SYSTEM			
None			
BODY CAVITIES			
None			
ALL OTHER SYSTEMS			
*Multiple organs	(50)	(50)	(50)
Carcinoma, NOS, metastatic			1 (2%)
Acinar cell carcinoma, metastatic			1 (2%)
Fibrosarcoma, metastatic		1 (2%)	
Rhabdomyosarcoma, metastatic	1 (2%)		

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Natural death	19	16	16
Moribund sacrifice	5	3	2
Terminal sacrifice	26	31	32
TUMOR SUMMARY			
Total animals with primary tumors**	35	37	35
Total primary tumors	54	54	60
Total animals with benign tumors	20	24	17
Total benign tumors	23	28	22
Total animals with malignant tumors	25	22	28
Total malignant tumors	31	25	37
Total animals with secondary tumors##	6	1	6
Total secondary tumors	6	1	7
Total animals with tumors uncertain-- benign or malignant		1	1
Total uncertain tumors		1	1

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
# Number of animals examined microscopically at this site
Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE: UNTREATED CONTROL

ANIMAL NUMBER	0 1 9	0 3 6	0 3 1	0 3 9	0 0 9	0 3 5	0 4 1	0 3 7	0 3 2	0 3 3	0 5 0	0 0 6	0 1 0	0 4 9	0 4 5	0 4 3	0 4 7	0 0 8	0 2 4	0 0 4	0 2 1	0 2 7	0 4 8	0 2 3	0 2 0
WEEKS ON STUDY	0 0 9	0 1 2	0 1 5	0 2 0	0 2 3	0 2 4	0 2 5	0 2 6	0 2 7	0 2 7	0 3 2	0 3 3	0 3 3	0 3 5	0 3 7	0 4 0	0 4 2	0 5 2	0 5 8	0 6 1	0 6 2	0 6 3	0 6 5	0 6 6	0 8 1
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic																									X
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Fibrosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma, metastatic																									
Thymus	+	–	+	–	+	+	+	–	–	+	–	–	+	–	–	+	–	+	+	+	–	–	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									X
Hepatocellular carcinoma																									X
Hemangiosarcoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	–	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	+	+	+	–	+	+	+	–	+	–	+	+	+	–	+	+	–	+	+	+	–	+	+	–	+
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenocarcinoma, NOS																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Fibrosarcoma, metastatic																									
Malig. lymphoma, lymphocytic type																									
Malignant lymphoma, mixed type																									
Base of tail																									
Fibroma																									

+ : Tissue Examined Microscopically
– : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: : No Tissue Information Submitted
C : Necropsy, No Histology Due To Protocol
A : Autolysis
M : Animal Missing
B : No Necropsy Performed

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	046	022	025	029	040	038	018	001	002	003	005	007	011	012	013	014	015	016	017	026	028	030	034	042	044	TOTAL
WEEKS ON STUDY	081	082	083	094	094	096	103	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibrosarcoma														X												1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibrosarcoma		X	X				X									X	X		X							6
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic				X																						2
Alveolar/bronchiolar adenoma																		X		X			X	X		4
Alveolar/bronchiolar carcinoma											X									X						2
Fibrosarcoma, metastatic		X																								1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma														X												1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma, metastatic		X																								1
Thymus	–	+	–	–	+	–	–	–	+	–	–	–	–	+	–	+	–	+	–	+	+	+	+	–	+	25
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma								X																X	X	4
Hepatocellular carcinoma	X			X		X						X														5
Hemangiosarcoma					X																					1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	48
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cortical adenoma																							X			1
Pheochromocytoma														X												1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid	+	+	+	–	+	–	+	+	+	+	+	–	+	+	–	+	+	+	+	–	+	+	+	+	+	38
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	+	N	+	N	+	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenocarcinoma, NOS															X											1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Fibrosarcoma, metastatic			X																							1
Malig. lymphoma, lymphocytic type												X														1
Malignant lymphoma, mixed type																							X			1
Base of tail																										
Fibroma								X																		1

* Animals Necropsied

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE: LOW DOSE

ANIMAL NUMBER	118	134	145	228	330	550	441	443	227	338	466	108	449	110	229	114	331	117	426	109	221	105	113	335	123
WEEKS ON STUDY	002	006	009	010	016	033	034	063	065	066	072	076	082	083	084	088	088	090	090	092	092	095	095	096	100
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																									
Fibrosarcoma											X	X			X							X	X	X	
Hemangioma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic														X											
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Fibrosarcoma, metastatic											X											X			
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Malig. lymphoma, undiffer type																									
Malignant lymphoma, mixed type																									
Lymph nodes	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma, metastatic																						X			
Hemangioma																									X
Thymus	+	–	–	–	+	–	–	–	–	+	–	–	–	–	–	+	–	–	+	–	–	–	–	–	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									X
Hepatocellular carcinoma											X			X		X	X		X	X					
Hemangioma																									
Hemangiosarcoma																					X				
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	N	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS													X												
Malignant lymphoma, mixed type																									
Large intestine	–	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																			X						
Follicular cell carcinoma																									
Parathyroid	+	–	–	+	+	+	+	+	–	–	+	+	–	+	+	+	+	–	+	–	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Papillary adenocarcinoma																			X	X					
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malig. lymphoma, undiffer type													X												
Malig. lymphoma, lymphocytic type																			X						
Malignant lymphoma, mixed type																									
Base of tail																									
Fibrosarcoma																									

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: LOW DOSE (Continued)

ANIMAL NUMBER	101	102	103	104	106	107	111	112	115	116	119	120	122	124	125	132	133	136	137	139	140	142	144	147	148	TOTAL
WEEKS ON STUDY	103	103	103	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS	X																									1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroma					X	X											X									3
Fibrosarcoma																X									X	8
Hemangioma						X																				1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic																										1
Alveolar/bronchiolar adenoma											X															1
Alveolar/bronchiolar carcinoma	X			X							X									X						4
Fibrosarcoma, metastatic																										2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma												X														1
Malig. lymphoma, undiffer type	X																									1
Malignant lymphoma, mixed type							X																			1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibrosarcoma, metastatic																										1
Hemangioma																										1
Thymus	–	+	+	+	–	+	–	–	+	–	+	+	+	–	–	–	+	–	–	+	+	–	–	+	+	19
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma		X		X					X		X	X					X	X	X	X			X	X		12
Hepatocellular carcinoma						X	X		X	X	X				X		X		X							14
Hemangioma	X							X																		2
Hemangiosarcoma																										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	N	+	+	*50
Pancreas	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenomatous polyp, NOS																										1
Malignant lymphoma, mixed type								X																		1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cortical adenoma				X													X									2
Pheochromocytoma					X																	X				2
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell adenoma									X						X											3
Follicular cell carcinoma	X																									1
Parathyroid	–	+	+	+	+	+	–	+	–	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	38
Pancreatic islets	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Islet cell carcinoma													X													1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Papillary adenocarcinoma																			X							3
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malig. lymphoma, undiffer type																										1
Malig. lymphoma, lymphocytic type																				X						2
Malignant lymphoma, mixed type		X																								1
Base of tail																										
Fibrosarcoma						X																				1

* Animals Necropsied

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE: HIGH DOSE

ANIMAL NUMBER	22208	20709	22930	23015	21544	24545	21146	21760	21161	23464	24971	20972	21673	23976	22183	22232	23546	22090	20402	20023	22636	21919
WEEKS ON STUDY	00001	00019	01010	01020	02323	03535	05404	06000	06061	06364	07111	07272	07373	07676	08083	08383	09090	09091	09292	09595	09696	09797	10101
INTEGUMENTARY SYSTEM																							
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma									X		X	X	X	X					X	X			
RESPIRATORY SYSTEM																							
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic																							
Alveolar/bronchiolar adenoma						X														X			
Alveolar/bronchiolar carcinoma																							
Fibrosarcoma, metastatic											X												
Rhabdomyosarcoma, metastatic														X									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																							
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	–	+	–	+	–	+	+	+	+	–	–	+	+	+	+	–	+	+	+	+	+	+	–
CIRCULATORY SYSTEM																							
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																							
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma									X					X		X		X			X		
Hepatocellular carcinoma														X	X			X					
Hemangiosarcoma												X											
Kupffer cell sarcoma																							
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	–	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																							
Adenomatous polyp, NOS																							
Small intestine	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																							
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																							
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																				X			
Cortical adenoma																							
Pheochromocytoma																				X			
Pheochromocytoma, malignant																	X						
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																							
Parathyroid	+	–	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	–	+	–	+	+	–
REPRODUCTIVE SYSTEM																							
Mammary gland	+	N	N	N	N	+	N	N	N	N	N	+	N	N	N	N	N	N	N	N	+	+	N	N
Testis	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor																								
Prostate	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																								
NERVOUS SYSTEM																							
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUSCULOSKELETAL SYSTEM																							
Muscle	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Rhabdomyosarcoma															X		X						
BODY CAVITIES																							
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Fibrosarcoma, metastatic												X											
ALL OTHER SYSTEMS																							
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Hepatocellular carcinoma, metastatic																			X					
Fibrosarcoma, metastatic																				X				
Malig. lymphoma, lymphocytic type																								
Malig. lymphoma, histiocytic type																								
Malignant lymphoma, mixed type																								
Granulocytic leukemia																				X				

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: HIGH DOSE (Continued)

ANIMAL NUMBER	227	201	205	206	208	210	212	213	218	223	224	225	231	232	233	236	237	238	240	241	242	243	247	248	250	TOTAL
WEEKS ON STUDY	101	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibrosarcoma											X							X		X						10
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic	X																									1
Alveolar/bronchiolar adenoma					X										X										4
Alveolar/bronchiolar carcinoma																				X						1
Fibrosarcoma, metastatic																										1
Rhabdomyosarcoma, metastatic																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thymus	+	+	–	–	–	–	+	+	–	+	–	+	+	+	+	–	–	–	–	+	+	+	+	–	+	32
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma				X	X							X	X			X		X					X			12
Hepatocellular carcinoma	X		X					X						X								X				8
Hemangiosarcoma										X																2
Kupffer cell sarcoma											X															1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma														X												1
Adenomatous polyp, NOS																					X					1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	47
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma, NOS													X													2
Cortical adenoma															X											1
Pheochromocytoma																										1
Pheochromocytoma, malignant																										1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell adenoma					X								X			X										3
Parathyroid	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	–	+	+	–	+	–	+	+	+	+	40
REPRODUCTIVE SYSTEM																										
Mammary gland	N	+	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Interstitial cell tumor													X											X		2
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																					X					1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MUSCULOSKELETAL SYSTEM																										
Muscle	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Rhabdomyosarcoma																										2
BODY CAVITIES																										
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Fibrosarcoma, metastatic																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Hepatocellular carcinoma, metastatic																										1
Fibrosarcoma, metastatic																										1
Malig. lymphoma, lymphocytic type																	X									1
Malig. lymphoma, histiocytic type		X																						X		2
Malignant lymphoma, mixed type																X										1
Granulocytic leukemia																				X						2

*Animals Necropsied

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE: UNTREATED CONTROL

ANIMAL NUMBER	07781	09771	05551	09881	06021	06691	09961	05221	07741	06651	09931	07771	09911	05561	05591	05541	06061	06331	06671	07751	06001	06681	07731	10101	05111
WEEKS ON STUDY	05001	05031	06051	07001	07771	07781	07881	08331	08441	08551	08991	09011	09911	09931	09931	09951	09951	09951	09951	09951	09980	09991	10011	10031	10041
INTEGUMENTARY SYSTEM																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Rhabdomyosarcoma													X												
Neurofibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic											X														
Hepatocellular carcinoma, metastatic																							X		
Alveolar/bronchiolar adenoma																	X								
Alveolar/bronchiolar carcinoma																X									
Papillary adenocarcinoma, metastatic																	X								
Granulosa cell carcinoma, metastatic																						X			
Pheochromocytoma, metastatic																									
Trachea	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Malig. lymphoma, undiffer type																X									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	–	+	+	+	+	+	–	–	–	+	+	–	–	+	–	–	–	–	+	–	–	+	+	–	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma								X																	
Hepatocellular carcinoma																							X	X	
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	–	–	–	–	–	–	+	+	+	+	–	+	+	+
Adenoma, NOS		X			X														X		X				X
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+
Pheochromocytoma, malignant																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																		X							
C-cell carcinoma								X																	
Parathyroid	+	–	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	–	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	N	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS								X			X														
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																									
Hemangioma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell carcinoma																						X			
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																									
Papillary adenoma																									
Papillary adenocarcinoma																	X								
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Rhabdomyosarcoma, metastatic													X												
Malig. lymphoma, undiffer type									X						X										
Malig. lymphoma, lymphocytic type												X						X			X				
Malig. lymphoma, histiocytic type																									
Malignant lymphoma, mixed type																			X						X

+ : Tissue Examined Microscopically
– : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: No Tissue Information Submitted
C : Necropsy, No Histology Due To Protocol
A : Autolysis
M : Animal Missing
B : No Necropsy Performed

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	053	057	058	064	066	070	071	072	076	079	080	081	082	083	084	085	086	087	088	089	090	092	094	095	099	TOTAL
WEEKS ON STUDY	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Rhabdomyosarcoma																										1
Neurofibrosarcoma																								X		1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, NOS, metastatic																										1
Hepatocellular carcinoma, metastatic																										1
Alveolar/bronchiolar adenoma		X						X								X										4
Alveolar/bronchiolar carcinoma																					X					2
Papillary adenocarcinoma, metastatic																										1
Granulosa cell carcinoma, metastatic																										1
Pheochromocytoma, metastatic																						X				1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Malig. lymphoma, undiffer type																										1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	–	–	–	+	–	–		31
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma					X											X		X			X					5
Hepatocellular carcinoma										X																3
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma						X																				1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
Pituitary	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+		40
Adenoma, NOS				X													X		X							8
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pheochromocytoma, malignant																						X				1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell adenoma																										1
C-cell carcinoma																										1
Parathyroid	+	–	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	–	+	+	+	+	–	+	+	41
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenocarcinoma, NOS																										2
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroma																		X								1
Hemangioma																						X				1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	49
Granulosa cell carcinoma																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenoma, NOS																		X								1
Papillary adenoma													X													1
Papillary adenocarcinoma		X																								2
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Rhabdomyosarcoma, metastatic																										1
Malig. lymphoma, undiffer type			X																							3
Malig. lymphoma, lymphocytic type										X													X			5
Malig. lymphoma, histiocytic type				X																				X		2
Malignant lymphoma, mixed type		X									X							X				X				6

* Animals Necropsied

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE: LOW DOSE

ANIMAL NUMBER	18 85	17 73	19 55	19 96	18 82	19 99	17 79	18 83	17 71	15 55	16 88	19 93	16 64	19 98	18 88	19 94	15 53	18 81	16 67	15 51	15 52	15 54	15 56	15 57	15 58
WEEKS ON STUDY	02 00	06 65	06 66	07 72	08 80	08 84	08 86	08 88	09 01	09 91	09 91	09 91	09 93	09 94	09 97	09 97	10 00	10 00	10 02	10 44	10 44	10 44	10 44	10 44	10 44
INTEGUMENTARY SYSTEM																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma												X			X										
Neurofibrosarcoma									X																
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																				X		X			
Alveolar/bronchiolar carcinoma																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	–	+	+	+	–	–	+	–	–	–	+	+	–	–	–	+	–	+	+	–	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																			X		X				
Hepatocellular carcinoma													X							X					
Hemangioma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	+	+	+	+	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Malig. lymphoma, undiffer type							X																		
Urinary bladder	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS									X						X					X		X		X	
Adrenal	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma					X								X												
Parathyroid	–	+	+	+	+	+	–	–	+	–	+	+	+	–	+	+	–	–	–	–	+	+	–	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–
Islet cell adenoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+
Adenocarcinoma, NOS												X													
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrial stromal polyp																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Teratoma, NOS	X																								
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Fibrosarcoma, metastatic												X													
Malignant lymphoma, NOS										X															
Malig. lymphoma, undiffer type											X														
Malig. lymphoma, lymphocytic type			X					X									X								
Malig. lymphoma, histiocytic type		X													X										
Malignant lymphoma, mixed type					X																X				
Granulocytic leukemia																		X							

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: LOW DOSE (Continued)

ANIMAL NUMBER	159	160	161	162	163	165	166	169	170	172	174	175	176	177	178	180	184	186	187	189	190	191	192	197	200	TOTAL
WEEKS ON STUDY	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibrosarcoma																										2
Neurofibrosarcoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma												X										X				2
Alveolar/bronchiolar carcinoma																										2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	–	+	+	+	–	+	+	+	+	+	+	+	+	–	+	–	+	–	+	34
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma	X		X		X		X		X				X				X					X				10
Hepatocellular carcinoma					X									X												4
Hemangioma							X																			1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	48
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																					X					1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Malig. lymphoma, undiffer type																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
Pituitary	–	+	+	–	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Adenoma, NOS											X															6
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma											X															1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell adenoma		X																								3
Parathyroid	–	+	+	–	–	+	–	+	+	–	–	+	–	+	–	+	+	–	+	–	+	+	–	–	+	28
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	48
Islet cell adenoma								X																		1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenocarcinoma, NOS																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endometrial stromal polyp			X															X					X			3
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Teratoma, NOS																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Fibrosarcoma, metastatic																										1
Malignant lymphoma, NOS																										1
Malig. lymphoma, undiffer type																										1
Malig. lymphoma, lymphocytic type																				X						4
Malig. lymphoma, histiocytic type																										2
Malignant lymphoma, mixed type				X			X														X					5
Granulocytic leukemia																										1

* Animals Necropsied

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE: HIGH DOSE

ANIMAL NUMBER	29 98	27 77	25 53	25 54	26 65	27 76	27 78	29 96	28 83	28 86	28 81	29 97	30 00	26 01	27 75	28 88	28 82	27 73	25 51	25 52	25 55	25 56	25 57	25 58	25 59
WEEKS ON STUDY	00 07	07 47	08 80	08 87	08 87	08 87	08 88	08 88	08 89	08 89	09 96	09 97	09 97	09 99	09 99	09 99	10 01	10 02	10 03	10 03	10 03	10 03	10 03	10 03	10 03
INTEGUMENTARY SYSTEM																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic						X			X																
Alveolar/bronchiolar adenoma																								X	
Alveolar/bronchiolar carcinoma				X																					
Osteosarcoma, metastatic																				X					
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	–	–	+	+	+	–	–	–	+	–	+	–	–	–	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Hepatocellular carcinoma											X														
Osteosarcoma, metastatic																				X					
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	+	N	+	+	+	N	N	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell carcinoma																X									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																	X								
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma																				X					
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS														X			X								X
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS																									
Adenocarcinoma, NOS, metastatic																									
Pheochromocytoma																									
Thyroid	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																									
Parathyroid	–	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS			X																						
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS						X																			
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Papillary adenoma																									
Endometrial stromal polyp																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Papillary adenocarcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																							X		
Adenocarcinoma, NOS									X																
Papillary adenocarcinoma																				X					
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS, metastatic																							X		
Acinar cell carcinoma, metastatic																X									
Malig. lymphoma, lymphocytic type																									
Malig. lymphoma, histiocytic type					X				X				X												
Malignant lymphoma, mixed type														X						X					

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: HIGH DOSE (Continued)

ANIMAL NUMBER	260	262	263	264	266	267	268	269	270	271	272	274	279	280	284	285	287	289	290	291	292	293	294	295	299	TOTAL
WEEKS ON STUDY	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	103	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	*50
Fibrosarcoma													X													1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, NOS, metastatic																										2
Alveolar/bronchiolar adenoma			X																							2
Alveolar/bronchiolar carcinoma											X															2
Osteosarcoma, metastatic																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	40
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma	X	X		X				X											X			X		X		7
Hepatocellular carcinoma	X					X						X	X	X			X						X			7
Osteosarcoma, metastatic																										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+		49
Acinar cell carcinoma																										1
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																										1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma, NOS	X				X																		X			6
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplasm, NOS																									X	1
Adenocarcinoma, NOS, metastatic							X																			1
Pheochromocytoma																								X		1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Follicular cell adenoma											X												X			2
Follicular cell carcinoma																				X						1
Parathyroid	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma, NOS																										1
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	49
Islet cell carcinoma									X																	1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	*50
Adenocarcinoma, NOS																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, NOS							X																			1
Papillary adenoma												X														1
Endometrial stromal polyp																							X			1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Papillary adenocarcinoma				X																						1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																										1
Adenocarcinoma, NOS																										1
Papillary adenocarcinoma																										1
ALL OTHER SYSTEMS																										
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS, metastatic																										1
Acinar cell carcinoma, metastatic																										1
Malig. lymphoma, lymphocytic type					X																					1
Malig. lymphoma, histiocytic type	X			X																						5
Malignant lymphoma, mixed type						X					X			X	X		X		X	X			X	X		11

* Animals Necropsied

APPENDIX C

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*Skin	(50)	(50)	(50)
Hyperkeratosis	2 (4%)		
*Subcutaneous tissue	(50)	(50)	(50)
Epidermal inclusion cyst	1 (2%)		
Hematoma, NOS		1 (2%)	
Hematoma, organized	1 (2%)		
RESPIRATORY SYSTEM			
#Trachea	(50)	(50)	(49)
Inflammation, suppurative		1 (2%)	
Inflammation, acute suppurative			1 (2%)
#Lung/bronchiole	(50)	(50)	(49)
Hyperplasia, NOS			1 (2%)
Hyperplasia, focal	1 (2%)		
#Lung	(50)	(50)	(49)
Bronchiectasis	1 (2%)		
Congestion, NOS	4 (8%)	2 (4%)	5 (10%)
Edema, NOS		1 (2%)	2 (4%)
Hemorrhage	1 (2%)	2 (4%)	3 (6%)
Inflammation, focal	2 (4%)	4 (8%)	2 (4%)
Inflammation, multifocal	3 (6%)	1 (2%)	3 (6%)
Inflammation, diffuse	1 (2%)	1 (2%)	
Inflammation, acute focal	3 (6%)		
Inflammation, acute suppurative		1 (2%)	1 (2%)
Abscess, NOS	1 (2%)		
Pneumonia, chronic murine	1 (2%)		
Inflammation, chronic	35 (70%)	43 (86%)	42 (86%)
Fibrosis, focal	1 (2%)		
Necrosis, focal	1 (2%)		1 (2%)
Pigmentation, NOS			2 (4%)
Alveolar macrophages		1 (2%)	
Hyperplasia, alveolar epithelium	2 (4%)	2 (4%)	1 (2%)
#Lung/alveoli	(50)	(50)	(49)
Pigmentation, NOS	1 (2%)		
HEMATOPOIETIC SYSTEM			
#Bone marrow	(50)	(50)	(50)
Congestion, NOS	1 (2%)		1 (2%)
Hemorrhage		1 (2%)	1 (2%)
Hypoplasia, NOS	1 (2%)	3 (6%)	
Hyperplasia, NOS	2 (4%)	2 (4%)	
Myelofibrosis		1 (2%)	
#Spleen	(49)	(50)	(49)
Congestion, NOS		1 (2%)	
Fibrosis, focal	4 (8%)	3 (6%)	10 (20%)
Fibrosis, multifocal		1 (2%)	1 (2%)
Fibrosis, diffuse	1 (2%)	4 (8%)	2 (4%)
Necrosis, NOS	1 (2%)	2 (4%)	
Necrosis, focal	1 (2%)	2 (4%)	3 (6%)
Metamorphosis, fatty			1 (2%)
Hematopoiesis	1 (2%)	1 (2%)	
#Splenic follicles	(49)	(50)	(49)
Atrophy, NOS	1 (2%)	1 (2%)	1 (2%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM (Continued)			
#Mandibular lymph node	(50)	(50)	(49)
Congestion, NOS		1 (2%)	1 (2%)
Necrosis, NOS		1 (2%)	
Hyperplasia, reticulum cell	1 (2%)		
Hyperplasia, lymphoid	4 (8%)	6 (12%)	13 (27%)
#Mediastinal lymph node	(50)	(50)	(49)
Congestion, NOS		3 (6%)	1 (2%)
Hemorrhage			1 (2%)
Pigmentation, NOS	3 (6%)	1 (2%)	1 (2%)
Atrophy, NOS	1 (2%)		1 (2%)
Erythrophagocytosis	2 (4%)	2 (4%)	
Hyperplasia, reticulum cell	1 (2%)		
Hyperplasia, lymphoid	3 (6%)	1 (2%)	3 (6%)
#Pancreatic lymph node	(50)	(50)	(49)
Hyperplasia, reticulum cell		1 (2%)	
#Mesenteric lymph node	(50)	(50)	(49)
Hemorrhage			1 (2%)
Abscess, NOS			1 (2%)
Atrophy, NOS	1 (2%)		1 (2%)
Erythrophagocytosis		2 (4%)	
Hyperplasia, reticulum cell	26 (52%)	4 (8%)	19 (39%)
Hyperplasia, lymphoid	1 (2%)	1 (2%)	1 (2%)
#Renal lymph node	(50)	(50)	(49)
Pigmentation, NOS	2 (4%)		1 (2%)
Erythrophagocytosis	1 (2%)		
Hyperplasia, lymphoid		1 (2%)	
#Iliac lymph node	(50)	(50)	(49)
Pigmentation, NOS	1 (2%)		
Hyperplasia, lymphoid	1 (2%)		
#Lung	(50)	(50)	(49)
Leukocytosis, NOS		1 (2%)	
#Liver	(50)	(50)	(49)
Leukocytosis, NOS	2 (4%)		
Hematopoiesis	1 (2%)	1 (2%)	
#Thymus	(47)	(40)	(44)
Congestion, NOS		1 (3%)	
Hyperplasia, lymphoid	1 (2%)		
CIRCULATORY SYSTEM			
*Multiple organs	(50)	(50)	(50)
Thrombosis, NOS			1 (2%)
Periarteritis		1 (2%)	
#Bone marrow	(50)	(50)	(50)
Thrombosis, NOS		1 (2%)	
#Mandibular lymph node	(50)	(50)	(49)
Lymphangiectasis	1 (2%)	1 (2%)	2 (4%)
#Mediastinal lymph node	(50)	(50)	(49)
Lymphangiectasis			1 (2%)
#Mesenteric lymph node	(50)	(50)	(49)
Lymphangiectasis	4 (8%)		
#Lung	(50)	(50)	(49)
Thrombosis, NOS	1 (2%)	1 (2%)	2 (4%)
Thrombus, fibrin			1 (2%)
#Heart	(50)	(50)	(49)
Thrombosis, NOS			1 (2%)
Inflammation, chronic			1 (2%)
Fibrosis	2 (4%)	2 (4%)	
Degeneration, NOS		1 (2%)	

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM (Continued)			
#Heart/atrium	(50)	(50)	(49)
Thrombosis, NOS	3 (6%)	11 (22%)	6 (12%)
Fibrosis		1 (2%)	
#Heart/ventricle	(50)	(50)	(49)
Thrombosis, NOS		1 (2%)	
#Myocardium	(50)	(50)	(49)
Mineralization		2 (4%)	1 (2%)
Inflammation, acute focal	1 (2%)		
Inflammation, chronic	1 (2%)		
Inflammation, chronic focal	27 (54%)	20 (40%)	25 (51%)
Inflammation, chronic diffuse	9 (18%)	13 (26%)	17 (35%)
Fibrosis	1 (2%)	7 (14%)	3 (6%)
Necrosis, focal	1 (2%)		1 (2%)
*Coronary artery	(50)	(50)	(50)
Inflammation, chronic	1 (2%)		
*Mediastinal artery	(50)	(50)	(50)
Inflammation, chronic		1 (2%)	
*Superior pancreatico-duodenal artery	(50)	(50)	(50)
Inflammation, chronic		3 (6%)	
*Vena cava	(50)	(50)	(50)
Thrombosis, NOS		1 (2%)	
#Liver	(50)	(50)	(49)
Thrombosis, NOS	1 (2%)		9 (18%)
#Hepatic sinusoid	(50)	(50)	(49)
Pigmentation, NOS	2 (4%)		
#Testis	(47)	(50)	(49)
Periarteritis	2 (4%)		
#Adrenal medulla	(49)	(50)	(49)
Thrombosis, NOS	2 (4%)	1 (2%)	
DIGESTIVE SYSTEM			
#Salivary gland	(49)	(50)	(48)
Necrosis, focal	1 (2%)		
Atrophy, focal	1 (2%)		2 (4%)
Hyperplasia, diffuse			1 (2%)
#Liver	(50)	(50)	(49)
Hernia, NOS	1 (2%)	3 (6%)	
Congestion, NOS	2 (4%)	2 (4%)	
Spongiosis	1 (2%)	1 (2%)	
Hemorrhage	1 (2%)		1 (2%)
Hematoma, NOS	1 (2%)		
Inflammation, chronic	1 (2%)	3 (6%)	2 (4%)
Granuloma, NOS	7 (14%)	5 (10%)	2 (4%)
Fibrosis, focal		1 (2%)	1 (2%)
Hepatitis, toxic	8 (16%)	13 (26%)	12 (24%)
Degeneration, NOS	10 (20%)	16 (32%)	21 (43%)
Degeneration, cystic	2 (4%)	2 (4%)	1 (2%)
Necrosis, focal	9 (18%)	5 (10%)	9 (18%)
Necrosis, coagulative	2 (4%)		
Metamorphosis, fatty	8 (16%)	13 (26%)	11 (22%)
Pigmentation, NOS	4 (8%)	4 (8%)	10 (20%)
Focal cellular change	21 (42%)	25 (50%)	27 (55%)
Hepatocytomegaly		2 (4%)	
Atrophy, focal			1 (2%)
Regeneration, NOS	2 (4%)	2 (4%)	2 (4%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#Liver/centrilobular	(50)	(50)	(49)
Degeneration, NOS	1 (2%)	1 (2%)	
Necrosis, NOS		1 (2%)	
Necrosis, coagulative			1 (2%)
Cytoplasmic vacuolization		2 (4%)	
Hepatocytomegaly			1 (2%)
#Bile duct	(50)	(50)	(49)
Inflammation, chronic	17 (34%)	2 (4%)	6 (12%)
Fibrosis	5 (10%)	3 (6%)	11 (22%)
Hyperplasia, NOS	29 (58%)	26 (52%)	25 (51%)
#Pancreas	(49)	(50)	(49)
Ectopia	1 (2%)		
Dilatation/ducts	1 (2%)		
Hemorrhage			1 (2%)
Atrophy, NOS		2 (4%)	
Atrophy, focal	7 (14%)	2 (4%)	9 (18%)
Atrophy, diffuse		3 (6%)	4 (8%)
#Pancreatic duct	(49)	(50)	(49)
Hyperplasia, NOS		1 (2%)	
#Esophagus	(50)	(50)	(49)
Dilatation, NOS		1 (2%)	
Hyperkeratosis		2 (4%)	
#Stomach	(49)	(50)	(49)
Mineralization	1 (2%)		
Ulcer, NOS	1 (2%)	4 (8%)	
#Glandular stomach	(49)	(50)	(49)
Embryonal rest			1 (2%)
Mineralization	1 (2%)	1 (2%)	1 (2%)
Hemorrhage	1 (2%)		
Ulcer, NOS		2 (4%)	
Inflammation, acute diffuse			1 (2%)
Necrosis, focal	7 (14%)	4 (8%)	9 (18%)
Hyperplasia, diffuse		1 (2%)	
#Forestomach	(49)	(50)	(49)
Embryonal rest	1 (2%)		
Mineralization			1 (2%)
Ulcer, NOS		1 (2%)	
Inflammation, chronic	2 (4%)		
Inflammation, chronic focal			4 (8%)
Inflammation, chronic diffuse	1 (2%)	1 (2%)	2 (4%)
Perforation, inflammatory		1 (2%)	
Fibrosis		1 (2%)	
Necrosis, focal	2 (4%)	2 (4%)	5 (10%)
Hyperkeratosis			1 (2%)
Acanthosis		3 (6%)	5 (10%)
#Large intestine	(47)	(49)	(48)
Parasitism			1 (2%)
#Colon	(47)	(49)	(48)
Inflammation, suppurative		1 (2%)	
Parasitism		1 (2%)	1 (2%)
Necrosis, NOS		1 (2%)	
#Cecum	(47)	(49)	(48)
Edema, NOS			1 (2%)
Inflammation, acute focal			1 (2%)
Inflammation, acute diffuse			1 (2%)
Abscess, NOS			1 (2%)
Necrosis, NOS		1 (2%)	
Necrosis, focal			1 (2%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
URINARY SYSTEM			
#Kidney	(48)	(50)	(49)
Hamartoma		1 (2%)	
Mineralization		1 (2%)	
Congestion, NOS	2 (4%)	1 (2%)	1 (2%)
Hemorrhage	1 (2%)		
Nephropathy	45 (94%)	46 (92%)	47 (96%)
Necrosis, coagulative	1 (2%)		
Infarct, acute			1 (2%)
Pigmentation, NOS		1 (2%)	
#Kidney/cortex	(48)	(50)	(49)
Cyst, NOS		4 (8%)	
Multiple cysts			1 (2%)
#Kidney/tubule	(48)	(50)	(49)
Necrosis, focal	2 (4%)		
Pigmentation, NOS	35 (73%)	12 (24%)	13 (27%)
#Urinary bladder	(47)	(48)	(49)
Hemorrhage	1 (2%)	1 (2%)	1 (2%)
ENDOCRINE SYSTEM			
#Pituitary	(50)	(50)	(50)
Congestion, NOS		1 (2%)	1 (2%)
#Anterior pituitary	(50)	(50)	(50)
Cyst, NOS	3 (6%)	2 (4%)	2 (4%)
Hemorrhage	1 (2%)		
Hemorrhagic cyst	1 (2%)	1 (2%)	
Necrosis, focal	1 (2%)		1 (2%)
Pigmentation, NOS	2 (4%)	1 (2%)	
Hyperplasia, focal	6 (12%)	3 (6%)	3 (6%)
Angiectasis	3 (6%)	1 (2%)	1 (2%)
#Adrenal	(49)	(50)	(49)
Metamorphosis, fatty		1 (2%)	
#Adrenal/capsule	(49)	(50)	(49)
Fibrosis		1 (2%)	
#Adrenal cortex	(49)	(50)	(49)
Congestion, NOS	1 (2%)	1 (2%)	
Metamorphosis, fatty	3 (6%)	3 (6%)	2 (4%)
Cytoplasmic vacuolization		1 (2%)	
Hypertrophy, focal		1 (2%)	
Hyperplasia, focal		3 (6%)	1 (2%)
#Adrenal medulla	(49)	(50)	(49)
Hemorrhage	1 (2%)		
Pigmentation, NOS			1 (2%)
Hyperplasia, focal	11 (22%)	12 (24%)	6 (12%)
#Thyroid	(50)	(49)	(49)
Ultimobranchial cyst	1 (2%)		1 (2%)
Cyst, NOS	1 (2%)		
Cystic follicles	1 (2%)	3 (6%)	3 (6%)
Follicular cyst, NOS	1 (2%)		
Pigmentation, NOS	1 (2%)		
Hyperplasia, C-cell	12 (24%)	6 (12%)	2 (4%)
Hyperplasia, follicular cell	1 (2%)		
#Parathyroid	(49)	(48)	(47)
Hyperplasia, NOS	16 (33%)	7 (15%)	10 (21%)
#Pancreatic islets	(49)	(50)	(49)
Hyperplasia, focal	3 (6%)		

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*Mammary gland	(50)	(50)	(50)
Dilatation/ducts	8 (16%)	1 (2%)	3 (6%)
Galactocele		2 (4%)	1 (2%)
Hyperplasia, diffuse	1 (2%)		
*Preputial gland	(50)	(50)	(50)
Dilatation/ducts	1 (2%)	4 (8%)	2 (4%)
Abscess, NOS	2 (4%)	3 (6%)	1 (2%)
Inflammation, chronic	1 (2%)		1 (2%)
Hyperplasia, NOS	1 (2%)		1 (2%)
Hyperplasia, epithelial	1 (2%)		
Hyperplasia, focal		1 (2%)	
Hyperplasia, diffuse		1 (2%)	
Hyperkeratosis	1 (2%)	1 (2%)	1 (2%)
#Prostate	(47)	(49)	(49)
Hemorrhage	1 (2%)		
Inflammation, suppurative		1 (2%)	1 (2%)
Inflammation, acute	1 (2%)		
Inflammation, acute focal	1 (2%)		
Abscess, NOS	8 (17%)	3 (6%)	4 (8%)
Inflammation, active chronic		2 (4%)	1 (2%)
Inflammation, chronic			1 (2%)
Inflammation, chronic focal	8 (17%)	3 (6%)	4 (8%)
Hyperplasia, epithelial	5 (11%)	2 (4%)	6 (12%)
Hyperplasia, focal	3 (6%)		
*Seminal vesicle	(50)	(50)	(50)
Dilatation/ducts			1 (2%)
Cyst, NOS			1 (2%)
Inflammation, suppurative		1 (2%)	
#Testis	(47)	(50)	(49)
Mineralization	1 (2%)		
Granuloma, spermatic			1 (2%)
Degeneration, NOS	6 (13%)	4 (8%)	2 (4%)
Aspermatogenesis	1 (2%)	1 (2%)	
Spermatogenic arrest		1 (2%)	
Hypospermatogenesis	1 (2%)	3 (6%)	
Hyperplasia, interstitial cell	5 (11%)	8 (16%)	6 (12%)
*Epididymis	(50)	(50)	(50)
Granuloma, spermatic	1 (2%)		
Necrosis, fat	1 (2%)	1 (2%)	
NERVOUS SYSTEM			
#Cerebrum	(50)	(50)	(50)
Hemorrhage		1 (2%)	3 (6%)
Necrosis, focal		2 (4%)	
Necrosis, lamellar		1 (2%)	
#Cerebellum	(50)	(50)	(50)
Hemorrhage	1 (2%)	1 (2%)	2 (4%)
#Medulla oblongata	(50)	(50)	(50)
Cyst, NOS			1 (2%)
SPECIAL SENSE ORGANS			
*Eye	(50)	(50)	(50)
Synechia, anterior	1 (2%)		
Cataract	3 (6%)	1 (2%)	2 (4%)
Phthisis bulbi		1 (2%)	

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
SPECIAL SENSE ORGANS (Continued)			
*Eye/cornea	(50)	(50)	(50)
Inflammation, acute focal			1 (2%)
Inflammation, chronic	1 (2%)		1 (2%)
Inflammation, chronic diffuse		1 (2%)	
Necrosis, focal			1 (2%)
*Eye/retina	(50)	(50)	(50)
Degeneration, NOS	5 (10%)	1 (2%)	2 (4%)
*Zymbal gland	(50)	(50)	(50)
Abscess, NOS			1 (2%)
MUSCULOSKELETAL SYSTEM			
*Skull	(50)	(50)	(50)
Exostosis			1 (2%)
*Sternum	(50)	(50)	(50)
Fracture, NOS			1 (2%)
*Muscle of neck	(50)	(50)	(50)
Fibrosis, focal			1 (2%)
Degeneration, NOS			1 (2%)
BODY CAVITIES			
*Mediastinum	(50)	(50)	(50)
Edema, NOS			1 (2%)
*Abdominal cavity	(50)	(50)	(50)
Necrosis, fat	3 (6%)	3 (6%)	6 (12%)
ALL OTHER SYSTEMS			
*Multiple organs	(50)	(50)	(50)
Dilatation/ducts	1 (2%)		
Congestion, NOS		3 (6%)	1 (2%)
Inflammation, suppurative		1 (2%)	
Inflammation, chronic	2 (4%)	3 (6%)	
Pigmentation, NOS	1 (2%)		
Adipose tissue			
Edema, NOS			1
Inflammation, chronic	1		
Inflammation, chronic focal			1
SPECIAL MORPHOLOGY SUMMARY			
None			

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically.
# Number of animals examined microscopically at this site

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*Skin	(50)	(50)	(50)
Hyperplasia, focal	1 (2%)		
Acanthosis	1 (2%)		
*Subcutaneous tissue	(50)	(50)	(50)
Edema, NOS			1 (2%)
Necrosis, fat	1 (2%)		
RESPIRATORY SYSTEM			
*Tracheal lumen	(50)	(50)	(50)
Foreign body, NOS			1 (2%)
#Trachea	(50)	(49)	(50)
Inflammation, suppurative			1 (2%)
#Lung	(50)	(49)	(50)
Congestion, NOS	1 (2%)	3 (6%)	
Hematoma, organized		1 (2%)	
Inflammation, focal	2 (4%)	5 (10%)	1 (2%)
Inflammation, multifocal	3 (6%)		2 (4%)
Pneumonia, aspiration			1 (2%)
Inflammation, acute diffuse			1 (2%)
Abscess, NOS	1 (2%)		1 (2%)
Inflammation, chronic	44 (88%)	40 (82%)	44 (88%)
Necrosis, focal		1 (2%)	1 (2%)
Pigmentation, NOS	2 (4%)		
Hyperplasia, alveolar epithelium	1 (2%)		1 (2%)
HEMATOPOIETIC SYSTEM			
#Bone marrow	(50)	(50)	(50)
Hyperplasia, NOS		2 (4%)	1 (2%)
#Spleen	(49)	(48)	(50)
Hemorrhage		1 (2%)	
Pigmentation, NOS	25 (51%)	22 (46%)	18 (36%)
Hemosiderosis	1 (2%)	1 (2%)	
Depletion, lymphoid	1 (2%)	1 (2%)	
Hyperplasia, reticulum cell		4 (8%)	1 (2%)
Hyperplasia, lymphoid		1 (2%)	1 (2%)
Hematopoiesis	12 (24%)	24 (50%)	17 (34%)
#Splenic capsule	(49)	(48)	(50)
Inflammation, NOS	1 (2%)		
#Splenic follicles	(49)	(48)	(50)
Atrophy, NOS		1 (2%)	
#Mandibular lymph node	(50)	(49)	(50)
Hyperplasia, reticulum cell			1 (2%)
Hyperplasia, lymphoid	1 (2%)	3 (6%)	3 (6%)
#Mediastinal lymph node	(50)	(49)	(50)
Hemorrhage		1 (2%)	
Pigmentation, NOS	7 (14%)	3 (6%)	4 (8%)
Depletion, lymphoid	1 (2%)		
Erythrophagocytosis	8 (16%)	3 (6%)	3 (6%)
Hyperplasia, reticulum cell	1 (2%)	2 (4%)	1 (2%)
#Pancreatic lymph node	(50)	(49)	(50)
Pigmentation, NOS	1 (2%)		1 (2%)
Hyperplasia, reticulum cell		1 (2%)	
Hyperplasia, lymphoid			1 (2%)

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM (Continued)			
#Mesenteric lymph node	(50)	(49)	(50)
Hemorrhage	1 (2%)	1 (2%)	
Pigmentation, NOS	2 (4%)		
Depletion, lymphoid	1 (2%)	1 (2%)	
Erythrophagocytosis			2 (4%)
Hyperplasia, reticulum cell	34 (68%)	23 (47%)	22 (44%)
Hyperplasia, lymphoid		1 (2%)	
#Renal lymph node	(50)	(49)	(50)
Hemorrhage	1 (2%)		
Pigmentation, NOS	1 (2%)		
#Liver	(50)	(49)	(50)
Leukocytosis, NOS	7 (14%)	3 (6%)	5 (10%)
Hematopoiesis	1 (2%)	1 (2%)	1 (2%)
#Adrenal	(50)	(48)	(50)
Hematopoiesis			1 (2%)
CIRCULATORY SYSTEM			
#Mandibular lymph node	(50)	(49)	(50)
Lymphangiectasis		1 (2%)	1 (2%)
#Mesenteric lymph node	(50)	(49)	(50)
Lymphangiectasis	3 (6%)		
#Heart	(50)	(49)	(50)
Mineralization			1 (2%)
Inflammation, chronic	1 (2%)		1 (2%)
Fibrosis			1 (2%)
#Heart/atrium	(50)	(49)	(50)
Thrombosis, NOS		1 (2%)	1 (2%)
#Myocardium	(50)	(49)	(50)
Mineralization		1 (2%)	
Inflammation, chronic focal	26 (52%)	20 (41%)	16 (32%)
Inflammation, chronic diffuse	10 (20%)	11 (22%)	8 (16%)
Fibrosis	1 (2%)	2 (4%)	2 (4%)
Degeneration, NOS	1 (2%)		
*Pulmonary artery	(50)	(50)	(50)
Hyperplasia, NOS			1 (2%)
*Mesenteric artery	(50)	(50)	(50)
Inflammation, chronic	1 (2%)	1 (2%)	
DIGESTIVE SYSTEM			
*Tongue	(50)	(50)	(50)
Hyperkeratosis		1 (2%)	
#Salivary gland	(50)	(49)	(50)
Inflammation, chronic	1 (2%)	1 (2%)	
Fibrosis, diffuse		1 (2%)	
Atrophy, NOS	1 (2%)		
Atrophy, focal		1 (2%)	1 (2%)
#Liver	(50)	(49)	(50)
Hernia, NOS	6 (12%)	4 (8%)	4 (8%)
Congestion, NOS	1 (2%)	2 (4%)	1 (2%)
Hemorrhage	1 (2%)		
Inflammation, chronic	1 (2%)	1 (2%)	
Granuloma, NOS	23 (46%)	13 (27%)	17 (34%)
Fibrosis, focal	1 (2%)		1 (2%)
Hepatitis, toxic	4 (8%)	6 (12%)	6 (12%)
Necrosis, focal	2 (4%)	2 (4%)	5 (10%)
Metamorphosis, fatty	9 (18%)	5 (10%)	4 (8%)
Pigmentation, NOS	16 (32%)	8 (16%)	5 (10%)
Focal cellular change	37 (74%)	32 (65%)	31 (62%)
Hepatocytomegaly	2 (4%)	1 (2%)	
Angiectasis	2 (4%)		

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#Liver/centrilobular	(50)	(49)	(50)
Necrosis, coagulative		1 (2%)	
Cytoplasmic vacuolization			1 (2%)
#Liver/hepatocytes	(50)	(49)	(50)
Cytoplasmic vacuolization	1 (2%)		
#Bile duct	(50)	(49)	(50)
Inflammation, chronic	5 (10%)	3 (6%)	2 (4%)
Fibrosis		1 (2%)	
Hyperplasia, NOS	4 (8%)	8 (16%)	4 (8%)
#Pancreas	(49)	(48)	(49)
Ectopia		1 (2%)	
Hemorrhage			1 (2%)
Atrophy, focal	8 (16%)	8 (17%)	11 (22%)
Atrophy, diffuse		2 (4%)	1 (2%)
#Pancreatic acinus	(49)	(48)	(49)
Hyperplasia, focal	2 (4%)		
#Esophagus	(50)	(48)	(50)
Hyperkeratosis	2 (4%)		1 (2%)
#Stomach	(49)	(48)	(50)
Ulcer, NOS	1 (2%)		4 (8%)
Inflammation, chronic diffuse			1 (2%)
Necrosis, focal			1 (2%)
Amyloidosis		1 (2%)	
#Glandular stomach	(49)	(48)	(50)
Edema, NOS		1 (2%)	
Ulcer, NOS	1 (2%)		
Inflammation, chronic diffuse		1 (2%)	
Necrosis, focal	3 (6%)	4 (8%)	4 (8%)
Hyperkeratosis		1 (2%)	
Acanthosis		1 (2%)	
#Forestomach	(49)	(48)	(50)
Hemorrhage		1 (2%)	
Inflammation, chronic focal	2 (4%)		
Inflammation, chronic diffuse		1 (2%)	
Necrosis, focal	3 (6%)	1 (2%)	
Hyperkeratosis	1 (2%)	1 (2%)	1 (2%)
Acanthosis	3 (6%)	1 (2%)	3 (6%)
#Small intestine	(49)	(47)	(50)
Diverticulum	1 (2%)		
#Cecum	(49)	(49)	(49)
Hemorrhage	1 (2%)		1 (2%)
Necrosis, focal	1 (2%)		1 (2%)
URINARY SYSTEM			
#Kidney	(50)	(49)	(50)
Mineralization		1 (2%)	1 (2%)
Congestion, NOS	1 (2%)		1 (2%)
Abscess, NOS	1 (2%)		
Nephropathy	42 (84%)	44 (90%)	49 (98%)
Metamorphosis, fatty		1 (2%)	
Pigmentation, NOS		1 (2%)	
#Kidney/cortex	(50)	(49)	(50)
Cyst, NOS			1 (2%)
#Kidney/tubule	(50)	(49)	(50)
Mineralization			1 (2%)
Necrosis, focal			2 (4%)
Pigmentation, NOS	43 (86%)	35 (71%)	39 (78%)
#Urinary bladder	(49)	(48)	(49)
Distention	1 (2%)		

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#Pituitary	(50)	(50)	(50)
Cyst, NOS		1 (2%)	1 (2%)
Hemorrhage	1 (2%)		
Hyperplasia, focal	1 (2%)	1 (2%)	
Angiectasis	1 (2%)	1 (2%)	
#Anterior pituitary	(50)	(50)	(50)
Cyst, NOS	12 (24%)	9 (18%)	11 (22%)
Multiple cysts	2 (4%)		1 (2%)
Hemorrhage	1 (2%)	1 (2%)	
Hemorrhagic cyst	1 (2%)	1 (2%)	1 (2%)
Pigmentation, NOS	2 (4%)	2 (4%)	1 (2%)
Hyperplasia, focal	3 (6%)	1 (2%)	3 (6%)
Angiectasis	2 (4%)	5 (10%)	2 (4%)
#Adrenal	(50)	(48)	(50)
Congestion, NOS	1 (2%)		1 (2%)
Infarct, NOS			1 (2%)
Metamorphosis, fatty	1 (2%)		
#Adrenal cortex	(50)	(48)	(50)
Accessory structure	1 (2%)		
Congestion, NOS	3 (6%)	1 (2%)	
Degeneration, NOS			1 (2%)
Necrosis, focal			2 (4%)
Metamorphosis, fatty	6 (12%)	2 (4%)	10 (20%)
Pigmentation, NOS			1 (2%)
Cytoplasmic vacuolization	1 (2%)		
Hyperplasia, focal	3 (6%)	4 (8%)	4 (8%)
#Adrenal medulla	(50)	(48)	(50)
Hyperplasia, focal	2 (4%)	5 (10%)	1 (2%)
#Periadrenal tissue	(50)	(48)	(50)
Fibrosis			1 (2%)
#Thyroid	(50)	(49)	(50)
Cystic follicles		2 (4%)	1 (2%)
Hyperplasia, C-cell	14 (28%)	7 (14%)	2 (4%)
#Parathyroid	(49)	(49)	(47)
Hyperplasia, NOS	1 (2%)		1 (2%)
REPRODUCTIVE SYSTEM			
*Mammary gland	(50)	(50)	(50)
Dilatation/ducts	25 (50%)	24 (48%)	24 (48%)
Galactocele	2 (4%)	2 (4%)	2 (4%)
*Clitoral gland	(50)	(50)	(50)
Dilatation/ducts	1 (2%)		1 (2%)
Cystic ducts			1 (2%)
Inflammation, suppurative		1 (2%)	
Inflammation, acute focal	1 (2%)		
Abscess, NOS	1 (2%)		
Fibrosis, diffuse	1 (2%)		
Hyperplasia, NOS	1 (2%)		
#Uterus	(49)	(49)	(50)
Hydrometra	3 (6%)	3 (6%)	4 (8%)
Hemorrhage	1 (2%)	1 (2%)	
Pyometra	1 (2%)		
Inflammation, acute focal			1 (2%)
Fibrosis	1 (2%)		
Pigmentation, NOS		1 (2%)	
#Cervix uteri	(49)	(49)	(50)
Cyst, NOS		2 (4%)	1 (2%)
Abscess, NOS			2 (4%)
Fibrosis	6 (12%)	1 (2%)	5 (10%)

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM (Continued)			
#Uterus/endometrium	(49)	(49)	(50)
Cyst, NOS	1 (2%)		
Hyperplasia, cystic	2 (4%)	4 (8%)	4 (8%)
#Ovary	(48)	(48)	(50)
Cyst, NOS	1 (2%)	2 (4%)	4 (8%)
#Ovary/follicle	(48)	(48)	(50)
Hyperplasia, NOS			1 (2%)
NERVOUS SYSTEM			
#Cerebrum	(49)	(50)	(49)
Hemorrhage		2 (4%)	
Cytoplasmic vacuolization			1 (2%)
#Brain	(49)	(50)	(49)
Hemorrhage	2 (4%)		
Necrosis, NOS	1 (2%)		
#Cerebral basal surface	(49)	(50)	(49)
Compression, NOS			1 (2%)
#Cerebellum	(49)	(50)	(49)
Hemorrhage		2 (4%)	
Necrosis, focal		1 (2%)	
SPECIAL SENSE ORGANS			
*Eye	(50)	(50)	(50)
Hemorrhage		2 (4%)	
Pannus		1 (2%)	
Synechia, posterior	3 (6%)	3 (6%)	1 (2%)
Cataract	8 (16%)	8 (16%)	1 (2%)
Phthisis bulbi	1 (2%)		
*Eye/cornea	(50)	(50)	(50)
Inflammation, NOS		1 (2%)	
Inflammation, acute		1 (2%)	
*Eye/retina	(50)	(50)	(50)
Degeneration, NOS	5 (10%)	15 (30%)	1 (2%)
*Harderian gland	(50)	(50)	(50)
Granuloma, NOS			1 (2%)
MUSCULOSKELETAL SYSTEM			
*Skull	(50)	(50)	(50)
Exostosis		1 (2%)	
*Sternum	(50)	(50)	(50)
Exostosis	5 (10%)	3 (6%)	5 (10%)
BODY CAVITIES			
*Abdominal cavity	(50)	(50)	(50)
Necrosis, fat	1 (2%)	1 (2%)	
*Mesentery	(50)	(50)	(50)
Fibrosis			1 (2%)

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
*Multiple organs	(50)	(50)	(50)
Congestion, NOS	1 (2%)	2 (4%)	3 (6%)
Inflammation, chronic	1 (2%)	1 (2%)	
Pigmentation, NOS	2 (4%)		2 (4%)
Adipose tissue			
Inflammation, chronic focal	1		
SPECIAL MORPHOLOGY SUMMARY			
None			

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically.
# Number of animals examined microscopically at this site

APPENDIX D

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*Skin	(50)	(50)	(50)
Edema, NOS			1 (2%)
Ulcer, NOS	3 (6%)		2 (4%)
Inflammation, chronic		1 (2%)	
Inflammation, chronic focal	1 (2%)		
Fibrosis	1 (2%)		
Parasitism		1 (2%)	
Hyperkeratosis			1 (2%)
Acanthosis	†4 (8%)	4 (8%)	3 (6%)
Metaplasia, osseous	1 (2%)		
*Subcutaneous tissue	(50)	(50)	(50)
Epidermal inclusion cyst			1 (2%)
Edema, NOS		1 (2%)	1 (2%)
Abscess, NOS	2 (4%)	1 (2%)	1 (2%)
Inflammation, chronic		1 (2%)	
RESPIRATORY SYSTEM			
#Lung	(50)	(50)	(50)
Atelectasis		1 (2%)	
Congestion, NOS	19 (38%)	13 (26%)	17 (34%)
Edema, NOS			1 (2%)
Hemorrhage		1 (2%)	
Inflammation, chronic	22 (44%)	34 (68%)	27 (54%)
Infection, fungal			1 (2%)
Alveolar macrophages	1 (2%)	6 (12%)	2 (4%)
Hyperplasia, alveolar epithelium	1 (2%)	2 (4%)	2 (4%)
HEMATOPOIETIC SYSTEM			
#Brain	(50)	(50)	(50)
Leukocytosis, NOS		1 (2%)	
#Bone marrow	(49)	(50)	(50)
Leukemoid reaction	7 (14%)	2 (4%)	1 (2%)
Hyperplasia, hematopoietic	9 (18%)	12 (24%)	9 (18%)
Hyperplasia, granulocytic	1 (2%)		1 (2%)
#Spleen	(49)	(50)	(50)
Congestion, NOS		2 (4%)	2 (4%)
Necrosis, focal		1 (2%)	
Atrophy, NOS		2 (4%)	
Leukemoid reaction	5 (10%)	2 (4%)	2 (4%)
Hyperplasia, hematopoietic		1 (2%)	
Hyperplasia, lymphoid	1 (2%)		
Hematopoiesis	11 (22%)	8 (16%)	10 (20%)
#Lymph node	(50)	(49)	(49)
Hyperplasia, lymphoid		1 (2%)	1 (2%)
#Mandibular lymph node	(50)	(49)	(49)
Congestion, NOS		2 (4%)	
Infection, fungal			1 (2%)
Hyperplasia, lymphoid	3 (6%)	8 (16%)	9 (18%)
#Mediastinal lymph node	(50)	(49)	(49)
Hyperplasia, lymphoid		1 (2%)	1 (2%)
#Hepatic lymph node	(50)	(49)	(49)
Hyperplasia, lymphoid	1 (2%)		

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM (Continued)			
#Mesenteric lymph node	(50)	(49)	(49)
Congestion, NOS	6 (12%)	16 (33%)	13 (27%)
Hemorrhage	2 (4%)		1 (2%)
Angiectasis	1 (2%)	3 (6%)	2 (4%)
Leukocytosis, NOS	1 (2%)	2 (4%)	2 (4%)
Leukemoid reaction			1 (2%)
Plasmacytosis		1 (2%)	
Hyperplasia, lymphoid	1 (2%)	3 (6%)	2 (4%)
#Renal lymph node	(50)	(49)	(49)
Hyperplasia, lymphoid	6 (12%)	2 (4%)	
#Iliac lymph node	(50)	(49)	(49)
Necrosis, focal		1 (2%)	
Hyperplasia, lymphoid	15 (30%)	5 (10%)	4 (8%)
#Axillary lymph node	(50)	(49)	(49)
Hyperplasia, lymphoid	1 (2%)		1 (2%)
#Brachial lymph node	(50)	(49)	(49)
Hyperplasia, lymphoid	1 (2%)		
#Inguinal lymph node	(50)	(49)	(49)
Hyperplasia, lymphoid	3 (6%)	1 (2%)	1 (2%)
#Popliteal lymph node	(50)	(49)	(49)
Hyperplasia, lymphoid	1 (2%)		
#Lung	(50)	(50)	(50)
Leukocytosis, NOS	8 (16%)	7 (14%)	4 (8%)
#Heart	(50)	(50)	(50)
Leukocytosis, NOS	2 (4%)	2 (4%)	1 (2%)
#Liver	(50)	(50)	(50)
Leukocytosis, NOS	2 (4%)	1 (2%)	3 (6%)
Leukemoid reaction	1 (2%)		1 (2%)
Hematopoiesis			1 (2%)
#Kidney	(49)	(50)	(50)
Leukocytosis, NOS			1 (2%)
#Adrenal	(49)	(50)	(50)
Leukocytosis, NOS	1 (2%)		
#Thymus	(25)	(19)	(32)
Cyst, NOS		1 (5%)	3 (9%)
Congestion, NOS	1 (4%)		
CIRCULATORY SYSTEM			
*Subcutaneous tissue	(50)	(50)	(50)
Periarteritis	1 (2%)		
#Heart	(50)	(50)	(50)
Distention	4 (8%)		1 (2%)
Thrombosis, NOS	2 (4%)	1 (2%)	
Thrombus, mural	1 (2%)		
Congestion, NOS		1 (2%)	
Inflammation, suppurative		2 (4%)	1 (2%)
Inflammation, acute	1 (2%)		
Inflammation, chronic	6 (12%)	3 (6%)	5 (10%)
Fibrosis, focal			1 (2%)
Bacterial septicemia			1 (2%)
#Heart/atrium	(50)	(50)	(50)
Thrombosis, NOS	2 (4%)	3 (6%)	3 (6%)
#Heart/ventricle	(50)	(50)	(50)
Thrombosis, NOS		2 (4%)	1 (2%)
#Myocardium	(50)	(50)	(50)
Mineralization	2 (4%)	2 (4%)	
Inflammation, suppurative	1 (2%)		
Abscess, NOS	1 (2%)		
Fibrosis		1 (2%)	
Degeneration, NOS			1 (2%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM (Continued)			
#Endocardium	(50)	(50)	(50)
Inflammation, NOS	1 (2%)		
#Cardiac valve	(50)	(50)	(50)
Inflammation, active chronic	1 (2%)		
*Aorta	(50)	(50)	(50)
Thrombosis, NOS		1 (2%)	
Inflammation, active chronic	1 (2%)		
*Superior pancreaticoduodenal artery	(50)	(50)	(50)
Inflammation, NOS			1 (2%)
Periarteritis		1 (2%)	
*Renal artery	(50)	(50)	(50)
Inflammation, NOS			1 (2%)
*Portal vein	(50)	(50)	(50)
Thrombosis, NOS	1 (2%)		
#Liver	(50)	(50)	(50)
Thrombosis, NOS	1 (2%)	1 (2%)	
#Prostate	(50)	(50)	(49)
Periarteritis	1 (2%)		
DIGESTIVE SYSTEM			
#Salivary gland	(50)	(49)	(50)
Edema, NOS			1 (2%)
Inflammation, chronic	11 (22%)	12 (24%)	8 (16%)
#Liver	(50)	(50)	(50)
Congestion, NOS	7 (14%)	7 (14%)	10 (20%)
Hemorrhage	2 (4%)		
Inflammation, suppurative		1 (2%)	
Inflammation, chronic	1 (2%)	1 (2%)	
Inflammation, chronic focal	1 (2%)		1 (2%)
Granuloma, NOS	8 (16%)	22 (44%)	12 (24%)
Fibrosis		1 (2%)	1 (2%)
Necrosis, NOS	3 (6%)	1 (2%)	2 (4%)
Necrosis, focal	7 (14%)	6 (12%)	6 (12%)
Necrosis, coagulative		1 (2%)	
Infarct, NOS	2 (4%)	1 (2%)	2 (4%)
Metamorphosis, fatty	1 (2%)		
Hepatocytomegaly			1 (2%)
#Liver/centrilobular	(50)	(50)	(50)
Necrosis, NOS		1 (2%)	
Necrosis, focal			2 (4%)
Hypertrophy, NOS		34 (68%)	32 (64%)
#Liver/hepatocytes	(50)	(50)	(50)
Necrosis, NOS			5 (10%)
Cytoplasmic vacuolization	1 (2%)		
Focal cellular change		1 (2%)	1 (2%)
*Gallbladder	(50)	(50)	(50)
Distention			1 (2%)
#Bile duct	(50)	(50)	(50)
Dilatation, NOS	1 (2%)		
#Pancreas	(48)	(48)	(47)
Congestion, NOS			1 (2%)
Edema, interstitial			1 (2%)
Inflammation, chronic		1 (2%)	
Atrophy, NOS		1 (2%)	
#Pancreatic acinus	(48)	(48)	(47)
Hypertrophy, NOS		1 (2%)	
#Esophagus	(49)	(50)	(50)
Inflammation, acute		1 (2%)	

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#Stomach	(49)	(50)	(50)
Mineralization		1 (2%)	
Ulcer, NOS	1 (2%)		1 (2%)
Ulcer, acute	1 (2%)		
Keratin pearl formation		1 (2%)	
#Glandular stomach	(49)	(50)	(50)
Ulcer, NOS	3 (6%)	2 (4%)	3 (6%)
Hyperplasia, epithelial			3 (6%)
#Gastric submucosa	(49)	(50)	(50)
Cyst, NOS	1 (2%)		
#Forestomach	(49)	(50)	(50)
Ulcer, NOS		1 (2%)	1 (2%)
Hyperkeratosis	1 (2%)	2 (4%)	3 (6%)
Acanthosis		2 (4%)	4 (8%)
URINARY SYSTEM			
#Kidney	(49)	(50)	(50)
Ectopia	1 (2%)		1 (2%)
Mineralization	3 (6%)	2 (4%)	4 (8%)
Cyst, NOS		1 (2%)	
Congestion, NOS	10 (20%)	9 (18%)	11 (22%)
Pyelonephritis, NOS		1 (2%)	1 (2%)
Inflammation, suppurative		1 (2%)	
Glomerulonephritis, membranous			1 (2%)
Pyelonephritis, acute			1 (2%)
Inflammation, acute	1 (2%)		
Inflammation, acute focal	2 (4%)		1 (2%)
Abscess, NOS			1 (2%)
Inflammation, chronic	32 (65%)	41 (82%)	41 (82%)
Inflammation, chronic focal	2 (4%)		
Fibrosis, focal	1 (2%)		
Necrosis, NOS	1 (2%)		
Necrosis, focal	1 (2%)	1 (2%)	1 (2%)
Infarct, NOS		2 (4%)	
Pigmentation, NOS	1 (2%)		
#Kidney/cortex	(49)	(50)	(50)
Cyst, NOS	3 (6%)	1 (2%)	6 (12%)
Necrosis, focal	1 (2%)		
Cytoplasmic vacuolization			1 (2%)
#Kidney/tubule	(49)	(50)	(50)
Dilatation, NOS	2 (4%)	2 (4%)	2 (4%)
Cytoplasmic vacuolization	23 (47%)	32 (64%)	31 (62%)
#Kidney/pelvis	(49)	(50)	(50)
Dilatation, NOS	2 (4%)	1 (2%)	
Inflammation, suppurative	1 (2%)	1 (2%)	
*Ureter	(50)	(50)	(50)
Distention	3 (6%)		
Inflammation, suppurative		1 (2%)	
Inflammation, chronic	1 (2%)		

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
URINARY SYSTEM (Continued)			
#Urinary bladder	(50)	(50)	(50)
Calculus, microscopic examination	1 (2%)		
Dilatation, NOS			2 (4%)
Distention	10 (20%)	1 (2%)	4 (8%)
Congestion, NOS	1 (2%)	3 (6%)	1 (2%)
Edema, NOS			1 (2%)
Hemorrhage			1 (2%)
Inflammation, suppurative	1 (2%)	1 (2%)	
Inflammation, acute	2 (4%)		
Inflammation, acute focal			1 (2%)
Inflammation, acute diffuse	1 (2%)		1 (2%)
Inflammation, active chronic		1 (2%)	
Inflammation, chronic	2 (4%)		1 (2%)
Fibrosis, diffuse	1 (2%)		
Necrosis, NOS			2 (4%)
Hyperplasia, epithelial			1 (2%)
#Urinary bladder/submucosa	(50)	(50)	(50)
Edema, NOS		1 (2%)	
*Urethra	(50)	(50)	(50)
Inflammation, acute	2 (4%)		
ENDOCRINE SYSTEM			
#Pituitary	(50)	(49)	(47)
Cyst, NOS	1 (2%)	1 (2%)	3 (6%)
Congestion, NOS	2 (4%)	2 (4%)	2 (4%)
#Anterior pituitary	(50)	(49)	(47)
Cyst, NOS		1 (2%)	3 (6%)
#Adrenal	(49)	(50)	(50)
Congestion, NOS	1 (2%)	3 (6%)	2 (4%)
#Adrenal/capsule	(49)	(50)	(50)
Hyperplasia, NOS	22 (45%)	28 (56%)	28 (56%)
#Adrenal cortex	(49)	(50)	(50)
Ectopia			1 (2%)
Congestion, NOS			2 (4%)
Hypertrophy, focal	8 (16%)	2 (4%)	5 (10%)
#Adrenal medulla	(49)	(50)	(50)
Hyperplasia, NOS			1 (2%)
Hyperplasia, focal		1 (2%)	1 (2%)
#Thyroid	(50)	(50)	(50)
Cyst, NOS		1 (2%)	1 (2%)
Colloid cyst		4 (8%)	
Congestion, NOS		1 (2%)	
Inflammation, chronic	1 (2%)	1 (2%)	
Hyperplasia, follicular cell	2 (4%)	10 (20%)	19 (38%)
#Thyroid follicle	(50)	(50)	(50)
Crystals, NOS		3 (6%)	
#Pancreatic islets	(48)	(48)	(47)
Hyperplasia, NOS			2 (4%)
REPRODUCTIVE SYSTEM			
*Penis	(50)	(50)	(50)
Hemorrhage	1 (2%)	1 (2%)	
Inflammation, suppurative	1 (2%)		
Inflammation, chronic diffuse	1 (2%)		
Necrosis, NOS		1 (2%)	
Acanthosis	1 (2%)		

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM (Continued)			
*Prepuce	(50)	(50)	(50)
Hemorrhage	1 (2%)		
Inflammation, suppurative	2 (4%)		
Inflammation, acute	1 (2%)	1 (2%)	
Inflammation, acute diffuse	1 (2%)		
Abscess, NOS		1 (2%)	
Inflammation, chronic focal	1 (2%)		
Necrosis, NOS	1 (2%)		
Hyperkeratosis	1 (2%)		
Acanthosis	1 (2%)	1 (2%)	
*Preputial gland	(50)	(50)	(50)
Dilatation, NOS		2 (4%)	2 (4%)
Dilatation/ducts	2 (4%)		
Cyst, NOS	2 (4%)		1 (2%)
Cystic ducts	2 (4%)		
Hemorrhage	1 (2%)		
Inflammation, suppurative	5 (10%)		1 (2%)
Abscess, NOS	3 (6%)	3 (6%)	2 (4%)
Inflammation, active chronic		5 (10%)	5 (10%)
Inflammation, chronic	1 (2%)	4 (8%)	3 (6%)
Hyperplasia, diffuse	1 (2%)		
Hyperkeratosis	1 (2%)		
Metaplasia, squamous	1 (2%)		
#Prostate	(50)	(50)	(49)
Congestion, NOS	1 (2%)		
Inflammation, suppurative	1 (2%)	2 (4%)	2 (4%)
Inflammation, acute	2 (4%)		
Inflammation, acute focal		1 (2%)	
Inflammation, acute diffuse	2 (4%)		1 (2%)
Abscess, NOS	3 (6%)		1 (2%)
Inflammation, active chronic	1 (2%)	3 (6%)	
Inflammation, chronic	2 (4%)		1 (2%)
*Seminal vesicle	(50)	(50)	(50)
Mineralization			1 (2%)
Distention	6 (12%)	2 (4%)	5 (10%)
Retention of content	1 (2%)		
Cyst, NOS	4 (8%)		1 (2%)
Inflammation, suppurative		1 (2%)	
Inflammation, acute	1 (2%)		1 (2%)
Inflammation, acute focal	1 (2%)		
Inflammation, acute diffuse			1 (2%)
Inflammation, active chronic		1 (2%)	
Inflammation, chronic	1 (2%)		3 (6%)
Fibrosis			3 (6%)
Necrosis, fat			1 (2%)
*Coagulating gland	(50)	(50)	(50)
Distention	1 (2%)		
Inflammation, suppurative	1 (2%)		
Inflammation, acute			1 (2%)
Fibrosis			1 (2%)
#Testis	(50)	(50)	(48)
Mineralization	1 (2%)		2 (4%)
Congestion, NOS			1 (2%)
Inflammation, suppurative	1 (2%)		
Granuloma, spermatic	2 (4%)		1 (2%)
Fibrosis	1 (2%)		
Aspermatogenesis	1 (2%)		1 (2%)
Hypospermatogenesis		2 (4%)	4 (8%)
Hyperplasia, interstitial cell	1 (2%)		

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM (Continued)			
*Epididymis	(50)	(50)	(50)
Inflammation, suppurative	1 (2%)		
Inflammation, active chronic		1 (2%)	
Inflammation, chronic	1 (2%)	2 (4%)	6 (12%)
Granuloma, spermatic	3 (6%)	2 (4%)	
Aspermatogenesis		1 (2%)	1 (2%)
Hypospermatogenesis			1 (2%)
NERVOUS SYSTEM			
#Brain	(50)	(50)	(50)
Cyst, NOS		1 (2%)	
Congestion, NOS	1 (2%)		1 (2%)
Hemorrhage	1 (2%)	1 (2%)	
Infection, fungal			1 (2%)
Malacia			1 (2%)
SPECIAL SENSE ORGANS			
*Ear	(50)	(50)	(50)
Inflammation, suppurative			1 (2%)
MUSCULOSKELETAL SYSTEM			
None			
BODY CAVITIES			
None			
ALL OTHER SYSTEMS			
*Multiple organs	(50)	(50)	(50)
Congestion, NOS	1 (2%)		
Amyloidosis		1 (2%)	
Tail			
Exostosis			1
Adipose tissue			
Cyst, NOS		1	
SPECIAL MORPHOLOGY SUMMARY			
No lesion reported		1	

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically.
# Number of animals examined microscopically at this site
† Multiple occurrence of morphology in the same organ. Tissue is counted once only.

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*Subcutaneous tissue	(50)	(50)	(50)
Edema, NOS			1 (2%)
Abscess, NOS	1 (2%)		
RESPIRATORY SYSTEM			
*Nose	(50)	(50)	(50)
Inflammation, suppurative	1 (2%)		
Infection, bacterial	1 (2%)		
#Lung	(50)	(50)	(50)
Congestion, NOS	15 (30%)	9 (18%)	14 (28%)
Hemorrhage			1 (2%)
Pneumonia, aspiration			1 (2%)
Inflammation, suppurative			1 (2%)
Pneumonia, chronic murine	1 (2%)		
Inflammation, chronic	37 (74%)	33 (66%)	42 (84%)
Fibrosis, focal			1 (2%)
Bacterial septicemia		1 (2%)	1 (2%)
Infection, bacterial	1 (2%)		1 (2%)
Alveolar macrophages	2 (4%)	2 (4%)	2 (4%)
Hyperplasia, alveolar epithelium	1 (2%)	1 (2%)	1 (2%)
HEMATOPOIETIC SYSTEM			
*Multiple organs	(50)	(50)	(50)
Leukocytosis, NOS	2 (4%)		
Leukemoid reaction		1 (2%)	
#Bone marrow	(50)	(48)	(50)
Congestion, NOS	1 (2%)		
Leukemoid reaction	2 (4%)	3 (6%)	6 (12%)
Hyperplasia, hematopoietic	13 (26%)	5 (10%)	9 (18%)
#Spleen	(50)	(50)	(50)
Necrosis, NOS			1 (2%)
Leukemoid reaction	7 (14%)	3 (6%)	6 (12%)
Hyperplasia, lymphoid	1 (2%)	2 (4%)	
Hematopoiesis	5 (10%)	7 (14%)	10 (20%)
#Splenic capsule	(50)	(50)	(50)
Inflammation, NOS	1 (2%)		1 (2%)
Inflammation, suppurative	1 (2%)	1 (2%)	1 (2%)
Abscess, NOS			1 (2%)
#Lymph node	(50)	(50)	(50)
Angiectasis	1 (2%)	1 (2%)	
Hyperplasia, lymphoid	5 (10%)	2 (4%)	5 (10%)
#Mandibular lymph node	(50)	(50)	(50)
Congestion, NOS	3 (6%)	1 (2%)	1 (2%)
Necrosis, NOS			1 (2%)
Angiectasis		1 (2%)	
Hyperplasia, lymphoid	5 (10%)	10 (20%)	12 (24%)
#Mediastinal lymph node	(50)	(50)	(50)
Congestion, NOS	1 (2%)		1 (2%)
Inflammation, suppurative			4 (8%)
Leukocytosis, NOS	1 (2%)		
Hyperplasia, lymphoid	5 (10%)	4 (8%)	9 (18%)
#Pancreatic lymph node	(50)	(50)	(50)
Congestion, NOS	1 (2%)		
Necrosis, NOS	1 (2%)		

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM (Continued)			
#Mesenteric lymph node	(50)	(50)	(50)
Congestion, NOS	2 (4%)	2 (4%)	3 (6%)
Hemorrhagic cyst	1 (2%)		
Inflammation, suppurative		1 (2%)	
Inflammation, active chronic			1 (2%)
Necrosis, NOS			1 (2%)
Angiectasis	1 (2%)	3 (6%)	4 (8%)
Leukocytosis, NOS	3 (6%)		1 (2%)
Hyperplasia, lymphoid	3 (6%)	1 (2%)	9 (18%)
#Renal lymph node	(50)	(50)	(50)
Congestion, NOS		2 (4%)	1 (2%)
Necrosis, focal	1 (2%)		
Angiectasis		1 (2%)	
Hyperplasia, lymphoid	2 (4%)	2 (4%)	2 (4%)
#Iliac lymph node	(50)	(50)	(50)
Angiectasis	1 (2%)		
Hyperplasia, lymphoid	1 (2%)		
#Lung	(50)	(50)	(50)
Leukocytosis, NOS	7 (14%)	8 (16%)	9 (18%)
#Heart	(50)	(50)	(50)
Leukocytosis, NOS	1 (2%)		
#Liver	(50)	(50)	(50)
Leukocytosis, NOS	3 (6%)		3 (6%)
Leukemoid reaction	6 (12%)	3 (6%)	4 (8%)
Hematopoiesis	1 (2%)	3 (6%)	2 (4%)
#Peyers patch	(50)	(49)	(50)
Hyperplasia, lymphoid			1 (2%)
#Kidney	(50)	(50)	(50)
Hyperplasia, lymphoid		1 (2%)	1 (2%)
#Ovary/parovarian	(49)	(50)	(49)
Hyperplasia, lymphoid			1 (2%)
#Adrenal	(48)	(49)	(50)
Leukocytosis, NOS			1 (2%)
Leukemoid reaction	1 (2%)	1 (2%)	
Hematopoiesis		3 (6%)	1 (2%)
#Adrenal cortex	(48)	(49)	(50)
Leukemoid reaction	1 (2%)		2 (4%)
#Thymus	(31)	(34)	(40)
Cyst, NOS	1 (3%)	1 (3%)	1 (3%)
Inflammation, acute	1 (3%)		
Necrosis, NOS			1 (3%)
Hyperplasia, lymphoid	2 (6%)		
CIRCULATORY SYSTEM			
#Lymph node	(50)	(50)	(50)
Thrombosis, NOS		1 (2%)	
#Mesenteric lymph node	(50)	(50)	(50)
Thrombosis, NOS		1 (2%)	
#Heart	(50)	(50)	(50)
Inflammation, suppurative			1 (2%)
Inflammation, acute	2 (4%)		
Inflammation, chronic	4 (8%)	1 (2%)	4 (8%)
#Base of heart	(50)	(50)	(50)
Inflammation, suppurative	1 (2%)		
#Heart/atrium	(50)	(50)	(50)
Thrombosis, NOS	7 (14%)		5 (10%)
#Heart/ventricle	(50)	(50)	(50)
Thrombosis, NOS	1 (2%)		
#Myocardium	(50)	(50)	(50)
Inflammation, acute	1 (2%)		
Infection, bacterial	1 (2%)		

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM (Continued)			
*Cerebral artery	(50)	(50)	(50)
Infection, bacterial	1 (2%)		
*Superior pancreaticoduodenal artery	(50)	(50)	(50)
Thrombosis, NOS			1 (2%)
*Uterine artery	(50)	(50)	(50)
Inflammation, NOS		1 (2%)	
#Liver	(50)	(50)	(50)
Thrombosis, NOS	2 (4%)		
#Uterus	(50)	(50)	(50)
Thrombosis, NOS	1 (2%)		1 (2%)
#Adrenal	(48)	(49)	(50)
Thrombosis, NOS	2 (4%)		
DIGESTIVE SYSTEM			
#Salivary gland	(49)	(49)	(50)
Inflammation, chronic	11 (22%)	12 (24%)	13 (26%)
#Liver	(50)	(50)	(50)
Congestion, NOS	7 (14%)	6 (12%)	9 (18%)
Hemorrhage			1 (2%)
Inflammation, suppurative		1 (2%)	
Inflammation, chronic		2 (4%)	1 (2%)
Granuloma, NOS	23 (46%)	27 (54%)	24 (48%)
Necrosis, NOS		1 (2%)	4 (8%)
Necrosis, focal	3 (6%)	3 (6%)	3 (6%)
Infarct, NOS	1 (2%)		
Metamorphosis, fatty	1 (2%)		
Cytoplasmic vacuolization		1 (2%)	
Angiectasis	2 (4%)	1 (2%)	
#Hepatic capsule	(50)	(50)	(50)
Inflammation, NOS		1 (2%)	
Inflammation, suppurative	1 (2%)		3 (6%)
#Liver/centrilobular	(50)	(50)	(50)
Necrosis, focal			1 (2%)
#Liver/hepatocytes	(50)	(50)	(50)
Necrosis, NOS		1 (2%)	
Cytoplasmic vacuolization		1 (2%)	
Focal cellular change	1 (2%)	2 (4%)	2 (4%)
*Gallbladder	(50)	(50)	(50)
Inflammation, acute	1 (2%)		
Necrosis, NOS	1 (2%)		
*Gallbladder/serosa	(50)	(50)	(50)
Inflammation, suppurative	4 (8%)		
#Pancreas	(50)	(48)	(49)
Cyst, NOS	1 (2%)		1 (2%)
Inflammation, suppurative		1 (2%)	1 (2%)
Inflammation, active chronic	5 (10%)	1 (2%)	2 (4%)
Inflammation, chronic	2 (4%)	4 (8%)	3 (6%)
Necrosis, fat			1 (2%)
#Pancreatic acinus	(50)	(48)	(49)
Inflammation, active chronic			1 (2%)
#Esophagus	(50)	(50)	(50)
Inflammation, acute	1 (2%)		
#Stomach	(50)	(50)	(50)
Ulcer, NOS			1 (2%)
Ulcer, acute	1 (2%)		
#Glandular stomach	(50)	(50)	(50)
Cyst, NOS			1 (2%)
Ulcer, NOS		1 (2%)	6 (12%)
Hyperplasia, epithelial	5 (10%)	1 (2%)	

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#Gastric submucosa	(50)	(50)	(50)
Cyst, NOS		3 (6%)	
#Gastric serosa	(50)	(50)	(50)
Inflammation, suppurative		1 (2%)	
#Forestomach	(50)	(50)	(50)
Inflammation, NOS			1 (2%)
Ulcer, NOS			1 (2%)
Inflammation, acute			3 (6%)
Inflammation, acute focal	1 (2%)	2 (4%)	
Inflammation, active chronic	1 (2%)		
Inflammation, chronic	1 (2%)	1 (2%)	1 (2%)
Erosion			3 (6%)
Hyperkeratosis	5 (10%)	8 (16%)	6 (12%)
Acanthosis	9 (18%)	8 (16%)	6 (12%)
#Small intestine /serosa	(50)	(49)	(50)
Inflammation, chronic			1 (2%)
#Duodenum	(50)	(49)	(50)
Ulcer, NOS	1 (2%)		
#Duodenal serosa	(50)	(49)	(50)
Inflammation, NOS	1 (2%)		
#Colonic serosa	(50)	(50)	(49)
Inflammation, suppurative		1 (2%)	
URINARY SYSTEM			
#Kidney	(50)	(50)	(50)
Ectopia	1 (2%)	1 (2%)	1 (2%)
Mineralization	1 (2%)		
Hydronephrosis			1 (2%)
Congestion, NOS	10 (20%)	8 (16%)	9 (18%)
Pyelonephritis, NOS	1 (2%)		
Inflammation, chronic	41 (82%)	42 (84%)	47 (94%)
Infection, bacterial	1 (2%)		
Glomerulosclerosis, NOS	3 (6%)		1 (2%)
Infarct, healed	1 (2%)		
Hyperplasia, tubular cell			1 (2%)
#Kidney/capsule	(50)	(50)	(50)
Inflammation, active chronic	1 (2%)		
#Kidney/interstitium	(50)	(50)	(50)
Abscess, NOS	1 (2%)		
#Kidney/cortex	(50)	(50)	(50)
Cyst, NOS			1 (2%)
#Renal papilla	(50)	(50)	(50)
Inflammation, suppurative			1 (2%)
Necrosis, NOS	1 (2%)		
#Kidney/tubule	(50)	(50)	(50)
Dilatation, NOS			1 (2%)
#Urinary bladder	(50)	(48)	(49)
Inflammation, acute	1 (2%)		
Inflammation, active chronic	1 (2%)		
Inflammation, chronic	5 (10%)	2 (4%)	4 (8%)
#Urinary bladder/serosa	(50)	(48)	(49)
Necrosis, NOS		1 (2%)	
ENDOCRINE SYSTEM			
#Pituitary	(40)	(45)	(49)
Congestion, NOS	4 (10%)	2 (4%)	2 (4%)
Angiectasis		1 (2%)	

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM (Continued)			
#Anterior pituitary	(40)	(45)	(49)
Cyst, NOS	2 (5%)	3 (7%)	1 (2%)
Congestion, NOS	1 (3%)		2 (4%)
Hyperplasia, NOS	6 (15%)	11 (24%)	13 (27%)
Hyperplasia, focal	2 (5%)		
Angiectasis	6 (15%)	13 (29%)	9 (18%)
#Adrenal	(48)	(49)	(50)
Congestion, NOS	2 (4%)		1 (2%)
Abscess, NOS		1 (2%)	
Hyperplasia, NOS	1 (2%)		
#Adrenal/capsule	(48)	(49)	(50)
Inflammation, NOS			1 (2%)
Inflammation, active chronic	1 (2%)		1 (2%)
Hyperplasia, NOS	33 (69%)	36 (73%)	39 (78%)
Hyperplasia, focal	1 (2%)	1 (2%)	
#Adrenal cortex	(48)	(49)	(50)
Cyst, NOS			1 (2%)
Congestion, NOS		2 (4%)	1 (2%)
Cytoplasmic vacuolization	3 (6%)	4 (8%)	3 (6%)
Hypertrophy, focal	3 (6%)	2 (4%)	1 (2%)
Hypertrophy, diffuse		6 (12%)	6 (12%)
Hyperplasia, NOS		1 (2%)	
Hyperplasia, focal		1 (2%)	
#Periadrenal tissue	(48)	(49)	(50)
Inflammation, suppurative			1 (2%)
#Thyroid	(50)	(50)	(49)
Colloid cyst			1 (2%)
Inflammation, chronic	1 (2%)	3 (6%)	2 (4%)
Hyperplasia, focal			1 (2%)
Hyperplasia, follicular cell	4 (8%)	9 (18%)	7 (14%)
#Thyroid follicle	(50)	(50)	(49)
Crystals, NOS		1 (2%)	
REPRODUCTIVE SYSTEM			
*Mammary gland	(50)	(50)	(50)
Galactocele	5 (10%)	2 (4%)	5 (10%)
Inflammation, active chronic	1 (2%)		
#Uterus	(50)	(50)	(50)
Hemorrhagic cyst			1 (2%)
Inflammation, suppurative	8 (16%)	4 (8%)	12 (24%)
Inflammation, active chronic	1 (2%)		
Inflammation, chronic		1 (2%)	
Fibrosis		1 (2%)	
Necrosis, fat		1 (2%)	
#Uterine serosa	(50)	(50)	(50)
Abscess, NOS			1 (2%)
#Uterus/endometrium	(50)	(50)	(50)
Hyperplasia, cystic	40 (80%)	43 (86%)	39 (78%)
#Fallopian tube	(50)	(50)	(50)
Inflammation, suppurative		1 (2%)	1 (2%)
#Ovary/parovarian	(49)	(50)	(49)
Inflammation, active chronic			1 (2%)
#Ovary	(49)	(50)	(49)
Mineralization		1 (2%)	
Cyst, NOS	7 (14%)	5 (10%)	8 (16%)
Parovarian cyst	15 (31%)	9 (18%)	19 (39%)
Congestion, NOS		1 (2%)	
Hemorrhagic cyst	2 (4%)	2 (4%)	3 (6%)

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	CONTROL (UNTR)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
#Ovary (Continued)	(49)	(50)	(49)
Inflammation, suppurative	7 (14%)	4 (8%)	5 (10%)
Abscess, NOS	5 (10%)	3 (6%)	7 (14%)
Inflammation, active chronic	1 (2%)	3 (6%)	
Inflammation, chronic			1 (2%)
Fibrosis	1 (2%)	1 (2%)	
NERVOUS SYSTEM			
#Cerebral ventricle	(50)	(50)	(50)
Dilatation, NOS		1 (2%)	
#Brain	(50)	(50)	(50)
Congestion, NOS		1 (2%)	
Inflammation, chronic		1 (2%)	1 (2%)
Gliosis	1 (2%)		
#Brain stem	(50)	(50)	(50)
Atrophy, pressure		1 (2%)	
SPECIAL SENSE ORGANS			
*Eye/cornea	(50)	(50)	(50)
Inflammation, active chronic	1 (2%)		
Fibrosis	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*Sternum	(50)	(50)	(50)
Fibrous osteodystrophy	27 (54%)	27 (54%)	30 (60%)
BODY CAVITIES			
*Abdominal cavity	(50)	(50)	(50)
Steatitis	1 (2%)		
Necrosis, fat	1 (2%)	1 (2%)	
*Peritoneum	(50)	(50)	(50)
Inflammation, suppurative	1 (2%)		
Abscess, NOS	1 (2%)		
*Mesentery	(50)	(50)	(50)
Cyst, NOS			1 (2%)
Inflammation, active chronic			2 (4%)
ALL OTHER SYSTEMS			
*Multiple organs	(50)	(50)	(50)
Inflammation, suppurative		1 (2%)	
Inflammation, active chronic	1 (2%)		
Inflammation, chronic	2 (4%)	1 (2%)	
Adipose tissue			
Mineralization	1		
Cyst, NOS		1	
Inflammation, chronic		1	
Fibrosis		1	
Necrosis, fat	1	2	1
SPECIAL MORPHOLOGY SUMMARY			
None			

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically.
# Number of animals examined microscopically at this site

APPENDIX E

ANALYSES OF PRIMARY TUMORS IN RATS AND MICE IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	Control	25,000 ppm	50,000 ppm
Skin: Keratoacanthoma			
Overall Rates (a)	2/50 (4%)	3/50 (6%)	1/50 (2%)
Adjusted Rates (b)	5.1%	12.5%	3.8%
Terminal Rates (c)	1/35 (3%)	3/24 (13%)	1/26 (4%)
Week of First Observation	96	104	104
Life Table Tests (d)	P=0.522N	P=0.345	P=0.595N
Incidental Tumor Tests (d)	P=0.483N	P=0.373	P=0.530N
Cochran-Armitage Trend Test (d)	P=0.399N		
Fisher Exact Test (d)		P=0.500	P=0.500N
Subcutaneous Tissue: Fibroma			
Overall Rates (a)	3/50 (6%)	4/50 (8%)	3/50 (6%)
Adjusted Rates (b)	8.6%	12.5%	7.7%
Terminal Rates (c)	3/35 (9%)	2/24 (8%)	0/26 (0%)
Week of First Observation	104	77	86
Life Table Tests (d)	P=0.482	P=0.347	P=0.571
Incidental Tumor Tests (d)	P=0.491N	P=0.537	P=0.529N
Cochran-Armitage Trend Test (d)	P=0.579		
Fisher Exact Test (d)		P=0.500	P=0.661
Subcutaneous Tissue: Fibroma or Neurofibroma			
Overall Rates (a)	5/50 (10%)	6/50 (12%)	4/50 (8%)
Adjusted Rates (b)	14.3%	19.0%	11.3%
Terminal Rates (c)	5/35 (14%)	3/24 (13%)	1/26 (4%)
Week of First Observation	104	77	86
Life Table Tests (d)	P=0.548	P=0.300	P=0.634
Incidental Tumor Tests (d)	P=0.400N	P=0.462	P=0.443N
Cochran-Armitage Trend Test (d)	P=0.434N		
Fisher Exact Test (d)		P=0.500	P=0.500N
Subcutaneous Tissue: Fibrosarcoma			
Overall Rates (a)	4/50 (8%)	0/50 (0%)	1/50 (2%)
Adjusted Rates (b)	9.8%	0.0%	2.2%
Terminal Rates (c)	2/35 (6%)	0/24 (0%)	0/26 (0%)
Week of First Observation	75		87
Life Table Tests (d)	P=0.119N	P=0.104N	P=0.238N
Incidental Tumor Tests (d)	P=0.052N	P=0.044N	P=0.109N
Cochran-Armitage Trend Test (d)	P=0.082N		
Fisher Exact Test (d)		P=0.059N	P=0.181N
Integumentary System: Neurofibrosarcoma			
Overall Rates (a)	3/50 (6%)	2/50 (4%)	0/50 (0%)
Adjusted Rates (b)	8.6%	8.3%	0.0%
Terminal Rates (c)	3/35 (9%)	2/24 (8%)	0/26 (0%)
Week of First Observation	104	104	
Life Table Tests (d)	P=0.141N	P=0.670N	P=0.178N
Incidental Tumor Tests (d)	P=0.141N	P=0.670N	P=0.178N
Cochran-Armitage Trend Test (d)	P=0.082N		
Fisher Exact Test (d)		P=0.500N	P=0.121N
Integumentary System: Fibrosarcoma or Neurofibrosarcoma			
Overall Rates (a)	7/50 (14%)	2/50 (4%)	1/50 (2%)
Adjusted Rates (b)	18.0%	8.3%	2.2%
Terminal Rates (c)	5/35 (14%)	2/24 (8%)	0/26 (0%)
Week of First Observation	75	104	87
Life Table Tests (d)	P=0.035N	P=0.185N	P=0.066N
Incidental Tumor Tests (d)	P=0.017N	P=0.118N	P=0.027N
Cochran-Armitage Trend Test (d)	P=0.014N		
Fisher Exact Test (d)		P=0.080N	P=0.030N

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	Control	25,000 ppm	50,000 ppm
Subcutaneous Tissue: Fibroma or Fibrosarcoma			
Overall Rates (a)	7/50 (14%)	4/50 (8%)	4/50 (8%)
Adjusted Rates (b)	18.0%	12.5%	9.8%
Terminal Rates (c)	5/35 (14%)	2/24 (8%)	0/26 (0%)
Week of First Observation	75	77	86
Life Table Tests (d)	P=0.310N	P=0.440N	P=0.378N
Incidental Tumor Tests (d)	P=0.121N	P=0.205N	P=0.123N
Cochran-Armitage Trend Test (d)	P=0.202N		
Fisher Exact Test (d)		P=0.262N	P=0.262N
Integumentary System: Neurofibroma or Neurofibrosarcoma			
Overall Rates (a)	5/50 (10%)	4/50 (8%)	1/50 (2%)
Adjusted Rates (b)	14.3%	15.2%	3.8%
Terminal Rates (c)	5/35 (14%)	3/24 (13%)	1/26 (4%)
Week of First Observation	104	98	104
Life Table Tests (d)	P=0.165N	P=0.561	P=0.181N
Incidental Tumor Tests (d)	P=0.147N	P=0.579	P=0.181N
Cochran-Armitage Trend Test (d)	P=0.080N		
Fisher Exact Test (d)		P=0.500N	P=0.102N
Integumentary System: Fibroma, Neurofibroma, Fibrosarcoma, or Neurofibrosarcoma			
Overall Rates (a)	12/50 (24%)	8/50 (16%)	5/50 (10%)
Adjusted Rates (b)	31.7%	26.7%	13.3%
Terminal Rates (c)	10/35 (29%)	5/24 (21%)	1/26 (4%)
Week of First Observation	75	77	86
Life Table Tests (d)	P=0.124N	P=0.509N	P=0.143N
Incidental Tumor Tests (d)	P=0.038N	P=0.300N	P=0.036N
Cochran-Armitage Trend Test (d)	P=0.041N		
Fisher Exact Test (d)		P=0.227N	P=0.054N
Lung: Alveolar/Bronchiolar Adenoma			
Overall Rates (a)	1/50 (2%)	1/50 (2%)	3/49 (6%)
Adjusted Rates (b)	2.9%	4.2%	9.6%
Terminal Rates (c)	1/35 (3%)	1/24 (4%)	1/26 (4%)
Week of First Observation	104	104	93
Life Table Tests (d)	P=0.148	P=0.676	P=0.227
Incidental Tumor Tests (d)	P=0.186	P=0.676	P=0.298
Cochran-Armitage Trend Test (d)	P=0.196		
Fisher Exact Test (d)		P=0.753	P=0.301
Hematopoietic System: Mononuclear Cell Leukemia			
Overall Rates (a)	30/50 (60%)	33/50 (66%)	35/50 (70%)
Adjusted Rates (b)	67.9%	81.9%	82.8%
Terminal Rates (c)	21/35 (60%)	17/24 (71%)	19/26 (73%)
Week of First Observation	81	72	76
Life Table Tests (d)	P=0.028	P=0.029	P=0.031
Incidental Tumor Tests (d)	P=0.215	P=0.292	P=0.285
Cochran-Armitage Trend Test (d)	P=0.172		
Fisher Exact Test (d)		P=0.339	P=0.201
Salivary Gland: Sarcoma or Fibrosarcoma			
Overall Rates (a)	1/49 (2%)	0/50 (0%)	3/48 (6%)
Adjusted Rates (b)	2.9%	0.0%	10.5%
Terminal Rates (c)	1/35 (3%)	0/24 (0%)	2/26 (8%)
Week of First Observation	104		97
Life Table Tests (d)	P=0.127	P=0.575N	P=0.214
Incidental Tumor Tests (d)	P=0.148	P=0.575N	P=0.253
Cochran-Armitage Trend Test (d)	P=0.170		
Fisher Exact Test (d)		P=0.495N	P=0.301

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	Control	25,000 ppm	50,000 ppm
Liver: Neoplastic Nodule			
Overall Rates (a)	1/50 (2%)	7/50 (14%)	15/49 (31%)
Adjusted Rates (b)	2.9%	27.1%	52.7%
Terminal Rates (c)	1/35 (3%)	6/24 (25%)	13/26 (50%)
Week of First Observation	104	89	87
Life Table Tests (d)	P<0.001	P=0.008	P<0.001
Incidental Tumor Tests (d)	P<0.001	P=0.014	P<0.001
Cochran-Armitage Trend Test (d)	P<0.001		
Fisher Exact Test (d)		P=0.030	P<0.001
Liver: Neoplastic Nodule or Hepatocellular Carcinoma			
Overall Rates (a)	2/50 (4%)	8/50 (16%)	15/49 (31%)
Adjusted Rates (b)	5.2%	31.1%	52.7%
Terminal Rates (c)	1/35 (3%)	7/24 (29%)	13/26 (50%)
Week of First Observation	97	89	87
Life Table Tests (d)	P<0.001	P=0.012	P<0.001
Incidental Tumor Tests (d)	P<0.001	P=0.022	P<0.001
Cochran-Armitage Trend Test (d)	P<0.001		
Fisher Exact Test (d)		P=0.046	P<0.001
Pancreas: Acinar Cell Adenoma			
Overall Rates (a)	0/49 (0%)	0/50 (0%)	4/49 (8%)
Adjusted Rates (b)	0.0%	0.0%	13.7%
Terminal Rates (c)	0/35 (0%)	0/24 (0%)	2/25 (8%)
Week of First Observation			97
Life Table Tests (d)	P=0.010	(e)	P=0.037
Incidental Tumor Tests (d)	P=0.017	(e)	P=0.067
Cochran-Armitage Trend Test (d)	P=0.015		
Fisher Exact Test (d)		(e)	P=0.059
Pituitary: Adenoma			
Overall Rates (a)	10/50 (20%)	10/50 (20%)	9/50 (18%)
Adjusted Rates (b)	25.0%	33.1%	28.4%
Terminal Rates (c)	6/35 (17%)	6/24 (25%)	5/26 (19%)
Week of First Observation	85	69	93
Life Table Tests (d)	P=0.413	P=0.315	P=0.472
Incidental Tumor Tests (d)	P=0.460N	P=0.577	P=0.490N
Cochran-Armitage Trend Test (d)	P=0.450N		
Fisher Exact Test (d)		P=0.598	P=0.500N
Pituitary: Adenoma or Carcinoma			
Overall Rates (a)	10/50 (20%)	11/50 (22%)	9/50 (18%)
Adjusted Rates (b)	25.0%	36.8%	28.4%
Terminal Rates (c)	6/35 (17%)	7/24 (29%)	5/26 (19%)
Week of First Observation	85	69	93
Life Table Tests (d)	P=0.405	P=0.225	P=0.472
Incidental Tumor Tests (d)	P=0.471N	P=0.457	P=0.490N
Cochran-Armitage Trend Test (d)	P=0.450N		
Fisher Exact Test (d)		P=0.500	P=0.500N
Adrenal Gland: Cortical Adenoma			
Overall Rates (a)	4/49 (8%)	1/50 (2%)	1/49 (2%)
Adjusted Rates (b)	10.7%	2.8%	4.0%
Terminal Rates (c)	3/35 (9%)	0/24 (0%)	1/25 (4%)
Week of First Observation	96	89	104
Life Table Tests (d)	P=0.172N	P=0.289N	P=0.287N
Incidental Tumor Tests (d)	P=0.103N	P=0.154N	P=0.236N
Cochran-Armitage Trend Test (d)	P=0.100N		
Fisher Exact Test (d)		P=0.175N	P=0.181N

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	Control	25,000 ppm	50,000 ppm
Adrenal Gland: Pheochromocytoma			
Overall Rates (a)	31/49 (63%)	18/50 (36%)	18/49 (37%)
Adjusted Rates (b)	79.4%	59.1%	53.4%
Terminal Rates (c)	27/35 (77%)	12/24 (50%)	11/25 (44%)
Week of First Observation	95	85	87
Life Table Tests (d)	P=0.136N	P=0.234N	P=0.162N
Incidental Tumor Tests (d)	P=0.017N	P=0.075N	P=0.018N
Cochran-Armitage Trend Test (d)	P=0.006N		
Fisher Exact Test (d)		P=0.006N	P=0.007N
Adrenal Gland: Malignant Pheochromocytoma			
Overall Rates (a)	4/49 (8%)	1/50 (2%)	5/49 (10%)
Adjusted Rates (b)	11.4%	2.6%	16.2%
Terminal Rates (c)	4/35 (11%)	0/24 (0%)	3/25 (12%)
Week of First Observation	104	87	87
Life Table Tests (d)	P=0.296	P=0.294N	P=0.332
Incidental Tumor Tests (d)	P=0.404	P=0.186N	P=0.444
Cochran-Armitage Trend Test (d)	P=0.420		
Fisher Exact Test (d)		P=0.175N	P=0.500
Adrenal Gland: Pheochromocytoma or Malignant Pheochromocytoma			
Overall Rates (a)	32/49 (65%)	19/50 (38%)	23/49 (47%)
Adjusted Rates (b)	82.0%	60.1%	65.2%
Terminal Rates (c)	28/35 (80%)	12/24 (50%)	14/25 (56%)
Week of First Observation	95	85	87
Life Table Tests (d)	P=0.418N	P=0.254N	P=0.487N
Incidental Tumor Tests (d)	P=0.094N	P=0.063N	P=0.105N
Cochran-Armitage Trend Test (d)	P=0.043N		
Fisher Exact Test (d)		P=0.006N	P=0.051N
Thyroid Gland: C-Cell Adenoma			
Overall Rates (a)	6/50 (12%)	5/49 (10%)	1/49 (2%)
Adjusted Rates (b)	16.7%	19.2%	3.8%
Terminal Rates (c)	5/35 (14%)	4/24 (17%)	1/26 (4%)
Week of First Observation	103	98	104
Life Table Tests (d)	P=0.119N	P=0.510	P=0.118N
Incidental Tumor Tests (d)	P=0.095N	P=0.554	P=0.099N
Cochran-Armitage Trend Test (d)	P=0.052N		
Fisher Exact Test (d)		P=0.514N	P=0.059N
Thyroid Gland: C-Cell Adenoma or Carcinoma			
Overall Rates (a)	8/50 (16%)	6/49 (12%)	3/49 (6%)
Adjusted Rates (b)	22.2%	23.2%	9.6%
Terminal Rates (c)	7/35 (20%)	5/24 (21%)	2/26 (8%)
Week of First Observation	103	98	76
Life Table Tests (d)	P=0.188N	P=0.561	P=0.206N
Incidental Tumor Tests (d)	P=0.151N	P=0.601	P=0.166N
Cochran-Armitage Trend Test (d)	P=0.083N		
Fisher Exact Test (d)		P=0.403N	P=0.106N
Pancreatic Islets: Islet Cell Adenoma			
Overall Rates (a)	4/49 (8%)	1/50 (2%)	1/49 (2%)
Adjusted Rates (b)	11.4%	2.3%	4.0%
Terminal Rates (c)	4/35 (11%)	0/24 (0%)	1/25 (4%)
Week of First Observation	104	79	104
Life Table Tests (d)	P=0.171N	P=0.288N	P=0.292N
Incidental Tumor Tests (d)	P=0.129N	P=0.186N	P=0.292N
Cochran-Armitage Trend Test (d)	P=0.100N		
Fisher Exact Test (d)		P=0.175N	P=0.181N

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	Control	25,000 ppm	50,000 ppm
Mammary Gland: Fibroadenoma			
Overall Rates (a)	0/50 (0%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	0.0%	12.5%	0.0%
Terminal Rates (c)	0/35 (0%)	3/24 (13%)	0/26 (0%)
Week of First Observation		104	
Life Table Tests (d)	P=0.550	P=0.063	(e)
Incidental Tumor Tests (d)	P=0.550	P=0.063	(e)
Cochran-Armitage Trend Test (d)	P=0.640		
Fisher Exact Test (d)		P=0.121	(e)
Mammary Gland: Fibroadenoma or Adenocarcinoma			
Overall Rates (a)	1/50 (2%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	2.9%	12.5%	0.0%
Terminal Rates (c)	1/35 (3%)	3/24 (13%)	0/26 (0%)
Week of First Observation	104	104	
Life Table Tests (d)	P=0.482N	P=0.181	P=0.559N
Incidental Tumor Tests (d)	P=0.482N	P=0.181	P=0.559N
Cochran-Armitage Trend Test (d)	P=0.378N		
Fisher Exact Test (d)		P=0.309	P=0.500N
Preputial Gland: Carcinoma			
Overall Rates (a)	4/50 (8%)	4/50 (8%)	2/50 (4%)
Adjusted Rates (b)	11.4%	12.7%	7.7%
Terminal Rates (c)	4/35 (11%)	2/24 (8%)	2/26 (8%)
Week of First Observation	104	72	104
Life Table Tests (d)	P=0.403N	P=0.465	P=0.480N
Incidental Tumor Tests (d)	P=0.337N	P=0.646N	P=0.480N
Cochran-Armitage Trend Test (d)	P=0.274N		
Fisher Exact Test (d)		P=0.643	P=0.339N
Preputial Gland: Adenoma or Carcinoma			
Overall Rates (a)	4/50 (8%)	5/50 (10%)	4/50 (8%)
Adjusted Rates (b)	11.4%	16.7%	15.4%
Terminal Rates (c)	4/35 (11%)	3/24 (13%)	4/26 (15%)
Week of First Observation	104	72	104
Life Table Tests (d)	P=0.405	P=0.308	P=0.473
Incidental Tumor Tests (d)	P=0.459	P=0.478	P=0.473
Cochran-Armitage Trend Test (d)	P=0.571		
Fisher Exact Test (d)		P=0.500	P=0.643
Prostate: Adenoma			
Overall Rates (a)	3/47 (6%)	0/49 (0%)	3/49 (6%)
Adjusted Rates (b)	8.6%	0.0%	11.3%
Terminal Rates (c)	3/35 (9%)	0/24 (0%)	2/25 (8%)
Week of First Observation	104		103
Life Table Tests (d)	P=0.463	P=0.194N	P=0.507
Incidental Tumor Tests (d)	P=0.525	P=0.194N	P=0.585
Cochran-Armitage Trend Test (d)	P=0.585N		
Fisher Exact Test (d)		P=0.113N	P=0.641N
Testis: Interstitial Cell Tumor			
Overall Rates (a)	44/47 (94%)	47/50 (94%)	47/49 (96%)
Adjusted Rates (b)	97.7%	100.0%	97.9%
Terminal Rates (c)	34/35 (97%)	24/24 (100%)	24/25 (96%)
Week of First Observation	75	68	57
Life Table Tests (d)	P=0.010	P=0.003	P=0.009
Incidental Tumor Tests (d)	P=0.478	P=0.473	P=0.620
Cochran-Armitage Trend Test (d)	P=0.392		
Fisher Exact Test (d)		P=0.631	P=0.480

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (*Continued*)

	Control	25,000 ppm	50,000 ppm
Musculoskeletal System: Osteosarcoma			
Overall Rates (a)	0/50 (0%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	0.0%	7.3%	0.0%
Terminal Rates (c)	0/35 (0%)	0/24 (0%)	0/26 (0%)
Week of First Observation		71	
Life Table Tests (d)	P=0.617	P=0.108	(e)
Incidental Tumor Tests (d)	P=0.503N	P=0.301	(e)
Cochran-Armitage Trend Test (d)	P=0.640		
Fisher Exact Test (d)		P=0.121	(e)

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence at terminal kill
(d) Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).
(e) No P value is reported because no tumors were observed in the dosed and control groups.

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	Control	25,000 ppm	50,000 ppm
Subcutaneous Tissue: Sarcoma or Fibrosarcoma			
Overall Rates (a)	3/50 (6%)	1/50 (2%)	1/50 (2%)
Adjusted Rates (b)	6.9%	2.0%	2.9%
Terminal Rates (c)	2/40 (5%)	0/33 (0%)	1/34 (3%)
Week of First Observation	81	66	104
Life Table Tests (d)	P=0.239N	P=0.350N	P=0.359N
Incidental Tumor Tests (d)	P=0.159N	P=0.237N	P=0.388N
Cochran-Armitage Trend Test (d)	P=0.202N		
Fisher Exact Test (d)		P=0.309N	P=0.309N
Hematopoietic System: Mononuclear Cell Leukemia			
Overall Rates (a)	14/50 (28%)	21/50 (42%)	18/50 (36%)
Adjusted Rates (b)	30.6%	53.5%	42.8%
Terminal Rates (c)	9/40 (23%)	15/33 (45%)	11/34 (32%)
Week of First Observation	74	95	75
Life Table Tests (d)	P=0.124	P=0.043	P=0.157
Incidental Tumor Tests (d)	P=0.295	P=0.102	P=0.362
Cochran-Armitage Trend Test (d)	P=0.232		
Fisher Exact Test (d)		P=0.104	P=0.260
Liver: Neoplastic Nodule			
Overall Rates (a)	1/50 (2%)	3/49 (6%)	9/50 (18%)
Adjusted Rates (b)	2.5%	9.1%	24.4%
Terminal Rates (c)	1/40 (3%)	3/33 (9%)	7/34 (21%)
Week of First Observation	104	104	87
Life Table Tests (d)	P=0.002	P=0.239	P=0.005
Incidental Tumor Tests (d)	P=0.002	P=0.239	P=0.006
Cochran-Armitage Trend Test (d)	P=0.004		
Fisher Exact Test (d)		P=0.301	P=0.008
Liver: Neoplastic Nodule or Hepatocellular Carcinoma			
Overall Rates (a)	1/50 (2%)	5/49 (10%)	9/50 (18%)
Adjusted Rates (b)	2.5%	15.2%	24.4%
Terminal Rates (c)	1/40 (3%)	5/33 (15%)	7/34 (21%)
Week of First Observation	104	104	87
Life Table Tests (d)	P=0.003	P=0.064	P=0.005
Incidental Tumor Tests (d)	P=0.003	P=0.064	P=0.006
Cochran-Armitage Trend Test (d)	P=0.006		
Fisher Exact Test (d)		P=0.098	P=0.008
Pituitary Gland: Adenoma			
Overall Rates (a)	24/50 (48%)	22/50 (44%)	24/50 (48%)
Adjusted Rates (b)	58.4%	55.6%	64.6%
Terminal Rates (c)	23/40 (58%)	16/33 (48%)	21/34 (62%)
Week of First Observation	97	86	76
Life Table Tests (d)	P=0.259	P=0.418	P=0.274
Incidental Tumor Tests (d)	P=0.344	P=0.567	P=0.388
Cochran-Armitage Trend Test (d)	P=0.540		
Fisher Exact Test (d)		P=0.421N	P=0.579
Pituitary Gland: Adenoma or Carcinoma			
Overall Rates (a)	25/50 (50%)	24/50 (48%)	25/50 (50%)
Adjusted Rates (b)	59.3%	59.4%	65.3%
Terminal Rates (c)	23/40 (58%)	17/33 (52%)	21/34 (62%)
Week of First Observation	84	86	76
Life Table Tests (d)	P=0.257	P=0.335	P=0.278
Incidental Tumor Tests (d)	P=0.383	P=0.513	P=0.430
Cochran-Armitage Trend Test (d)	P=0.540		
Fisher Exact Test (d)		P=0.500N	P=0.579

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	Control	25,000 ppm	50,000 ppm
Adrenal Gland: Cortical Adenoma			
Overall Rates (a)	4/50 (8%)	0/48 (0%)	2/50 (4%)
Adjusted Rates (b)	10.0%	0.0%	5.9%
Terminal Rates (c)	4/40 (10%)	0/33 (0%)	2/34 (6%)
Week of First Observation	104		104
Life Table Tests (d)	P=0.279N	P=0.090N	P=0.414N
Incidental Tumor Tests (d)	P=0.279N	P=0.090N	P=0.414N
Cochran-Armitage Trend Test (d)	P=0.223N		
Fisher Exact Test (d)		P=0.064N	P=0.339N
Adrenal Gland: Pheochromocytoma			
Overall Rates (a)	3/50 (6%)	4/48 (8%)	2/50 (4%)
Adjusted Rates (b)	6.9%	11.2%	5.4%
Terminal Rates (c)	2/40 (5%)	3/33 (9%)	1/34 (3%)
Week of First Observation	74	91	96
Life Table Tests (d)	P=0.487N	P=0.417	P=0.558N
Incidental Tumor Tests (d)	P=0.387N	P=0.499	P=0.383N
Cochran-Armitage Trend Test (d)	P=0.417N		
Fisher Exact Test (d)		P=0.477	P=0.500N
Adrenal Gland: Pheochromocytoma or Malignant Pheochromocytoma			
Overall Rates (a)	4/50 (8%)	4/48 (8%)	2/50 (4%)
Adjusted Rates (b)	9.3%	11.2%	5.4%
Terminal Rates (c)	3/40 (7%)	3/33 (9%)	1/34 (3%)
Week of First Observation	74	91	96
Life Table Tests (d)	P=0.345N	P=0.552	P=0.402N
Incidental Tumor Tests (d)	P=0.257N	P=0.630	P=0.252N
Cochran-Armitage Trend Test (d)	P=0.275N		
Fisher Exact Test (d)		P=0.619	P=0.339N
Thyroid Gland: C-Cell Adenoma			
Overall Rates (a)	9/50 (18%)	6/49 (12%)	5/50 (10%)
Adjusted Rates (b)	22.5%	18.2%	13.6%
Terminal Rates (c)	9/40 (23%)	6/33 (18%)	3/34 (9%)
Week of First Observation	104	104	98
Life Table Tests (d)	P=0.242N	P=0.436N	P=0.294N
Incidental Tumor Tests (d)	P=0.210N	P=0.436N	P=0.241N
Cochran-Armitage Trend Test (d)	P=0.152N		
Fisher Exact Test (d)		P=0.303N	P=0.194N
Thyroid Gland: C-Cell Carcinoma			
Overall Rates (a)	2/50 (4%)	4/49 (8%)	3/50 (6%)
Adjusted Rates (b)	5.0%	11.8%	8.8%
Terminal Rates (c)	2/40 (5%)	3/33 (9%)	3/34 (9%)
Week of First Observation	104	103	104
Life Table Tests (d)	P=0.337	P=0.254	P=0.426
Incidental Tumor Tests (d)	P=0.367	P=0.287	P=0.426
Cochran-Armitage Trend Test (d)	P=0.417		
Fisher Exact Test (d)		P=0.329	P=0.500
Thyroid Gland: C-Cell Adenoma or Carcinoma			
Overall Rates (a)	11/50 (22%)	10/49 (20%)	8/50 (16%)
Adjusted Rates (b)	27.5%	29.4%	22.0%
Terminal Rates (c)	11/40 (28%)	9/33 (27%)	6/34 (18%)
Week of First Observation	104	103	98
Life Table Tests (d)	P=0.412N	P=0.499	P=0.450N
Incidental Tumor Tests (d)	P=0.358N	P=0.523	P=0.396N
Cochran-Armitage Trend Test (d)	P=0.264N		
Fisher Exact Test (d)		P=0.521N	P=0.306N

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	Control	25,000 ppm	50,000 ppm
Mammary Gland: Fibroadenoma			
Overall Rates (a)	24/50 (48%)	18/50 (36%)	21/50 (42%)
Adjusted Rates (b)	54.2%	46.2%	53.4%
Terminal Rates (c)	20/40 (50%)	13/33 (39%)	16/34 (47%)
Week of First Observation	74	86	86
Life Table Tests (d)	P=0.521	P=0.387N	P=0.546
Incidental Tumor Tests (d)	P=0.439N	P=0.210N	P=0.456N
Cochran-Armitage Trend Test (d)	P=0.306N		
Fisher Exact Test (d)		P=0.156N	P=0.344N
Mammary Gland: Adenoma or Fibroadenoma			
Overall Rates (a)	24/50 (48%)	18/50 (36%)	23/50 (46%)
Adjusted Rates (b)	54.2%	46.2%	57.2%
Terminal Rates (c)	20/40 (50%)	13/33 (39%)	17/34 (50%)
Week of First Observation	74	86	86
Life Table Tests (d)	P=0.366	P=0.387N	P=0.385
Incidental Tumor Tests (d)	P=0.485	P=0.210N	P=0.554
Cochran-Armitage Trend Test (d)	P=0.460N		
Fisher Exact Test (d)		P=0.156N	P=0.500N
Mammary Gland: Adenoma, Fibroadenoma, Adenocarcinoma, or Papillary Cystadenocarcinoma			
Overall Rates (a)	25/50 (50%)	18/50 (36%)	24/50 (48%)
Adjusted Rates (b)	56.5%	46.2%	59.8%
Terminal Rates (c)	21/40 (53%)	13/33 (39%)	18/34 (53%)
Week of First Observation	74	86	86
Life Table Tests (d)	P=0.358	P=0.323N	P=0.374
Incidental Tumor Tests (d)	P=0.476	P=0.161N	P=0.541
Cochran-Armitage Trend Test (d)	P=0.460N		
Fisher Exact Test (d)		P=0.113N	P=0.500N
Clitoral Gland: Carcinoma			
Overall Rates (a)	4/50 (8%)	3/50 (6%)	3/50 (6%)
Adjusted Rates (b)	10.0%	7.2%	8.8%
Terminal Rates (c)	4/40 (10%)	1/33 (3%)	3/34 (9%)
Week of First Observation	104	49	104
Life Table Tests (d)	P=0.497N	P=0.580N	P=0.589N
Incidental Tumor Tests (d)	P=0.471N	P=0.381N	P=0.589N
Cochran-Armitage Trend Test (d)	P=0.421N		
Fisher Exact Test (d)		P=0.500N	P=0.500N
Clitoral Gland: Adenoma or Carcinoma			
Overall Rates (a)	4/50 (8%)	4/50 (8%)	4/50 (8%)
Adjusted Rates (b)	10.0%	10.1%	11.8%
Terminal Rates (c)	4/40 (10%)	2/33 (6%)	4/34 (12%)
Week of First Observation	104	49	104
Life Table Tests (d)	P=0.487	P=0.555	P=0.552
Incidental Tumor Tests (d)	P=0.510	P=0.559N	P=0.552
Cochran-Armitage Trend Test (d)	P=0.573		
Fisher Exact Test (d)		P=0.643	P=0.643
Uterus: Endometrial Stromal Polyp			
Overall Rates (a)	9/49 (18%)	10/49 (20%)	11/50 (22%)
Adjusted Rates (b)	22.5%	26.7%	28.6%
Terminal Rates (c)	9/40 (23%)	7/33 (21%)	8/34 (24%)
Week of First Observation	104	86	72
Life Table Tests (d)	P=0.233	P=0.338	P=0.269
Incidental Tumor Tests (d)	P=0.333	P=0.402	P=0.422
Cochran-Armitage Trend Test (d)	P=0.373		
Fisher Exact Test (d)		P=0.500	P=0.421

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	Control	25,000 ppm	50,000 ppm
Uterus: Endometrial Stromal Polyp or Sarcoma			
Overall Rates (a)	10/49 (20%)	10/49 (20%)	12/50 (24%)
Adjusted Rates (b)	24.3%	26.7%	30.4%
Terminal Rates (c)	9/40 (23%)	7/33 (21%)	8/34 (24%)
Week of First Observation	99	86	72
Life Table Tests (d)	P=0.234	P=0.432	P=0.269
Incidental Tumor Tests (d)	P=0.369	P=0.532	P=0.481
Cochran-Armitage Trend Test (d)	P=0.377		
Fisher Exact Test (d)		P=0.599N	P=0.426
Zymbal Gland: Carcinoma			
Overall Rates (a)	0/50 (0%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	0.0%	7.4%	0.0%
Terminal Rates (c)	0/40 (0%)	1/33 (3%)	0/34 (0%)
Week of First Observation		72	
Life Table Tests (d)	P=0.609	P=0.104	(e)
Incidental Tumor Tests (d)	P=0.480N	P=0.177	(e)
Cochran-Armitage Trend Test (d)	P=0.640		
Fisher Exact Test (d)		P=0.121	(e)

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence at terminal kill
(d) Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).
(e) No P value is reported because no tumors were observed in the 50,000-ppm and control groups.

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	Control	25,000 ppm	50,000 ppm
Subcutaneous Tissue: Fibroma			
Overall Rates (a)	0/50 (0%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	0.0%	12.0%	0.0%
Terminal Rates (c)	0/19 (0%)	3/25 (12%)	0/24 (0%)
Week of First Observation		103	
Life Table Tests (d)	P=0.582N	P=0.171	(e)
Incidental Tumor Tests (d)	P=0.582N	P=0.171	(e)
Cochran-Armitage Trend Test (d)	P=0.640		
Fisher Exact Test (d)		P=0.121	(e)
Subcutaneous Tissue: Fibrosarcoma			
Overall Rates (a)	6/50 (12%)	8/50 (16%)	10/50 (20%)
Adjusted Rates (b)	27.6%	23.8%	28.2%
Terminal Rates (c)	4/19 (21%)	2/25 (8%)	3/24 (13%)
Week of First Observation	82	72	60
Life Table Tests (d)	P=0.378	P=0.561N	P=0.442
Incidental Tumor Tests (d)	P=0.420	P=0.593N	P=0.462
Cochran-Armitage Trend Test (d)	P=0.170		
Fisher Exact Test (d)		P=0.387	P=0.207
Integumentary System: Fibrosarcoma			
Overall Rates (a)	7/50 (14%)	8/50 (16%)	10/50 (20%)
Adjusted Rates (b)	32.5%	23.8%	28.2%
Terminal Rates (c)	5/19 (26%)	2/25 (8%)	3/24 (13%)
Week of First Observation	82	72	60
Life Table Tests (d)	P=0.490	P=0.437N	P=0.557
Incidental Tumor Tests (d)	P=0.542	P=0.459N	P=0.585
Cochran-Armitage Trend Test (d)	P=0.251		
Fisher Exact Test (d)		P=0.500	P=0.298
Integumentary System: Sarcoma or Fibrosarcoma			
Overall Rates (a)	7/50 (14%)	9/50 (18%)	10/50 (20%)
Adjusted Rates (b)	32.5%	27.1%	28.2%
Terminal Rates (c)	5/19 (26%)	3/25 (12%)	3/24 (13%)
Week of First Observation	82	72	60
Life Table Tests (d)	P=0.498	P=0.530N	P=0.557
Incidental Tumor Tests (d)	P=0.549	P=0.557N	P=0.585
Cochran-Armitage Trend Test (d)	P=0.254		
Fisher Exact Test (d)		P=0.393	P=0.298
Integumentary System: Fibroma, Sarcoma, or Fibrosarcoma			
Overall Rates (a)	7/50 (14%)	12/50 (24%)	10/50 (20%)
Adjusted Rates (b)	32.5%	37.1%	28.2%
Terminal Rates (c)	5/19 (26%)	6/25 (24%)	3/24 (13%)
Week of First Observation	82	72	60
Life Table Tests (d)	P=0.520	P=0.414	P=0.557
Incidental Tumor Tests (d)	P=0.535N	P=0.385	P=0.585
Cochran-Armitage Trend Test (d)	P=0.263		
Fisher Exact Test (d)		P=0.154	P=0.298
Integumentary System: Fibroma or Fibrosarcoma			
Overall Rates (a)	7/50 (14%)	11/50 (22%)	10/50 (20%)
Adjusted Rates (b)	32.5%	33.8%	28.2%
Terminal Rates (c)	5/19 (26%)	5/25 (20%)	3/24 (13%)
Week of First Observation	82	72	60
Life Table Tests (d)	P=0.513	P=0.499	P=0.557
Incidental Tumor Tests (d)	P=0.544N	P=0.475	P=0.585
Cochran-Armitage Trend Test (d)	P=0.261		
Fisher Exact Test (d)		P=0.218	P=0.298

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	Control	25,000 ppm	50,000 ppm
Lung: Alveolar/Bronchiolar Adenoma			
Overall Rates (a)	4/50 (8%)	1/50 (2%)	4/50 (8%)
Adjusted Rates (b)	21.1%	4.0%	13.5%
Terminal Rates (c)	4/19 (21%)	1/25 (4%)	2/24 (8%)
Week of First Observation	103	103	35
Life Table Tests (d)	P=0.466N	P=0.102N	P=0.503N
Incidental Tumor Tests (d)	P=0.536N	P=0.102N	P=0.583N
Cochran-Armitage Trend Test (d)	P=0.583		
Fisher Exact Test (d)		P=0.181N	P=0.643
Lung: Alveolar/Bronchiolar Carcinoma			
Overall Rates (a)	2/50 (4%)	4/50 (8%)	1/50 (2%)
Adjusted Rates (b)	10.5%	16.0%	4.2%
Terminal Rates (c)	2/19 (11%)	4/25 (16%)	1/24 (4%)
Week of First Observation	103	103	103
Life Table Tests (d)	P=0.306N	P=0.468	P=0.418N
Incidental Tumor Tests (d)	P=0.306N	P=0.468	P=0.418N
Cochran-Armitage Trend Test (d)	P=0.406N		
Fisher Exact Test (d)		P=0.339	P=0.500N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates (a)	5/50 (10%)	4/50 (8%)	5/50 (10%)
Adjusted Rates (b)	26.3%	16.0%	17.4%
Terminal Rates (c)	5/19 (26%)	4/25 (16%)	3/24 (13%)
Week of First Observation	103	103	35
Life Table Tests (d)	P=0.419N	P=0.324N	P=0.471N
Incidental Tumor Tests (d)	P=0.477N	P=0.324N	P=0.544N
Cochran-Armitage Trend Test (d)	P=0.568		
Fisher Exact Test (d)		P=0.500N	P=0.630
Hematopoietic System: Malignant Lymphoma, Mixed Type			
Overall Rates (a)	1/50 (2%)	3/50 (6%)	1/50 (2%)
Adjusted Rates (b)	5.3%	12.0%	4.2%
Terminal Rates (c)	1/19 (5%)	3/25 (12%)	1/24 (4%)
Week of First Observation	104	103	103
Life Table Tests (d)	P=0.531N	P=0.406	P=0.710N
Incidental Tumor Tests (d)	P=0.531N	P=0.406	P=0.710N
Cochran-Armitage Trend Test (d)	P=0.610		
Fisher Exact Test (d)		P=0.309	P=0.753N
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (a)	2/50 (4%)	7/50 (14%)	4/50 (8%)
Adjusted Rates (b)	10.5%	24.5%	16.7%
Terminal Rates (c)	2/19 (11%)	5/25 (20%)	4/24 (17%)
Week of First Observation	104	82	103
Life Table Tests (d)	P=0.431	P=0.174	P=0.447
Incidental Tumor Tests (d)	P=0.427	P=0.203	P=0.447
Cochran-Armitage Trend Test (d)	P=0.297		
Fisher Exact Test (d)		P=0.080	P=0.339
Hematopoietic System: Lymphoma or Leukemia			
Overall Rates (a)	2/50 (4%)	7/50 (14%)	6/50 (12%)
Adjusted Rates (b)	10.5%	24.5%	23.5%
Terminal Rates (c)	2/19 (11%)	5/25 (20%)	5/24 (21%)
Week of First Observation	104	82	92
Life Table Tests (d)	P=0.210	P=0.174	P=0.219
Incidental Tumor Tests (d)	P=0.203	P=0.203	P=0.224
Cochran-Armitage Trend Test (d)	P=0.122		

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	Control	25,000 ppm	50,000 ppm
Circulatory System: Hemangioma			
Overall Rates (a)	0/50 (0%)	4/50 (8%)	0/50 (0%)
Adjusted Rates (b)	0.0%	15.4%	0.0%
Terminal Rates (c)	0/19 (0%)	3/25 (12%)	0/24 (0%)
Week of First Observation		100	
Life Table Tests (d)	P=0.546N	P=0.105	(e)
Incidental Tumor Tests (d)	P=0.529N	P=0.104	(e)
Cochran-Armitage Trend Test (d)	P=0.622		
Fisher Exact Test (d)		P=0.059	(e)
Circulatory System: Hemangioma or Hemangiosarcoma			
Overall Rates (a)	2/50 (4%)	6/50 (12%)	2/50 (4%)
Adjusted Rates (b)	9.6%	21.8%	6.7%
Terminal Rates (c)	1/19 (5%)	4/25 (16%)	1/24 (4%)
Week of First Observation	94	92	72
Life Table Tests (d)	P=0.445N	P=0.247	P=0.589N
Incidental Tumor Tests (d)	P=0.414N	P=0.266	P=0.564N
Cochran-Armitage Trend Test (d)	P=0.579		
Fisher Exact Test (d)		P=0.134	P=0.691N
Liver: Hepatocellular Adenoma			
Overall Rates (a)	4/50 (8%)	12/50 (24%)	12/50 (24%)
Adjusted Rates (b)	19.0%	46.2%	39.0%
Terminal Rates (c)	3/19 (16%)	11/25 (44%)	7/24 (29%)
Week of First Observation	81	100	60
Life Table Tests (d)	P=0.078	P=0.081	P=0.095
Incidental Tumor Tests (d)	P=0.084	P=0.088	P=0.099
Cochran-Armitage Trend Test (d)	P=0.027		
Fisher Exact Test (d)		P=0.027	P=0.027
Liver: Hepatocellular Carcinoma			
Overall Rates (a)	5/50 (10%)	14/50 (28%)	8/50 (16%)
Adjusted Rates (b)	20.7%	42.9%	26.8%
Terminal Rates (c)	1/19 (5%)	8/25 (32%)	4/24 (17%)
Week of First Observation	81	72	76
Life Table Tests (d)	P=0.494	P=0.118	P=0.486
Incidental Tumor Tests (d)	P=0.523	P=0.139	P=0.542
Cochran-Armitage Trend Test (d)	P=0.258		
Fisher Exact Test (d)		P=0.020	P=0.277
Liver: Hepatocellular Adenoma or Carcinoma			
Overall Rates (a)	8/50 (16%)	22/50 (44%)	18/50 (36%)
Adjusted Rates (b)	33.9%	67.7%	56.5%
Terminal Rates (c)	4/19 (21%)	15/25 (60%)	11/24 (46%)
Week of First Observation	81	72	60
Life Table Tests (d)	P=0.124	P=0.036	P=0.115
Incidental Tumor Tests (d)	P=0.116	P=0.036	P=0.116
Cochran-Armitage Trend Test (d)	P=0.021		
Fisher Exact Test (d)		P=0.002	P=0.019
Thyroid Gland: Follicular Cell Adenoma			
Overall Rates (a)	0/50 (0%)	3/50 (6%)	3/50 (6%)
Adjusted Rates (b)	0.0%	10.8%	12.5%
Terminal Rates (c)	0/19 (0%)	2/25 (8%)	3/24 (13%)
Week of First Observation		90	103
Life Table Tests (d)	P=0.142	P=0.184	P=0.163
Incidental Tumor Tests (d)	P=0.138	P=0.210	P=0.163
Cochran-Armitage Trend Test (d)	P=0.101		
Fisher Exact Test (d)		P=0.121	P=0.121

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	Control	25,000 ppm	50,000 ppm
Thyroid: Follicular Cell Adenoma or Carcinoma			
Overall Rates (a)	0/50 (0%)	4/50 (8%)	3/50 (6%)
Adjusted Rates (b)	0.0%	14.7%	12.5%
Terminal Rates (c)	0/19 (0%)	3/25 (12%)	3/24 (13%)
Week of First Observation		90	103
Life Table Tests (d)	P=0.168	P=0.109	P=0.163
Incidental Tumor Tests (d)	P=0.164	P=0.124	P=0.163
Cochran-Armitage Trend Test (d)	P=0.118		
Fisher Exact Test (d)		P=0.059	P=0.121
Adrenal Gland: Adenoma or Cortical Adenoma			
Overall Rates (a)	1/49 (2%)	2/50 (4%)	3/50 (6%)
Adjusted Rates (b)	5.3%	8.0%	11.6%
Terminal Rates (c)	1/19 (5%)	2/25 (8%)	2/24 (8%)
Week of First Observation	103	103	96
Life Table Tests (d)	P=0.294	P=0.596	P=0.402
Incidental Tumor Tests (d)	P=0.305	P=0.596	P=0.418
Cochran-Armitage Trend Test (d)	P=0.228		
Fisher Exact Test (d)		P=0.508	P=0.316
Harderian Gland: Papillary Adenocarcinoma			
Overall Rates (a)	0/50 (0%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	0.0%	9.8%	0.0%
Terminal Rates (c)	0/19 (0%)	1/25 (4%)	0/24 (0%)
Week of First Observation		90	
Life Table Tests (d)	P=0.558N	P=0.194	(e)
Incidental Tumor Tests (d)	P=0.568N	P=0.246	(e)
Cochran-Armitage Trend Test (d)	P=0.640		
Fisher Exact Test (d)		P=0.121	(e)
Harderian Gland: Adenocarcinoma or Papillary Adenocarcinoma			
Overall Rates (a)	1/50 (2%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	5.3%	9.8%	0.0%
Terminal Rates (c)	1/19 (5%)	1/25 (4%)	0/24 (0%)
Week of First Observation	103	90	
Life Table Tests (d)	P=0.287N	P=0.433	P=0.453N
Incidental Tumor Tests (d)	P=0.282N	P=0.509	P=0.453N
Cochran-Armitage Trend Test (d)	P=0.378N		
Fisher Exact Test (d)		P=0.309	P=0.500N

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence at terminal kill
(d) Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).
(e) No P value is reported because no tumors were observed in the 50,000-ppm and control groups.

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	Control	25,000 ppm	50,000 ppm
Subcutaneous Tissue: Fibrosarcoma or Neurofibrosarcoma			
Overall Rates (a)	1/50 (2%)	3/50 (6%)	1/50 (2%)
Adjusted Rates (b)	3.7%	7.4%	3.1%
Terminal Rates (c)	1/27 (4%)	0/31 (0%)	1/32 (3%)
Week of First Observation	103	90	103
Life Table Tests (d)	P=0.563N	P=0.348	P=0.724N
Incidental Tumor Tests (d)	P=0.564N	P=0.336	P=0.724N
Cochran-Armitage Trend Test (d)	P=0.610		
Fisher Exact Test (d)		P=0.309	P=0.753
Lung: Alveolar/Bronchiolar Adenoma			
Overall Rates (a)	4/50 (8%)	2/50 (4%)	2/50 (4%)
Adjusted Rates (b)	13.7%	6.5%	6.3%
Terminal Rates (c)	3/27 (11%)	2/31 (6%)	2/32 (6%)
Week of First Observation	95	103	103
Life Table Tests (d)	P=0.192N	P=0.283N	P=0.265N
Incidental Tumor Tests (d)	P=0.209N	P=0.311N	P=0.290N
Cochran-Armitage Trend Test (d)	P=0.252N		
Fisher Exact Test (d)		P=0.339N	P=0.339N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates (a)	6/50 (12%)	4/50 (8%)	4/50 (8%)
Adjusted Rates (b)	19.7%	12.9%	11.3%
Terminal Rates (c)	4/27 (15%)	4/31 (13%)	3/32 (9%)
Week of First Observation	95	103	87
Life Table Tests (d)	P=0.218N	P=0.299N	P=0.276N
Incidental Tumor Tests (d)	P=0.240N	P=0.343N	P=0.308N
Cochran-Armitage Trend Test (d)	P=0.303N		
Fisher Exact Test (d)		P=0.370N	P=0.370N
Hematopoietic System: Malignant Lymphoma, Undifferentiated Type			
Overall Rates (a)	4/50 (8%)	2/50 (4%)	0/50 (0%)
Adjusted Rates (b)	11.2%	4.7%	0.0%
Terminal Rates (c)	1/27 (4%)	0/31 (0%)	0/32 (0%)
Week of First Observation	84	86	
Life Table Tests (d)	P=0.031N	P=0.311N	P=0.052N
Incidental Tumor Tests (d)	P=0.029N	P=0.310N	P=0.062N
Cochran-Armitage Trend Test (d)	P=0.037N		
Fisher Exact Test (d)		P=0.339N	P=0.059N
Hematopoietic System: Malignant Lymphoma, Lymphocytic Type			
Overall Rates (a)	5/50 (10%)	4/50 (8%)	1/50 (2%)
Adjusted Rates (b)	15.3%	10.2%	3.1%
Terminal Rates (c)	2/27 (7%)	1/31 (3%)	1/32 (3%)
Week of First Observation	91	66	103
Life Table Tests (d)	P=0.060N	P=0.440N	P=0.078N
Incidental Tumor Tests (d)	P=0.101N	P=0.552N	P=0.092N
Cochran-Armitage Trend Test (d)	P=0.080N		
Fisher Exact Test (d)		P=0.500N	P=0.103N
Hematopoietic System: Malignant Lymphoma, Histiocytic Type			
Overall Rates (a)	2/50 (4%)	2/50 (4%)	5/50 (10%)
Adjusted Rates (b)	7.4%	4.8%	12.7%
Terminal Rates (c)	2/27 (7%)	0/31 (0%)	2/32 (6%)
Week of First Observation	104	65	87
Life Table Tests (d)	P=0.200	P=0.649N	P=0.291
Incidental Tumor Tests (d)	P=0.121	P=0.626	P=0.281
Cochran-Armitage Trend Test (d)	P=0.146		
Fisher Exact Test (d)		P=0.691N	P=0.218

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	Control	25,000 ppm	50,000 ppm
Hematopoietic System: Malignant Lymphoma, Mixed Type			
Overall Rates (a)	6/50 (12%)	5/50 (10%)	11/50 (22%)
Adjusted Rates (b)	20.8%	14.8%	33.1%
Terminal Rates (c)	5/27 (19%)	4/31 (13%)	10/32 (31%)
Week of First Observation	95	80	99
Life Table Tests (d)	P=0.170	P=0.415N	P=0.243
Incidental Tumor Tests (d)	P=0.154	P=0.425N	P=0.208
Cochran-Armitage Trend Test (d)	P=0.102		
Fisher Exact Test (d)		P=0.500N	P=0.143
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (a)	17/50 (34%)	14/50 (28%)	17/50 (34%)
Adjusted Rates (b)	48.5%	32.6%	46.2%
Terminal Rates (c)	10/27 (37%)	5/31 (16%)	13/32 (41%)
Week of First Observation	84	65	87
Life Table Tests (d)	P=0.356N	P=0.245N	P=0.366N
Incidental Tumor Tests (d)	P=0.487N	P=0.320N	P=0.437N
Cochran-Armitage Trend Test (d)	P=0.543		
Fisher Exact Test (d)		P=0.333N	P=0.584N
Hematopoietic System: Lymphoma or Leukemia			
Overall Rates (a)	17/50 (34%)	15/50 (30%)	17/50 (34%)
Adjusted Rates (b)	48.5%	34.6%	46.2%
Terminal Rates (c)	10/27 (37%)	5/31 (16%)	13/32 (41%)
Week of First Observation	84	65	87
Life Table Tests (d)	P=0.353N	P=0.306N	P=0.366N
Incidental Tumor Tests (d)	P=0.494N	P=0.417N	P=0.437N
Cochran-Armitage Trend Test (d)	P=0.542		
Fisher Exact Test (d)		P=0.415N	P=0.584N
Liver: Hepatocellular Adenoma			
Overall Rates (a)	5/50 (10%)	10/50 (20%)	7/50 (14%)
Adjusted Rates (b)	16.8%	31.2%	21.9%
Terminal Rates (c)	4/27 (15%)	9/31 (29%)	7/32 (22%)
Week of First Observation	83	102	103
Life Table Tests (d)	P=0.466	P=0.196	P=0.497
Incidental Tumor Tests (d)	P=0.456	P=0.184	P=0.509
Cochran-Armitage Trend Test (d)	P=0.336		
Fisher Exact Test (d)		P=0.131	P=0.380
Liver: Hepatocellular Carcinoma			
Overall Rates (a)	3/50 (6%)	4/50 (8%)	7/50 (14%)
Adjusted Rates (b)	10.7%	12.1%	20.8%
Terminal Rates (c)	2/27 (7%)	3/31 (10%)	6/32 (19%)
Week of First Observation	101	93	96
Life Table Tests (d)	P=0.175	P=0.566	P=0.243
Incidental Tumor Tests (d)	P=0.139	P=0.499	P=0.196
Cochran-Armitage Trend Test (d)	P=0.114		
Fisher Exact Test (d)		P=0.500	P=0.159
Liver: Hepatocellular Adenoma or Carcinoma			
Overall Rates (a)	8/50 (16%)	13/50 (26%)	13/50 (26%)
Adjusted Rates (b)	26.7%	39.1%	39.1%
Terminal Rates (c)	6/27 (22%)	11/31 (35%)	12/32 (38%)
Week of First Observation	83	93	96
Life Table Tests (d)	P=0.259	P=0.256	P=0.290
Incidental Tumor Tests (d)	P=0.219	P=0.209	P=0.258
Cochran-Armitage Trend Test (d)	P=0.141		
Fisher Exact Test (d)		P=0.163	P=0.163

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

	Control	25,000 ppm	50,000 ppm
Pituitary: Adenoma			
Overall Rates (a)	8/40 (20%)	6/45 (13%)	6/49 (12%)
Adjusted Rates (b)	25.1%	19.2%	17.4%
Terminal Rates (c)	4/24 (17%)	4/27 (15%)	4/32 (13%)
Week of First Observation	53	90	99
Life Table Tests (d)	P=0.192N	P=0.317N	P=0.235N
Incidental Tumor Tests (d)	P=0.232N	P=0.323N	P=0.335N
Cochran-Armitage Trend Test (d)	P=0.198N		
Fisher Exact Test (d)		P=0.296N	P=0.239N
Thyroid Gland: Follicular Cell Adenoma			
Overall Rates (a)	1/50 (2%)	3/50 (6%)	2/49 (4%)
Adjusted Rates (b)	2.9%	7.8%	6.3%
Terminal Rates (c)	0/27 (0%)	1/31 (3%)	2/32 (6%)
Week of First Observation	95	80	103
Life Table Tests (d)	P=0.455	P=0.332	P=0.555
Incidental Tumor Tests (d)	P=0.419	P=0.279	P=0.514
Cochran-Armitage Trend Test (d)	P=0.391		
Fisher Exact Test (d)		P=0.309	P=0.492
Thyroid Gland: Follicular Cell Adenoma or Carcinoma			
Overall Rates (a)	1/50 (2%)	3/50 (6%)	3/49 (6%)
Adjusted Rates (b)	2.9%	7.8%	9.4%
Terminal Rates (c)	0/27 (0%)	1/31 (3%)	3/32 (9%)
Week of First Observation	95	80	103
Life Table Tests (d)	P=0.291	P=0.332	P=0.365
Incidental Tumor Tests (d)	P=0.263	P=0.279	P=0.331
Cochran-Armitage Trend Test (d)	P=0.231		
Fisher Exact Test (d)		P=0.309	P=0.301
Uterus: Endometrial Stromal Polyp			
Overall Rates (a)	0/50 (0%)	3/50 (6%)	1/50 (2%)
Adjusted Rates (b)	0.0%	9.7%	3.1%
Terminal Rates (c)	0/27 (0%)	3/31 (10%)	1/32 (3%)
Week of First Observation		103	103
Life Table Tests (d)	P=0.431	P=0.145	P=0.534
Incidental Tumor Tests (d)	P=0.431	P=0.145	P=0.534
Cochran-Armitage Trend Test (d)	P=0.378		
Fisher Exact Test (d)		P=0.121	P=0.500
Harderian Gland: Carcinoma or Adenocarcinoma (e)			
Overall Rates (a)	2/50 (4%)	0/50 (0%)	3/50 (6%)
Adjusted Rates (b)	6.5%	0.0%	8.5%
Terminal Rates (c)	1/27 (4%)	0/31 (0%)	2/32 (6%)
Week of First Observation	95		89
Life Table Tests (d)	P=0.440	P=0.222N	P=0.562
Incidental Tumor Tests (d)	P=0.429	P=0.262N	P=0.552
Cochran-Armitage Trend Test (d)	P=0.390		
Fisher Exact Test (d)		P=0.247N	P=0.500
Harderian Gland: Adenoma, Carcinoma, or Adenocarcinoma (f)			
Overall Rates (a)	4/50 (8%)	0/50 (0%)	3/50 (6%)
Adjusted Rates (b)	13.7%	0.0%	8.5%
Terminal Rates (c)	3/27 (11%)	0/31 (0%)	2/32 (6%)
Week of First Observation	95		89
Life Table Tests (d)	P=0.345N	P=0.051N	P=0.421N
Incidental Tumor Tests (d)	P=0.354N	P=0.061N	P=0.430N
Cochran-Armitage Trend Test (d)	P=0.406N		
Fisher Exact Test (d)		P=0.059N	P=0.500N

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE (Continued)

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence at terminal kill
(d) Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).
(e) Includes carcinoma, NOS, adenocarcinoma, NOS, and papillary adenocarcinoma
(f) Includes adenoma, NOS, papillary adenoma, carcinoma, NOS, adenocarcinoma, NOS, and papillary adenocarcinoma

APPENDIX F

HISTORICAL INCIDENCES OF TUMORS IN F344/N RATS AND B6C3F$_1$ MICE RECEIVING NO TREATMENT

TABLE F1. HISTORICAL INCIDENCE OF LEUKEMIA IN F344/N RATS RECEIVING NO TREATMENT (a)

	Incidence in Controls	
	Male	Female
No 2-year studies by Hazleton Laboratories America are included in the historical data base.		
Overall Historical Incidence		
TOTAL	458/1,727 (26.5%)	307/1,772 (17.3%)
SD (b)	8.83%	6.00%
Range (c)		
High	23/50	19/50
Low	5/50	3/50

(a) Data as of August 3, 1984, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE F2. HISTORICAL INCIDENCE OF SPLENIC TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT (a)

	Incidence of Sarcomas in Controls
No 2-year studies by Hazleton Laboratories America are included in the historical data base.	
Overall Historical Incidence	
TOTAL	5/1,705 (0.3%)
SD (b)	0.74%
Range (c)	
High	1/45
Low	0/90

(a) Data as of August 3, 1984, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE F3. HISTORICAL INCIDENCE OF HEPATOCELLULAR TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT (a)

	Incidence in Controls		
	Neoplastic Nodule	Carcinoma	Neoplastic Nodule or Carcinoma
No 2-year studies by Hazleton Laboratories America are included in the historical data base.			
Overall Historical Incidence			
TOTAL	61/1,719 (3.5%)	12/1,719 (0.7%)	73/1,719 (4.2%)
SD (b)	3.34%	0.98%	3.45%
Range (c)			
High	6/49	1/49	7/49
Low	0/50	0/90	0/50

(a) Data as of August 3, 1984, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE F4. HISTORICAL INCIDENCE OF PANCREATIC ACINAR CELL TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT (a)

	Incidence in Controls
No 2-year studies by Hazleton Laboratories America are included in the historical data base.	
Overall Historical Incidence	
TOTAL	(b) 3/1,667 (0.2%)
SD (c)	0.59%
Range (d)	
High	1/47
Low	0/88

(a) Data as of August 3, 1984, for studies of at least 104 weeks
(b) No acinar cell carcinomas have been observed.
(c) Standard deviation
(d) Range and SD are presented for groups of 35 or more animals.

TABLE F5. HISTORICAL INCIDENCE OF HEPATOCELLULAR TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT (a)

	Incidence in Controls		
	Neoplastic Nodule	Carcinoma	Neoplastic Nodule or Carcinoma
No 2-year studies by Hazleton Laboratories America are included in the historical data base.			
Overall Historical Incidence			
TOTAL	46/1,766 (2.6%)	3/1,766 (0.2%)	48/1,766 (2.7%)
SD (b)	2.77%	0.75%	2.99%
Range (c)			
High	4/50	2/50	5/50
Low	0/50	0/88	0/50

(a) Data as of August 3, 1984, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE F6. HISTORICAL INCIDENCE OF MUSCULOSKELETAL SYSTEM TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT (a)

	Incidence of Osteoma or Osteosarcoma in Controls
No 2-year studies by Hazleton Laboratories America are included in the historical data base.	
Overall Historical Incidence	
TOTAL	(b) 8/1,727 (0.5%)
SD (c)	0.96%
Range (d)	
High	2/50
Low	(e) 0/50

(a) Data as of August 3, 1984, for studies of at least 104 weeks
(b) Includes one osteoma and seven osteosarcomas
(c) Standard deviation
(d) Range and SD are presented for groups of 35 or more animals.
(e) The low range for osteosarcoma alone is 0/90.

TABLE F7. HISTORICAL INCIDENCE OF ZYMBAL GLAND TUMORS IN F344/N RATS RECEIVING NO TREATMENT (a)

	Incidence in Controls	
	Male	Female
No 2-year studies by Hazleton Laboratories America are included in the historical data base.		
Overall Historical Incidence		
TOTAL	(b) 11/1,772 (0.6%)	(c) 6/1,772 (0.3%)
SD (d)	1.28%	1.14%
Range (e)		
High	3/50	3/50
Low	0/90	0/88

(a) Data as of August 3, 1984, for studies of at least 104 weeks
(b) Total includes nine squamous cell carcinomas, one carcinoma, NOS, and one ceruminous carcinoma. One squamous cell papilloma, three squamous cell carcinomas, three sebaceous adenocarcinomas, and one ceruminous carcinoma of the ear canal were also observed; the inclusion of these tumors would not affect the reported range. No benign Zymbal gland tumors were observed.
(c) Total includes one adenocarcinoma, NOS, three squamous cell carcinomas, and two adenosquamous carcinomas. Three squamous cell carcinomas of the ear canal were also observed; the inclusion of these tumors would not affect the reported range. No benign tumors were observed.
(d) Standard deviation
(e) Range and SD are presented for groups of 35 or more animals.

TABLE F8. HISTORICAL INCIDENCE OF HEPATOCELLULAR TUMORS IN MALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
No 2-year studies by Hazleton Laboratories America are included in the historical data base.			
Overall Historical Incidence			
TOTAL	179/1,784 (10.0%)	377/1,784 (21.1%)	540/1,784 (30.3%)
SD (b)	7.36%	6.54%	8.04%
Range (c)			
High	(d) 22/50	16/50	(e) 29/50
Low	0/49	4/50	7/50

(a) Data as of August 3, 1984, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.
(d) Second high, 9/50
(e) Second high, 20/50

TABLE F9. HISTORICAL INCIDENCE OF THYROID GLAND FOLLICULAR CELL TUMORS IN MALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
No 2-year studies by Hazleton Laboratories America are included in the historical data base.			
Overall Historical Incidence			
TOTAL	(b) 26/1,680 (1.5%)	2/1,680 (0.1%)	28/1,680 (1.7%)
SD (c)	2.06%	0.49%	2.09%
Range (d)			
High	3/42	1/47	3/42
Low	0/50	0/50	0/50

(a) Data as of August 3, 1984, for studies of at least 104 weeks
(b) Total includes one papillary adenoma and one cystadenoma.
(c) Standard deviation
(d) Range and SD are presented for groups of 35 or more animals.

TABLE F10. HISTORICAL INCIDENCE OF TESTICULAR TUMORS IN MALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

	Incidence of Interstitial Cell Tumors in Controls
No 2-year studies by Hazleton Laboratories America are included in the historical data base.	
Overall Historical Incidence	
TOTAL	5/1,768 (0.3%)
SD (b)	0.71%
Range (c)	
High	1/48
Low	0/50

(a) Data as of August 3, 1984, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

APPENDIX G

GENETIC TOXICOLOGY OF DECABROMODIPHENYL OXIDE

TABLE G1. MUTAGENICITY OF DECABROMODIPHENYL OXIDE IN *SALMONELLA TYPHIMURIUM*

Strain	Dose (μg/plate)	Revertants/plate (a,b) −S9	+S9 (rat)	+S9 (hamster)
TA100	0	119 ± 4.2	121 ± 7.8	112 ± 6.7
	100	125 ± 6.4	142 ± 6.4	144 ± 5.0
	333	106 ± 5.5	131 ± 5.0	130 ± 18.1
	1,000	234 ± 6.8	137 ± 9.8	131 ± 8.7
	3,333	122 ± 18.4	178 ± 8.7	131 ± 9.0
	10,000	118 ± 13.5	130 ± 17.3	131 ± 1.7
TA1535	0	29 ± 0.9	13 ± 0.6	11 ± 1.8
	100	24 ± 3.2	9 ± 1.5	11 ± 2.8
	333	34 ± 2.0	4 ± 0.3	9 ± 1.7
	1,000	26 ± 1.5	8 ± 2.8	13 ± 3.3
	3,333	27 ± 1.2	12 ± 1.7	13 ± 2.0
	10,000	19 ± 3.0	12 ± 3.5	14 ± 1.2
TA1537	0	5 ± 0.7	8 ± 1.0	9 ± 1.8
	100	9 ± 0.9	10 ± 1.5	5 ± 2.1
	333	9 ± 4.2	10 ± 1.5	13 ± 2.1
	1,000	8 ± 2.1	7 ± 1.3	12 ± 1.9
	3,333	10 ± 2.5	13 ± 2.1	16 ± 2.0
	10,000	10 ± 2.3	11 ± 3.4	14 ± 0.3
TA98	0	23 ± 4.9	36 ± 3.3	28 ± 2.0
	100	22 ± 2.7	29 ± 2.7	33 ± 3.8
	333	17 ± 2.0	27 ± 6.2	38 ± 5.5
	1,000	18 ± 0.6	25 ± 5.2	39 ± 2.8
	3,333	20 ± 2.9	34 ± 1.8	43 ± 2.8
	10,000	20 ± 0.3	37 ± 5.3	56 ± 0.3

(a) The S9 fractions were prepared from the livers of Aroclor 1254-induced male Sprague-Dawley rats and male Syrian hamsters. Cells and study compound or solvent (DMSO) were incubated for 20 minutes at 37° C in the presence of either S9 or buffer. After the addition of soft agar, the contents of each tube were poured onto minimal medium, and the plates were incubated at 37° C for 48 hours (Haworth et al., 1983). The experiment was performed twice, each in triplicate; because the results were similar, data from only one experiment are shown.
(b) Mean ± standard error

TABLE G2. MUTAGENICITY OF DECABROMODIPHENYL OXIDE IN L5178Y/TK$^{+/-}$ MOUSE LYMPHOMA CELLS IN THE ABSENCE OF S9 (a)

Compound	Dose (µg/ml)	Total Mutant Clones	Cloning Efficiency (percent)	Relative Total Growth (percent)	Mutation Frequency (mutants/10^6 clonable cells)
DMSO					
		134	98	100	45
		103	105	100	33
		140	115	100	41
		178	100	100	59
Ethyl methanesulfonate					
	15	750	57	32	436
		762	70	36	365
Decabromodiphenyl oxide					
	7	77	89	87	29
		143	90	88	53
	8	97	81	85	40
		180	118	125	51
	9	49	90	86	35
		130	99	93	44
	10	115	97	91	40
		152	104	99	49

(a) Experiments were performed twice, all doses were tested in duplicate, except the solvent control (DMSO), which was tested in triplicate. Because the results were similar, data from only one experiment are shown. The protocol was basically that of Clive et al. (1979). Cells (6×10^5/ml) were treated for 4 hours at 37° C in medium, washed, resuspended in medium, and incubated for 48 hours at 37° C. After expression, 3×10^6 cells were plated in medium supplemented with trifluorothymidine for selection of cells that were mutant at the thymidine kinase (TK) locus, and 600 cells were plated in nonselective medium to determine the percentage of viable cells.

TABLE G3. MUTAGENICITY OF DECABROMODIPHENYL OXIDE IN L5178Y/TK$^{+/-}$ MOUSE LYMPHOMA CELLS IN THE PRESENCE OF S9 (a)

Compound	Dose (μg/ml)	Total Mutant Clones	Cloning Efficiency (percent)	Relative Total Growth (percent)	Mutation Frequency (mutants/10^6 clonable cells)
DMSO					
		117	78	100	50
		90	77	100	39
		90	66	100	45
		87	68	100	43
3-Methylcholanthrene					
	2.5	544	53	35	344
		474	36	31	437
Decabromodiphenyloxide					
	7	75	57	74	44
		91	53	84	57
	8	58	64	84	30
		97	124	158	26
	9	51	55	70	31
		85	60	76	48
	10	114	83	104	46
		94	52	72	61

(a) Experiments were performed twice, all doses were tested in duplicate, except the solvent control (DMSO), which was tested in triplicate. Because the results were similar, data from only one experiment are shown. The protocol was basically that of Clive et al. (1979). Cells (6×10^5/ml) were treated for 4 hours at 37° C in medium, washed, resuspended in medium, and incubated for 48 hours at 37° C. After expression, 3×10^6 cells were plated in medium supplemented with trifluorothymidine for selection of cells that were mutant at the thymidine kinase (TK) locus, and 600 cells were plated in nonselective medium to determine the percentage of viable cells. S9 was prepared from the livers of Aroclor 1254-induced male F344/N rats.

TABLE G4. INDUCTION OF SISTER-CHROMATID EXCHANGES IN CHINESE HAMSTER OVARY CELLS BY DECABROMODIPHENYL OXIDE (a)

−S9 (b)		+S9 (c)	
Dose (µg/ml)	SCE/Cell	Dose (µg/ml)	SCE/Cell
DMSO		DMSO	
10 µl	8.5	10 µl	9.3
Decabromodiphenyl oxide		Decabromodiphenyl oxide	
50	8.1	50	8.6
100	7.9	100	9.3
250	8.1	250	8.4
500	7.6	500	8.8
Mitomycin C		Cyclophosphamide	
0.001	11.1	0.3	12.9
0.010	49.0	2.0	35.6

(a) SCE = sister-chromatid exchange
(b) In the absence of S9, Chinese hamster ovary cells were incubated with study compound or solvent for 2 hours at 37° C. Then BrdU was added, and incubation was continued for 24 hours. Cells were washed, fresh medium containing BrdU (10 µM) and colcemid (0.1 µg/ml) was added, and incubation was continued for 2-3 hours. Cells were then collected by mitotic shake-off, treated for 3 minutes with potassium chloride (75 mM), washed twice with fixative, and dropped onto slides and air dried. Staining was by a modified technique (after Perry and Wolff, 1974; Goto et al., 1978).
(c) In the presence of S9, cells were incubated with study compound or solvent for 2 hours at 37° C. Then cells were washed, and medium containing 10 µM BrdU was added. Cells were incubated for a further 26 hours, with colcemid (0.1 µg/ml) present for the final 2-3 hours. S9 was from the livers of Aroclor 1254-induced male Sprague-Dawley rats.

TABLE G5. INDUCTION OF CHROMOSOMAL ABERRATIONS IN CHINESE HAMSTER OVARY CELLS BY DECABROMODIPHENYL OXIDE (a)

−S9 (b)		+S9 (c)	
Dose (µg/ml)	Abs/100 Cells (percent cells w/abs)	Dose (µg/ml)	Abs/100 Cells (percent cells w/abs)
DMSO		DMSO	
10 µl	1	10 µl	1
Decabromodiphenyl oxide		Decabromodiphenyl oxide	
50	0	50	0
100	0	100	2
250	1	250	0
500	0	500	1
Mitomycin C		Cyclophosphamide	
0.150	16	15.0	28
0.250	22	30.0	40

(a) Abs = aberrations
(b) In the absence of S9, Chinese hamster ovary cells were incubated with study compound or solvent for 8-10 hours at 37° C. Cells were then washed, and fresh medium containing colcemid (0.1 µg/ml) was added. After a further 2-3 hours of incubation, cells were harvested by mitotic shake-off, fixed, and stained in 6% Giemsa.
(c) In the presence of S9, cells were incubated with study compound or solvent for 2 hours at 37° C. Cells were then washed, medium was added, and incubation was continued for 8-10 hours. Colcemid (0.1 µg/ml) was added for the last 2-3 hours of incubation; then cells were harvested and fixed as described in footnote (b). S9 was from the livers of Aroclor 1254-induced male Sprague-Dawley rats.

APPENDIX H

CHEMICAL CHARACTERIZATION OF DECABROMODIPHENYL OXIDE

APPENDIX H. CHEMICAL CHARACTERIZATION

I. Identity and Purity Determinations of Decabromodiphenyl Oxide Performed by the Analytical Chemistry Laboratory

	Determined	Literature Values
A. Lot No. 08287-2		
1. Physical properties		
a. Appearance:	Fine, off-white, microcrystalline powder	
b. Melting point:	298.4°-302.5° C 299.0°-302.0° C (Dupont 900 DTA)	290°-306° C (Norris et al., 1973; Kociba et al., 1975; AIHA, 1981)
2. Spectral data		
a. Infrared		
Instrument:	Beckman IR-12	
Phase:	1% potassium bromide pellet	
Results:	See Figure 5	No literature reference found. Consistent with structure.
b. Ultraviolet/visible		
Instrument:	Cary 118	
Solvent:	*p*-Dioxane	
Results:	There was no absorbance between 800-350 nm.	No literature reference found. Consistent with structure.

λ_{max} (nm)	$\varepsilon \times 10^{-3}$
306 (shoulder)	2.480 ± 0.007
277	5.593 ± 0.033

3. **Water analysis (Karl Fischer):** 0.04% ± 0.01 (δ)%

4. **Elemental analysis**

Element	C	Br
Theory (T)	15.02	83.31
Determined (D)	15.02 15.20	83.39 83.26
Percent D/T	100.60	100.02

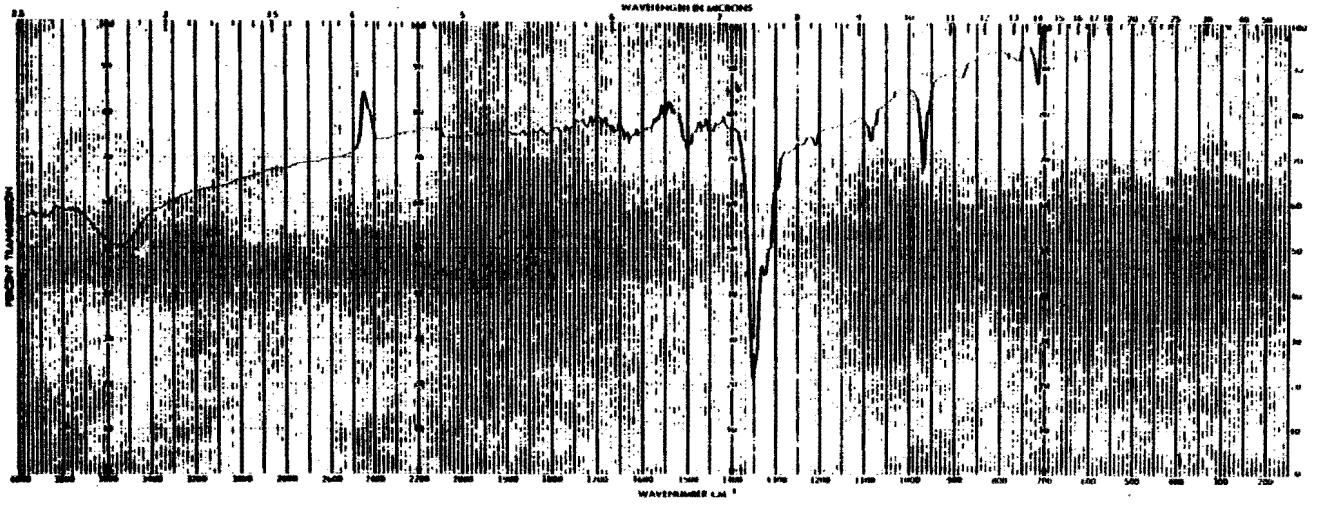


FIGURE 5. INFRARED ABSORPTION SPECTRUM OF DECABROMODIPHENYL OXIDE (LOT NO. 08287-2)

5. **Chromatographic analyses**

   a. **Thin-layer chromatography**

   Plates: System I--Whatman KC_{18} reversed-phase with fluorescent indicator
   System II--Silica Gel 60 F-254
   Reference standard: 2,4,6-Tribromophenol, 40 µg (10 µg/µl in toluene)
   Amount spotted: 100 and 300 µg (10 µg/µl in toluene)
   Visualization: Ultraviolet, 254 nm

   System 1: Methanol (100%)

   R_f: 0.47 (major)
   R_{st}: 0.56

   System 2: Hexane (100%)

   R_f: 0.68 (major)
   R_{st}: 6.48

   b. **High-performance liquid chromatography**

   Instrument: Waters Programmable Component System
   Column: µBondapak C_{18}, 300 mm × 4 mm, ID
   Detector: Ultraviolet, 254 nm
   Flow rate: 1 ml/min
   Sample injected: 10 µl of 0.5 mg/ml in tetrahydrofuran
   Solvent program: Methanol (Fischer HPLC):water (95:5)
   Results: Major peak, one minor peak, and one shoulder on the minor peak

Peak No.	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	9.1	0.76 }	1.31
2	9.8	0.82 }	
3	12.0	1.00	100

Note: Reducing the solvent ratio from 95% methanol to 70% methanol increased the retention time of the major peak to 18 minutes. No additional impurity peaks were detected.

   c. **Gas chromatography:** Gas chromatography was attempted with an SP-2100 column. The compound would not elute even at high isothermal temperatures.

6. **Conclusions:** The results of elemental analysis for carbon and bromine were consistent with the theoretical values. Thin-layer chromatography by two systems indicated a major spot only. High-performance liquid chromatography indicated two impurities before the major peak. The smaller of these impurities was detected as a shoulder on the larger impurity peak. The combined area of the two impurities was 1.3% of the major peak area. The infrared and the ultraviolet/visible spectra were consistent with the structure.

	Determined	Literature values
B. Lot no. D12478		
1. Physical properties		
Appearance:	White, microcrystalline powder	
2. Spectral data		
a. Infrared		
Instrument:	Beckman IR-12	
Phase:	1% in potassium bromide pellet	
Results:	See Figure 6	No literature reference found. Consistent with structure.
b. Ultraviolet/visible		
Instrument:	Cary 118	
Solvent:	1,4-dioxane	
Results:	No maximum from 800 to 350 nm, but a gradual increase in absorbance toward 350 nm.	No literature reference found. Consistent with structure.

λ_{max} (nm)	$\varepsilon \times 10^{-3}$
306	2.314 ± 0.02(δ)
277	5.313 ± 0.09(δ)

3. Water analysis (Karl Fischer): <0.05%

4. Elemental analysis

Element	C	Br
Theory (T)	15.02	83.31
Determined (D)	14.79 14.75	83.55 83.74
Percent D/T	98.34	100.40

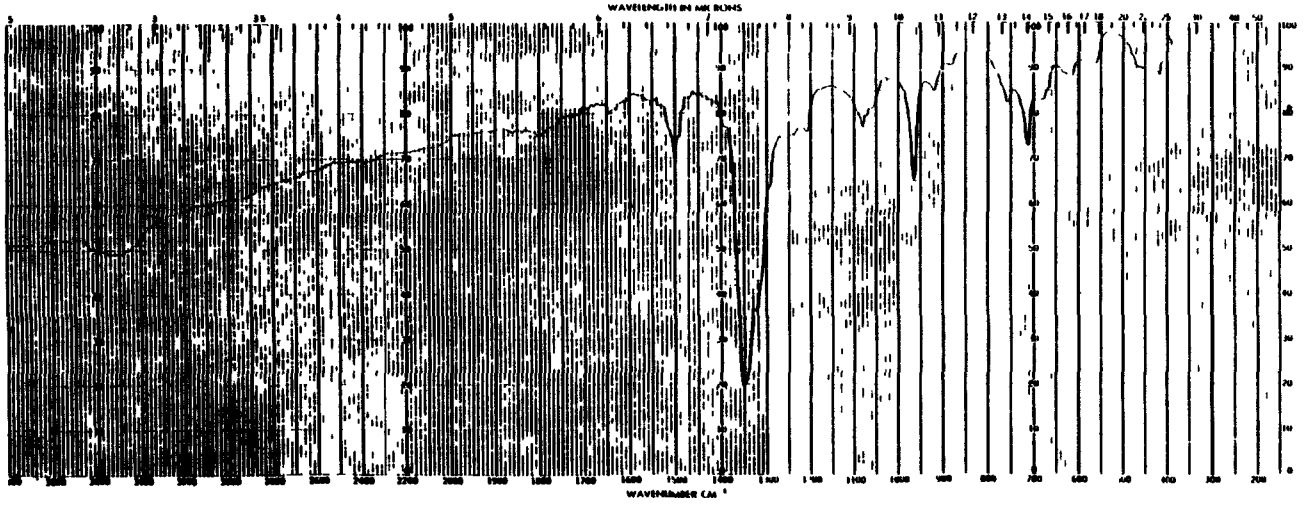


FIGURE 6. INFRARED ABSORPTION SPECTRUM OF DECABROMODIPHENYL OXIDE (LOT NO. D12478)

5. **Chromatographic analysis**

   a. **Thin-layer chromatography**

   Plates: Silica Gel 60 F-254, 0.25 mm layer
   Reference standard: 2,4,6-Tribromophenol (10 mg/ml in toluene)
   Amount spotted: 10 and 30 µg (1 mg/ml in toluene)
   Visualization: Ultraviolet (254 nm)
   Solvent system: Hexane (100%)

   Results

   R_f: 0.35 (major)
   R_{st}: 9.6

   b. **High-performance liquid chromatography (HPLC)**

   Instrument system
   Pump(s): Waters 6000A
   Programmer: Waters 660
   Detector: Waters 440
   Injector: Waters U6K
   Column: µBondapak C_{18}, 300 mm × 3.9 mm, ID
   Detection: Ultraviolet, 254 nm
   Guard column: CO:PELL ODS, 72 mm × 2.3 mm, ID
   Solvent system: Acetonitrile:water (90:10)
   Flow rate: 1 ml/min
   Samples injected: 10 µl solution of 0.4 mg decabromodiphenyl oxide per 1 ml tetrahydrofuran

   Results: Major peak and two impurities before the major peak with relative areas of 1.5% and 1.3%. A system using 100% acetonitrile, isocratic, revealed no additional impurities, and the retention time of the major peak was 7.5 minutes.

Peak No.	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	13.5	0.81	1.5
2	14.5	0.87	1.3
3	16.75	1.00	100

6. **Conclusions:** The result of elemental analysis for bromine was in agreement with the theoretical value, whereas that for carbon was slightly low. Thin-layer chromatography indicated a major spot only. High-performance liquid chromatography indicated two impurities before the major peak with areas totaling 2.8% of the area of the major peak. The two impurities had areas 1.5% and 1.3% of the major peak area. This HPLC analysis compares with two impurities before the major peak with a combined area of 1.3% of the major peak for lot no. 08287-2. The infrared and ultraviolet/visible spectra were consistent with the structure of decabromodiphenyl oxide and with the spectra for lot no. 08287-2.

	Determined	Literature Values
C. Lot no. MM04080-1		
1. Appearance:	White, microcrystalline powder	
2. Spectral data		
a. Infrared		
Instrument:	Beckman IR-12	
Phase:	1% potassium bromide pellet	
Results:	See Figure 7	No literature reference found. Consistent with structure.
b. Ultraviolet/visible		
Instrument:	Cary 118	
Solvent:	*p*-Dioxane	
Results:	There was no absorbance between 800-350 nm at a concentration of 0.13 mg/ml	No literature reference found. Consistent with structure.

λ_{max} (nm)	$\varepsilon \times 10^{-3}$
306	2.46 ± 0.03
(a) 296	2.77 ± 0.02
276	5.57 ± 0.08

(a) Observed in spectrum of lot no. D12478 but not calculated or reported

3. Water analysis (Karl Fischer): <0.1%

4. Elemental analysis

Element	C	Br
Theory (T)	15.02	83.31
Determined (D)	14.52 14.34	82.73 82.79
Percent D/T	96.07	99.34

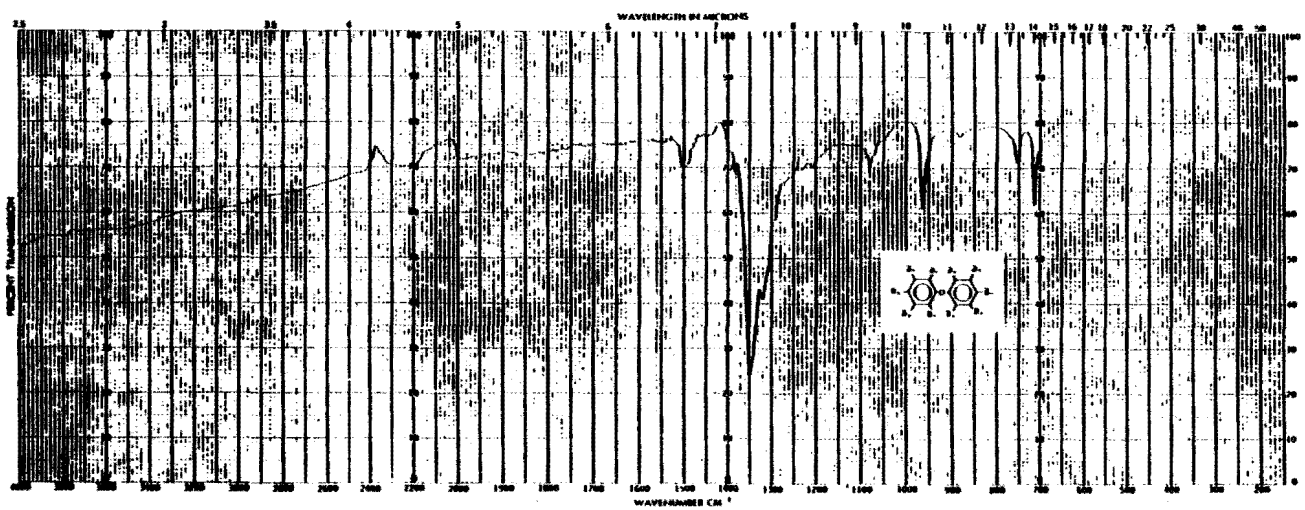


FIGURE 7. INFRARED ABSORPTION SPECTRUM OF DECABROMODIPHENYL OXIDE (LOT NO. MM04080-1)

5. **Chromatographic analyses**

a. **Thin-layer chromatography**

Plates: System I--Silica Gel 60 F-254, 0.25 mm layer; System II--Whatman KC_{18} reversed-phase with fluorescent indicator, 0.25 mm layer
Reference standard: 2,4,6-Tribromophenol, 10 µg (1 µl of a 10 µg/µl solution in toluene)
Amount spotted: 1, 10, and 30 µg (1, 10, and 30 µl of a 1 µg/µl solution in toluene)
Visualization: Ultraviolet, 254 nm

System 1: Hexane (100%)
System 2: Methanol (100%)

Results

Spot Intensity	R_f	R_{st}
System 1		
Major	0.52	5.2
Trace	origin	--
Reference	0.10	--
System 2		
Major	0.21	0.29
Trace	origin	--
Reference	0.72	--

b. **High-performance liquid chromatography**

Instrument system
Pump: Varian 5020 liquid chromatograph
Detector: Waters 440
Injector: Waters U6K
Column: µBondapak C_{18}, 300 mm × 3.9 mm, ID
Guard column: Whatman CO:PELL ODS, 72 × 2.3 mm, ID
Detector: Ultraviolet, 254 nm
Solvent system: Water:acetonitrile (23:77), isocratic
Flow rate: 1 ml/min
Sample injected: 10 µl of 0.5 mg/ml in tetrahydrofuran, filtered

Results: Major peak and three impurities before the major peak with relative areas of 0.23%, 2.0%, and 2.3% that of the major peak. Another impurity before the major peak had a relative area of less than 0.1% that of the major peak. No additional impurities were observed when the sample solution was injected at 100%, 90%, and 80% acetonitrile. A visual comparison of profiles between lot no. D12478 and lot no. MM04080-1 indicated the same impurities in both samples but at lower levels in lot no. D12478.

Peak No.	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	13.1	0.68	0.23
2	14.8	0.76	2.0
3	16.0	0.82	2.3
4	19.4	1.00	100

6. **Conclusions:** The results of the elemental analysis for carbon and bromine were low when compared with the theoretical values. Water content was found to be less than 0.1% by Karl Fischer analysis, compared with less than 0.05% for lot no. D12478. Thin-layer chromatography indicated a major spot and a trace impurity on each of two systems. High-performance liquid chromatography indicated three impurities before the major peak with relative areas that were 0.23%, 2.0%, and 2.3%. One additional impurity before the major peak had a relative area of less than 0.1% that of the major peak. Major peak comparison of lot nos. D12478 and MM04080-1 indicated that lot no. MM04080-1 was 95.2% $\pm$ 1.0(δ)% when normalized to lot no. D12478. The infrared and ultraviolet/visible spectra were consistent with the structure of decabromodiphenyl oxide and with the spectra for lot no. D12478.

	Determined	Literature Values
D. Lot no. MM811102-3-1		
1. Appearance:	White, crystalline powder	
2. Spectral data		
a. Infrared		
Instrument:	Perkin-Elmer 283	
Phase:	2% in potassium bromide pellet	
Results:	See Figure 8	No literature reference found. Consistent with structure.
b. Ultraviolet/visible		
Instrument:	Cary 219	
Solvent:	*p*-Dioxane	
Results:	No absorbance observed from 800 to 350 nm at a concentration of 0.12 mg/ml	No literature reference found; spectra consistent with structure.

λ_{max} (nm)	$\varepsilon \times 10^{-3}$
306	2.46 ± 0.01(δ)
(a) 296 (shoulder)	2.74 ± 0.01(δ)
276 (shoulder)	5.55 ± 0.02(δ)

(a) Observed in spectrum of lot no. D12478 but not calculated or reported

3. Water analysis (Karl Fischer): 0.010% ± 0.001(δ)%

4. Elemental analysis

Element	C	Br
Theory (T)	15.02	83.31
Determined (D)	14.87 14.83	83.30 83.42
Percent D/T	98.87	100.06

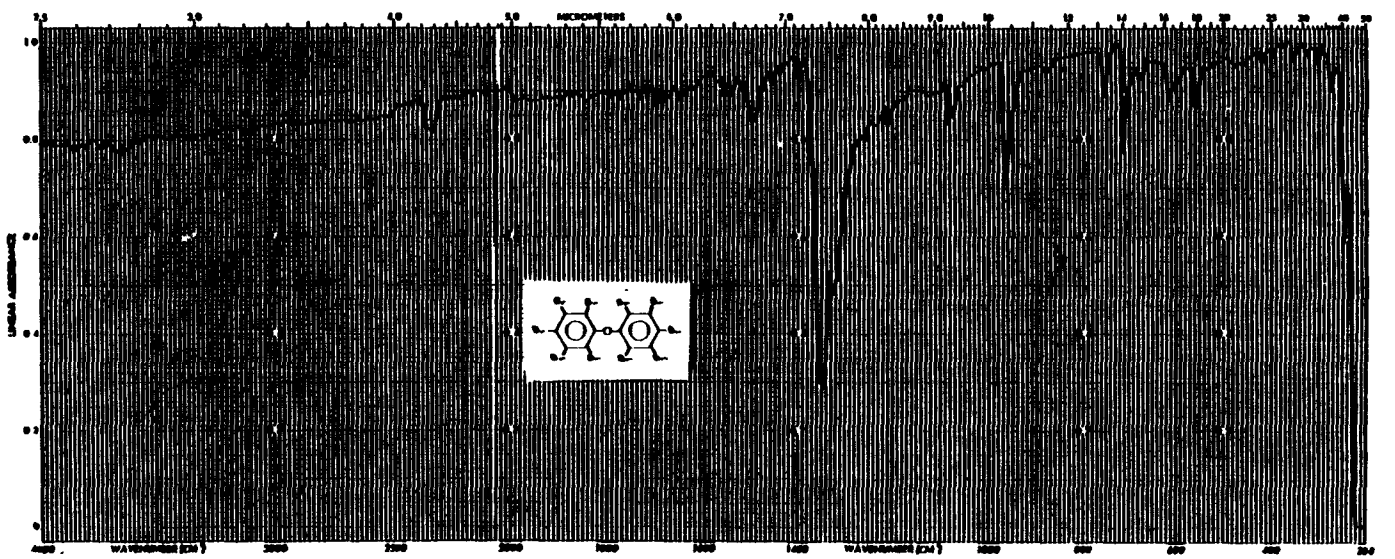


FIGURE 8. INFRARED ABSORPTION SPECTRUM OF DECABROMODIPHENYL OXIDE (LOT NO. MM811102-3-1)

5. **Chromatographic analysis**

a. **Thin-layer chromatography**

Plates: System 1--Silica Gel 60 F-254, 0.25 mm layer; System 2--Whatman KC_{18} reversed-phase with fluorescent indicator, 0.20 mm layer
Reference standard: 2,4,6-Tribromophenol, 10 µg (1 µl of a 10 µg/µl solution in toluene)
Amount spotted: 1, 10, and 30 µg (1, 10, and 30 µl of a 1 µg/µl solution in toluene)
Visualization: Ultraviolet (254 nm)

System 1: Hexanes (100%)
System 2: Methanol (100%)

Results

Spot Intensity	R_f	R_{st}
System 1		
Major	0.39	6.5
Reference	0.06	--
System 2		
Major	0.23	0.32
Minor	origin	--
Reference	0.72	--

b. **High-performance liquid chromatography**

(1) **Impurity profile**

Instrument system
Pump(s): Waters 6000A
Programmer: Waters 660
Detector: Waters 440
Injector: Rheodyne 7125 with 10 µl loop
Column: µBondapak C_{18}, 300 mm × 3.9 mm, ID
Detection: Ultraviolet, 254nm
Guard column: Whatman CO:PELL ODS, 72 mm × 2.3 mm, ID
Solvent system: Water:acetonitrile (12:88), isocratic
Flow rate: 1 ml/min
Samples injected: 0.45 mg/ml decabromodiphenyl oxide in tetrahydrofuran, filtered
Volume injected: 10 µl

Results: Major peak and three impurities before the major peak with relative areas greater than or equal to 0.1% of the major peak area. Two of the impurities had areas 1.3% that of the major peak. A system using 100% and 90% acetonitrile showed no additional peaks.

Peak No.	Retention Time (min)	Retention Time Relative to Major Peak	Area (a) (percent of major peak)
1	15.2	0.70	0.1
2	17.0	0.78	1.3
3	18.4	0.85	1.3
4	21.7	1.00	100

(a) Detector response is very dependent on the absorbance of a substance at the detection wavelength used. The values reported are absolute areas expressed as percentages of the area of the major peak and do not take into account the different molar absorptivity values of the compound and its impurities. Therefore, the areas reported do not necessarily reflect the actual weight percentages of the impurities in the sample.

(2) **Major peak lot comparison:** Lot no. MM811102-3-1 and lot no. D12478 were analyzed for content of decabromodiphenyl oxide by high-performance liquid chromatography. Major peak areas were compared with internal standard peak areas, and the percent of decabromodiphenyl oxide in lot MM811102-3-1 was calculated relative to lot no. D12478. The instrument system described in I.D.5.b.(1) was used with the following changes.

Integrator: Varian CDS111L
Guard column: None
Solvent system: Water:acetonitrile (6:94), isocratic
Samples injected: Accurately weighed solutions containing approximately 0.24 mg/ml of decabromodiphenyl oxide and 8.86×10^{-3} mg/ml of the internal standard, anthracene, in tetrahydrofuran. The solutions were filtered into amber septum vials.
Retention times: Anthracene--4.0 min; decabromodiphenyl oxide--10.5 min

Results

Sample	Percent Decabromodiphenyl Oxide Compared with Lot No. D12478
Lot no. D12478	100.0 ± 0.1(δ)
Lot no. MM811102-3-1	100.5 ± 0.2(δ)

6. **Conclusions:** The results of the elemental analysis for carbon and bromine were consistent with the theoretical values. Water content (Karl Fischer titration) was 0.010% ± 0.001(δ)% compared with less than 0.05% for lot no. D12478. Thin-layer chromatography indicated a major spot and a minor impurity by one system and a major spot only by a second system. High-performance liquid chromatography indicated three impurities with areas totaling 2.7% that of the major peak. The three impurities before the major peak had relative areas of 0.1%, 1.3%, and 1.3% that of the major peak. A similar impurity profile was detected for lot no. D12478: three impurities before the major peak with relative areas of 0.1%, 1.6%, and 1.3% that of the major peak. Major peak comparison of lot no. D12478 and lot no. MM811102-3-1 indicated that lot no. MM811102-3-1 was 100.5% ± 2.0(δ)% pure when normalized to lot no. D12478. The infrared and ultraviolet/visible spectra were consistent with the spectra for lot no. D12478 and with the structure of decabromodiphenyl oxide.

II. Chemical Stability Study Performed by the Analytical Chemistry Laboratory

A. Sample storage: The decabromodiphenyl oxide samples were stored at −20°, 5°, 25°, and 60° C for 2 weeks in glass tubes with Teflon®-lined lids.

B. Analytical method: The high-performance liquid chromatographic system used is described below. The major peak areas of the 5°, 25°, and 60° C samples were compared with the average of the major peak areas for the −20° C sample injections, which served as the standard. Each area was adjusted for the weight of the sample.

Instrument: Waters Programmable Component System
Column: μBondapak C_{18}, 300 × 4 mm, ID
Detector: Ultraviolet, 254 nm
Solvent: Acetonitrile (100%), 1 ml/min
Retention time: 5.9 min

C. Results

Storage Temperature	Percent Purity
−20° C	100.0 ± 0.9
5° C	99.2 ± 0.9
25° C	100.3 ± 0.9
60° C	99.6 ± 0.9

D. Conclusion: Decabromodiphenyl oxide is stable as the bulk chemical for 2 weeks at temperatures up to 60° C.

III. Chemical Stability Study at the Study Laboratory

A. Identity determination by infrared spectroscopy

Instrument: Perkin-Elmer 597
Phase: 1% Potassium bromide pellet

B. Purity determination

1. **Thin-layer chromatography:** Solutions of decabromodiphenyl oxide were prepared and processed simultaneously with an internal standard solution of 2,4,6-tribromophenol.

   Plates: Silica gel 60, F-254 nm, 0.25-mm layer
   Solvent system: 100% Hexane at ambient temperature
   Visualization: Ultraviolet lamp at 254 nm
   Reference standard: 2,4,6-tribromophenol (10 mg/ml in toluene)
   Sample solutions: Decabromodiphenyl oxide (1 mg/ml in toluene)
   Amount spotted: 20 µl of each

2. **High-performance liquid chromatography**

   Instrument: Waters HPLC model 440 with ultraviolet detector at 254 nm
   Column: µBondapak C_{18} (3.9 mm × 300 mm) with CO:PELL ODS guard column
   Mobile phase: Water:acetonitrile (10:90), isocratic, 1.0 ml/min
   Chart speed: 0.5 in/min
   Attenuation: 0.1
   Standard: Solutions of 0.4 mg/ml decabromodiphenyl oxide in tetrahydrofuran
   Injection volume: 10 µl

C. Results

1. **Thin-layer chromatography**

Date of Analysis	Lot No.	Reference R_f	Reference R_{st}	Bulk R_f	Bulk R_{st}
04/02/79	08287-2	0.69	5.31	0.66	6.25
04/13/79	08287-2	0.58	5.80	0.57	5.70
08/13/79	D12478	0.70	7.00	0.70	7.00
12/09/79	D12478	0.60	5.00	0.60	5.00

2. High-performance liquid chromatography

Date of Analysis	Lot No.	Purity (percent) Reference	Bulk
02/11/80	08287-2	97.24	97.09
02/11/80	D12478	97.24	97.28
05/09/80	MM04080-1	97.75	96.67
09/24/80	MM04080-1	96.47	96.47
01/07/81	MM04080-1	95.36	95.34
05/12/81	MM04080-1	95.56	95.65
09/25/81	MM04080-1	95.99	95.56
01/27/82	MM04080-1	96.22	95.60
03/18/82	MM811102-3-1	95.50	97.30
10/18/82	MM811102-3-1	97.75	97.70

High-performance liquid chromatography replaced thin-layer chromatography as the purity analytical method because the purity results obtained from the thin-layer chromatography analyses were not consistent.

D. **Conclusion:** No notable degradation of the test material occurred during the studies.

IV. Isolation and Identification of Impurities in Decabromodiphenyl Oxide

A. Introduction: The purpose of this analysis was to isolate and identify two impurities previously observed in the lot no. MM811102-3-1 of decabromodiphenyl oxide by high-performance liquid chromatography (HPLC). The two impurity peak areas were 1.3% and 1.6% relative to the major peak in the previous HPLC analysis.

The HPLC method developed by the Dow Chemical USA was used without modification for the impurity profile analysis and subsequent isolation of the major impurities in this lot of decabromodiphenyl oxide. These HPLC fractions were then analyzed by direct inlet mass spectrometry to identify the two impurities.

B. High-performance liquid chromatography

1. **Sample preparation:** A solution (approximately 0.5 mg/ml) of decabromodiphenyl oxide was prepared in tetrahydrofuran and filtered for HPLC analysis.

2. **Instrumental system**

Solvent delivery system: Varian 5020 HPLC
Detector: Tracor 970A
Injector: Waters WISP 710B
Electronic integration: Nelson 4400 Data System
Detection: Ultraviolet, 220 nm (254 nm was used in the previous analysis)
Column: Dupont Zorbax ODS, 250 × 4.6 mm ID
Guard column: Whatman CO:PELL ODS, 23 × 3.9 mm ID
Mobile phase: 100% Acetonitrile, 1.2 ml/min
Volume injected: 10 µl
Column temperature: 40° C

3. **Results:** A major peak and three impurity peaks, with areas greater than 0.1% relative to the major peak (Figure 9), were observed. All the impurity peaks eluted before the major peak.

Peak No.	Retention Time (min)	Retention Time (relative to major peak)	Area (a) (percent of major peak)
1	7.7	0.73	0.3
2	8.2	0.78	3.7
3	9.3	0.89	1.7
4	10.5	1.00	100

(a) Detector response is very dependent on the absorbance of a substance at the detection wavelength used. The values reported are absolute areas expressed as percentages of the area of the major peak and do not take into account the different ε values of the compound and its impurities. Therefore, the areas reported do not necessarily reflect the actual weight percentages of the impurities in the sample.

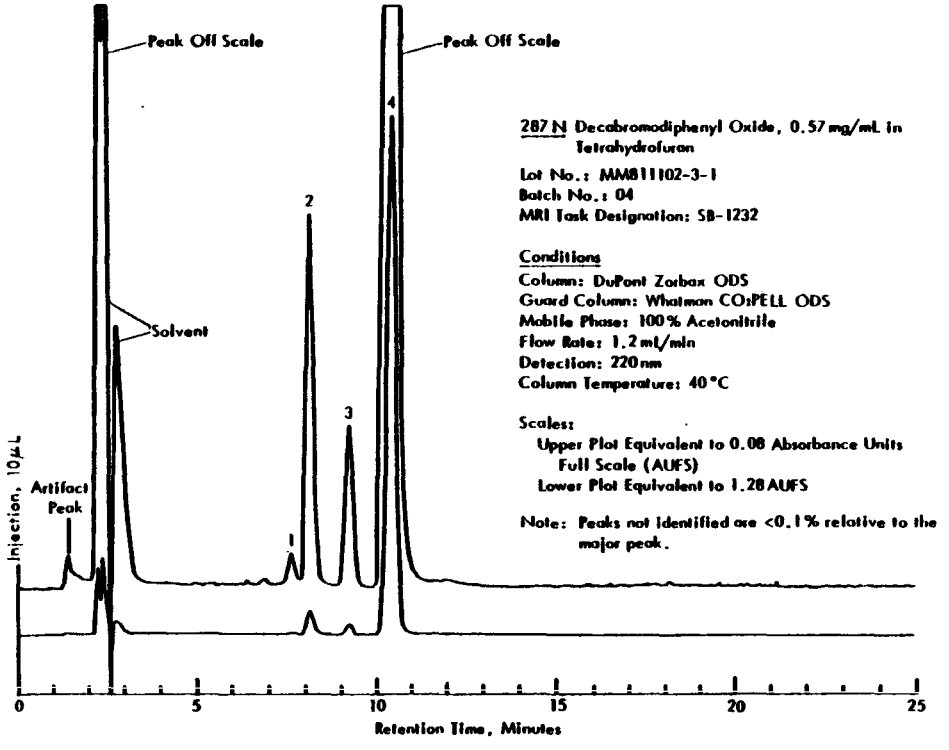


FIGURE 9. HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC PROFILE OF DECABROMODIPHENYL OXIDE (LOT NO. MM811102-3-1)

C. Ultraviolet/visible spectra of the major component and impurities

1. **Sample preparation:** A 2.3 mg/ml solution of decabromodiphenyl oxide was prepared volumetrically in tetrahydrofuran. The solution was filtered for HPLC analysis.

2. **Instrument system:** Ultraviolet/visible spectra of the major peak and the impurity peaks were obtained with a Hewlett-Packard 1040A high-speed spectrophotometric HPLC detector. The HPLC conditions described above were used, with the following exceptions:

   Injector: Rheodyne 7125
   Detector: Hewlett-Packard 1040A
   Monitoring wavelength: 220 nm
   Lamp current: Low
   Scanning range: 190-600 nm
   Scanning step: 2 nm

3. **Results:** The spectra of decabromodiphenyl oxide and its major impurities are presented in Figure 10. The spectra are very similar, indicating that the two impurities are probably compounds that have structures closely related to the major component. The absorbance maxima of the three peaks are also quite near the detection wavelength used in the impurity profile analysis. The relative area percent values reported for the impurities in the impurity profile should therefore closely approximate their actual concentrations in the sample.

D. Isolation of the major component and two impurities

1. **Procedure:** A concentrated solution of decabromodiphenyl oxide was prepared in tetrahydrofuran and repeatedly injected into an HPLC system similar to that used for the impurity profile. The fractions containing the two largest impurities and the major peak were collected as they eluted from the analytical column. The fractions were immersed in a 50° C water bath and evaporated to dryness under a stream of purified nitrogen. The samples were then stored at −20° C before analysis by direct inlet mass spectrometry (Section IV.E.).

2. **Instrument system:** The instrumental parameters described in IV.B.2. were used with the following exceptions:

   Injector: Rheodyne 7125
   Samples injected: Solutions of 6.0 mg/ml decabromodiphenyl oxide in tetrahydrofuran, filtered

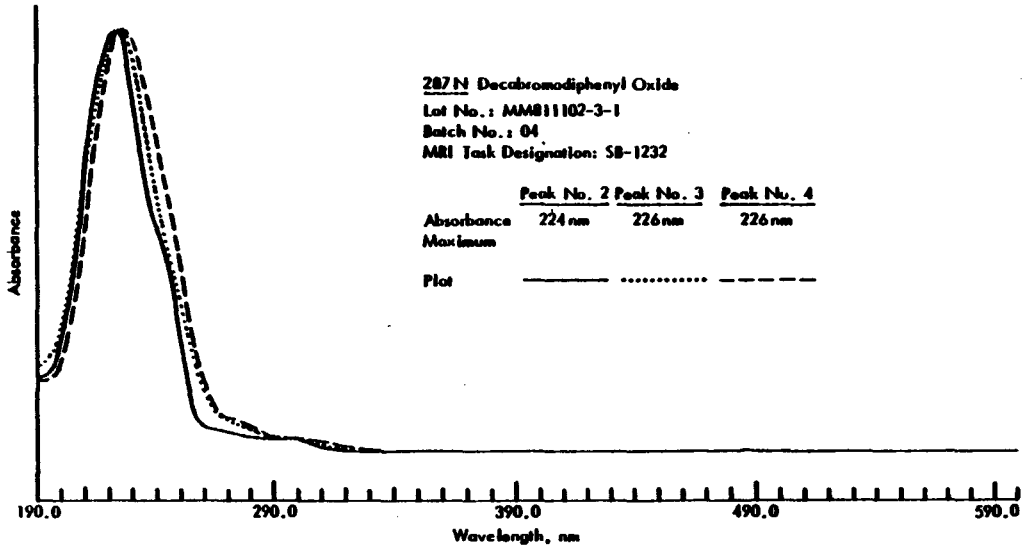


FIGURE 10. ULTRAVIOLET/VISIBLE SPECTRUM OF DECABROMODIPHENYL OXIDE AND TWO MAJOR IMPURITIES

E. Identification of impurities by mass spectrometry

1. **Sample preparation:** The three HPLC fractions were reconstituted in 50 µl of acetonitrile. Aliquots (1-5 µl) of the reconstituted samples were evaporated in a gold cup for direct inlet mass spectrophotometric analysis.

2. **Instrument system**

Instrument: Finnigan MAT 311-A mass spectrometer
Data processor: Incos 2400 Data System
Electron energy: 70 eV
Scan range: 50-1,075 amu
Scan rate: 7.00 sec/scan
Scan times: Up: 5.70 Top: 0.30
Down: 0.00 Bottom: 1.00
Electron multiplier voltage: −1800 V
Emission current: 1 mA
Resolution: 1,000
Accelerator voltage: 3000 V
Sample introduction: Direct inlet probe (gold cup)
Probe temperature program: 30°-450° C in 1,000 sec
Probe temperature at sampling point: Approximately 250° C

3. **Results**

Peak no. 4 (major component of decabromodiphenyl oxide): The mass list is presented in Table H1. The spectrum was found to be consistent with a literature reference mass spectrum of decabromodiphenyl oxide (EPA/NIH, 1980). An abundant molecular ion cluster (m/z 950-m/z 958) was observed with an isotopic ratio consistent with that for a molecule containing 10 bromine atoms. The fragmentation observed indicated several losses of Br and Br_2 from the molecular ion. A mass spectrum of the major component is presented in Figure 11.

Peak no. 2: The mass list obtained from peak no. 2 is presented in Table H2. This impurity was identified from the mass spectrum as an isomer of nonabromodiphenyl oxide ($C_{12}HOBr_9$). A molecular ion was observed at m/z 871 (nominal mass for ^{79}Br, 78.9183, was used for molecular weight calculations). The isotopic ratio for the molecular ion cluster was consistent with the theoretical isotopic pattern for a molecule containing nine bromine atoms. An initial loss of 80 amu (HBr) from the molecular ion was observed. Subsequent losses of 79 (Br) and 159 amu (Br_2) were repeatedly observed, yielding a fragmentation pathway analogous to that observed for the major component. The loss of 28 amu from the m/z 640 ion was observed at m/z 612, indicating the loss of CO which is characteristic of aromatic diphenylethers. A specific isomer of nonabromodiphenyl oxide was not identified. A mass spectrum of the impurity is presented in Figure 12.

TABLE H1. TABULATED MASS SPECTRUM FOR DECABROMODIPHENYL OXIDE (PEAK NO. 4)

Mass	Relative Abundance (percent of base peak)	Mass	Relative Abundance (percent of base peak)
35.32	1.08	302.75	5.23
43.98	2.45	303.78	1.55
60.03	1.53	304.78	2.91
66.02	1.27	305.78	4.09
72.02	1.77	306.75	3.04
78.96	3.05	307.75	1.13
79.97	3.40	308.78	2.87
80.95	3.14	310.78	8.08
81.97	3.27	312.75	8.10
106.97	0.27	314.75	2.51
132.00	5.50	317.75	3.73
138.92	7.49	318.75	8.68
140.92	7.50	319.25	1.25
144.92	1.88	319.75	12.06
145.92	3.34	320.25	1.59
146.94	2.04	320.75	8.71
150.92	4.94	321.75	1.26
152.92	5.00	321.75	3.51
166.92	1.31	343.25	1.04
168.95	2.46	344.25	3.06
186.42	1.53	345.25	5.11
210.94	1.78	346.25	5.12
217.84	6.66	347.25	2.90
219.84	13.29	358.25	1.64
220.86	1.22	358.75	2.04
221.84	6.30	359.22	2.86
224.84	1.24	359.75	3.38
225.84	1.74	360.22	2.98
226.84	1.19	360.75	3.24
229.84	10.14	361.22	1.71
231.84	20.14	361.75	1.89
232.84	1.67	368.78	1.56
233.84	9.87	370.78	4.26
234.86	1.07	372.78	4.28
238.87	1.22	374.75	1.48
239.84	1.22	377.69	1.79
240.87	1.10	379.69	2.68
247.84	1.31	381.69	1.68
265.31	5.94	387.69	1.67
265.81	1.46	389.69	6.24
266.31	6.20	391.69	9.43
267.28	3.33	393.69	6.13
274.75	1.12	395.69	2.54
276.75	1.07	396.69	7.65
289.84	1.74	397.19	1.07
291.84	3.42	397.69	24.93
293.84	1.78	398.19	3.34
296.75	5.67	398.69	49.90
298.78	15.79	399.19	6.66
300.75	15.76	399.69	60.61

TABLE H1. TABULATED MASS SPECTRUM FOR DECABROMODIPHENYL OXIDE (PEAK NO. 4)
(Continued)

Mass	Relative Abundance (percent of base peak)	Mass	Relative Abundance (percent of base peak)
400.19	8.10	715.44	1.14
400.69	47.95	716.44	2.53
401.19	6.41	717.44	3.49
401.69	23.00	718.44	4.64
402.19	3.27	719.44	5.62
402.69	6.57	720.44	4.62
403.69	1.93	721.44	5.63
405.69	4.03	722.44	3.02
407.69	5.61	723.44	3.22
409.69	3.65	724.44	1.15
438.16	1.30	725.44	1.10
439.16	2.09	791.37	1.62
440.16	2.15	793.37	12.50
441.16	1.29	794.37	1.63
454.62	1.59	795.37	41.89
456.62	6.29	796.37	5.64
458.62	11.77	797.37	82.89
460.62	11.47	798.37	11.11
462.62	5.48	799.37	100.00
464.62	1.10	800.37	13.39
470.62	1.20	801.37	78.40
472.62	1.15	802.37	10.69
477.69	1.80	803.37	38.71
479.69	2.64	804.37	4.96
481.69	1.67	805.37	11.29
486.62	1.21	806.37	1.48
488.62	1.38	807.37	1.26
528.62	3.88	875.31	1.02
530.62	8.00	876.31	1.15
531.62	1.02	877.31	2.38
532.62	7.75	878.31	1.89
534.62	3.79	879.31	3.38
558.62	1.61	880.31	1.86
560.62	1.42	881.31	3.55
609.56	1.51	882.31	1.43
611.56	1.71	883.31	2.09
613.56	1.57	951.19	2.54
635.56	4.23	953.25	11.58
637.56	10.68	955.19	31.23
638.56	1.49	957.12	55.13
639.50	14.13	958.25	6.76
640.50	2.14	959.19	60.51
641.50	10.51	960.25	7.80
642.56	1.42	961.25	48.97
643.50	4.22	962.25	6.43
686.44	1.11	963.25	27.66
688.44	3.28	964.25	3.89
690.50	5.03	965.25	10.28
692.50	4.88	966.87	3.65
694.50	3.09		

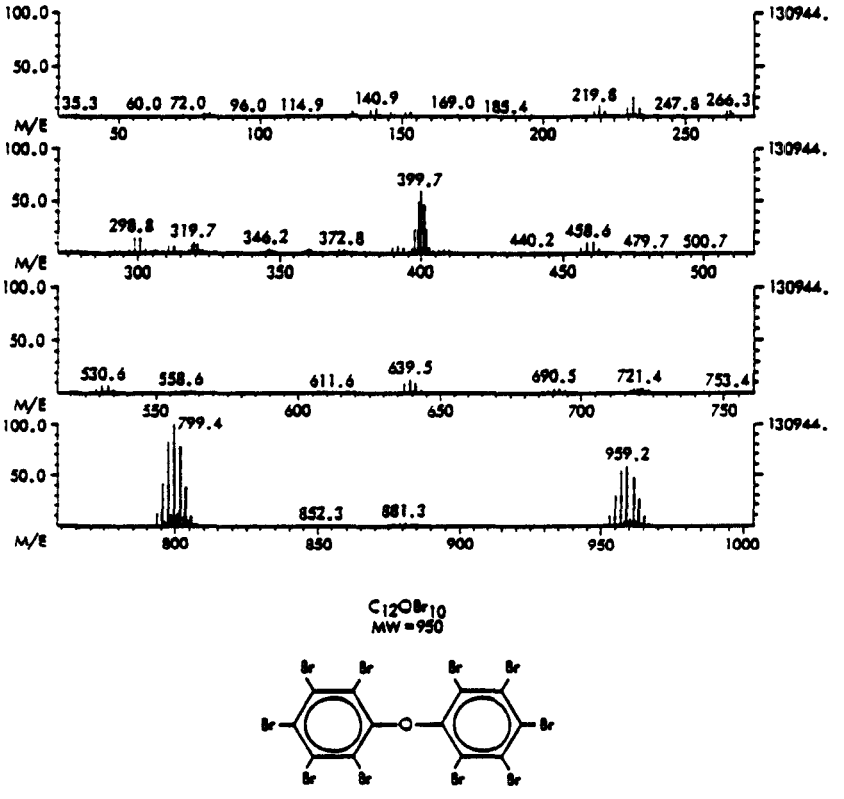


FIGURE 11. MASS SPECTRUM OF DECABROMODIPHENYL OXIDE (PEAK NO. 4)

TABLE H2. TABULATED MASS SPECTRUM FOR NONABROMODIPHENYL OXIDE ISOMER (PEAK NO. 2)

Mass	Relative Abundance (percent of base peak)	Mass	Relative Abundance (percent of base peak)
35.26	1.94	87.09	3.42
35.31	4.05	88.09	1.77
35.36	2.54	89.07	1.86
35.40	6.84	90.96	1.46
35.45	9.07	91.10	1.52
36.88	2.27	92.95	1.52
37.93	7.61	93.11	1.25
38.98	13.20	95.12	3.81
40.00	28.07	96.03	13.34
41.02	61.34	96.12	1.63
42.02	3.84	97.02	15.24
43.01	4.94	97.12	4.43
43.05	4.40	98.09	2.45
43.99	100.00	99.11	1.63
45.00	3.66	100.01	3.10
48.01	4.20	101.05	1.83
49.02	1.62	105.09	1.64
50.02	1.44	105.48	4.04
53.06	1.01	105.99	42.06
54.06	1.54	106.49	9.11
55.07	9.99	109.99	41.59
56.09	3.87	107.10	1.18
57.10	8.28	107.49	4.56
60.04	30.67	108.03	5.88
61.04	20.58	109.02	7.18
62.04	1.34	109.12	1.48
66.02	56.50	109.95	3.30
66.52	34.13	110.11	1.94
67.02	6.41	110.94	1.51
67.07	3.10	111.14	2.33
68.07	1.45	112.13	1.05
69.01	24.22	113.12	1.44
69.08	7.06	114.94	4.06
70.09	3.95	115.09	1.05
71.10	7.13	115.94	1.57
72.02	14.74	116.94	2.87
73.04	21.93	119.02	10.25
74.05	2.63	120.01	6.94
75.05	4.18	121.01	3.50
76.05	1.07	123.13	1.28
77.06	2.83	125.14	1.33
78.97	11.80	127.13	1.35
79.09	1.83	129.09	1.13
79.98	13.51	131.00	3.83
80.55	2.46	132.02	46.42
80.96	11.25	133.03	57.10
81.10	4.59	134.02	8.74
81.98	13.59	135.00	3.40
82.12	2.42	138.94	12.89
83.13	6.00	139.94	11.83
84.05	10.23	140.94	13.45
84.14	1.98	141.94	10.07
85.05	6.39	143.00	1.16
85.15	4.16	144.94	2.90
86.06	1.03	145.44	8.13

TABLE H2. TABULATED MASS SPECTRUM FOR NONABROMODIPHENYL OXIDE ISOMER (PEAK NO. 2)
(Continued)

Mass	Relative Abundance (percent of base peak)	Mass	Relative Abundance (percent of base peak)
145.94	5.91	233.86	8.19
146.44	13.60	234.87	6.35
146.98	21.75	235.02	4.17
147.44	6.43	239.87	1.60
147.95	1.80	240.41	1.45
149.05	1.24	241.91	1.13
150.02	4.56	263.03	1.24
150.94	7.64	264.84	2.17
151.95	20.20	265.84	4.29
152.94	8.50	266.34	1.72
153.95	20.58	266.81	4.25
154.95	2.04	267.81	2.63
161.08	1.28	274.78	1.14
162.94	1.21	276.78	1.21
164.94	1.31	277.84	1.33
166.95	1.19	278.81	5.96
169.00	37.77	279.84	11.41
169.97	1.78	280.34	1.26
178.02	1.92	280.84	12.26
184.98	4.63	281.34	1.60
185.44	1.33	281.81	5.36
185.94	9.19	282.81	1.07
186.44	2.30	285.00	4.63
186.95	9.23	290.87	10.90
187.45	1.05	291.87	2.34
187.95	3.94	292.87	20.73
188.95	1.03	293.87	2.73
189.95	1.39	294.87	9.61
193.91	1.13	295.87	1.03
195.89	1.61	296.78	3.65
198.94	1.57	298.78	11.50
199.94	3.80	299.78	2.93
200.94	3.28	300.78	10.95
210.95	1.51	301.78	3.04
211.95	11.74	302.78	3.41
212.95	5.10	303.78	1.28
213.95	11.74	304.28	1.95
214.95	2.58	305.28	4.25
217.86	6.24	306.28	5.37
218.89	8.93	307.28	3.66
219.86	12.59	308.28	1.69
220.87	15.81	308.78	1.13
221.87	6.39	309.81	2.16
222.87	7.03	310.78	3.46
224.39	1.98	311.78	6.48
225.36	10.68	312.78	4.43
225.87	1.96	313.03	1.15
226.36	14.83	313.78	5.96
226.87	2.39	314.78	1.51
227.36	10.77	315.78	1.89
227.87	1.31	319.28	1.46
228.36	2.02	319.78	1.63
229.86	6.45	320.28	2.51
230.87	5.78	320.81	2.82
231.86	13.81	321.28	2.10
232.87	11.08	321.78	1.12

TABLE H2. TABULATED MASS SPECTRUM FOR NONABROMODIPHENYL OXIDE ISOMER (PEAK NO. 2) (Continued)

Mass	Relative Abundance (percent of base peak)	Mass	Relative Abundance (percent of base peak)
325.78	1.03	532.62	1.05
327.78	4.11	533.69	2.43
329.81	3.59	535.69	1.24
331.78	1.00	557.62	6.59
335.00	5.33	558.62	1.14
357.75	4.66	559.62	13.17
358.75	14.23	560.69	1.55
359.25	1.54	561.62	13.04
359.75	22.37	562.62	1.98
360.25	3.18	563.62	6.09
360.75	22.40	565.62	1.20
361.25	3.51	608.56	2.57
361.75	12.90	610.56	5.91
362.25	1.60	612.56	7.03
362.75	3.91	614.56	5.02
369.84	1.10	616.56	1.80
371.78	4.18	636.56	1.40
372.81	1.83	637.62	1.07
373.78	4.31	638.56	3.98
374.81	1.10	639.56	2.71
375.78	1.54	640.56	5.38
376.75	1.13	641.56	2.55
377.69	1.16	642.56	3.57
378.72	2.80	643.56	2.33
379.72	2.36	644.56	1.39
380.72	4.47	645.56	1.10
381.72	1.19	713.56	1.29
382.72	2.34	715.50	11.56
389.72	2.66	716.44	1.31
391.72	3.67	717.50	33.29
393.72	2.46	718.50	5.10
397.81	1.57	719.50	54.53
399.78	4.23	720.50	7.17
400.78	1.50	721.50	52.80
401.78	4.09	722.50	6.70
403.78	1.75	723.50	29.65
405.72	1.91	724.50	4.06
407.72	2.62	725.50	9.77
409.72	1.69	726.50	1.04
448.72	2.71	727.50	1.31
450.72	11.26	799.44	1.28
451.72	1.56	801.37	1.09
452.72	16.35	803.37	1.00
453.72	2.05	873.37	1.66
454.72	11.63	875.31	6.90
455.72	1.01	876.37	1.00
456.69	4.60	877.37	15.93
458.66	4.82	878.31	1.64
460.62	5.47	879.37	22.61
462.66	2.09	880.37	2.76
464.62	0.56	881.31	21.45
478.75	3.16	882.31	2.96
480.72	5.36	883.31	14.42
481.75	1.13	884.31	1.93
482.72	3.34	885.31	5.76
531.62	2.32	887.37	1.61

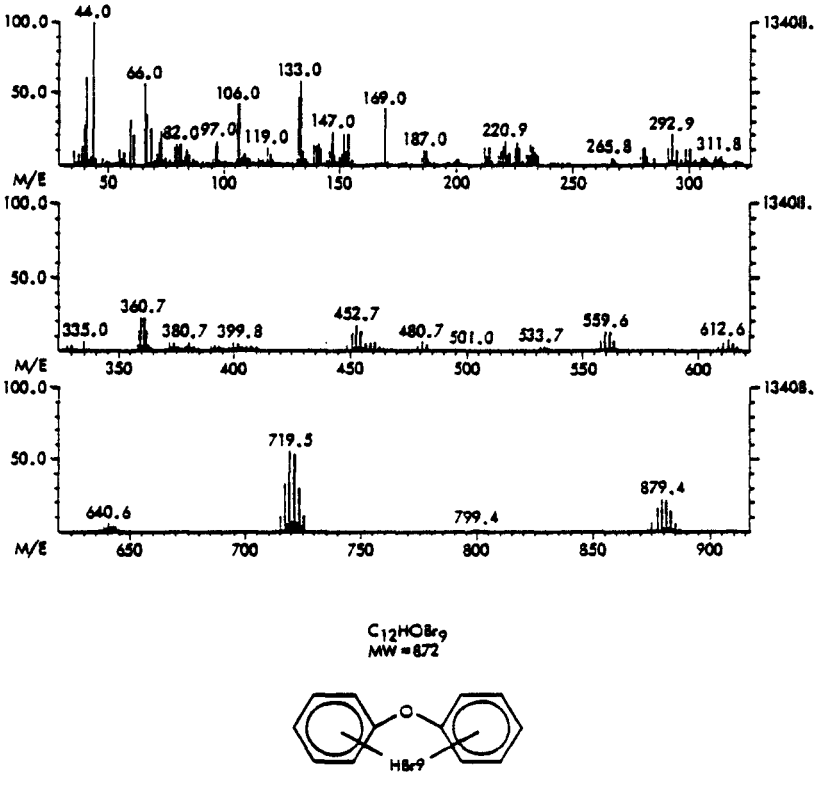


FIGURE 12. MASS SPECTRUM OF NONABROMODIPHENYL OXIDE ISOMER (PEAK NO. 2)

Peak no. 3: The mass list obtained from peak no. 3 is presented in Table H3. This impurity was identified as a second isomer of nonabromodiphenyl oxide ($C_{12}HOBr_9$). The mass spectrum obtained from peak no. 3 resembled the mass spectrum obtained from peak no. 2. A specific isomer on nonabromodiphenyl oxide was not identified. A mass spectrum of this impurity is presented in Figure 13.

4. **Conclusions:** High-performance liquid chromatographic analysis detected two impurities that were estimated at 3.7% and 1.7% relative to the major component by peak area comparison at 220 nm. HPLC analysis with a spectrophotometric detector revealed similar ultraviolet/visible spectra for the major component and the two impurities. These two impurities were isolated by HPLC and identified by direct inlet mass spectrometry as two isomers of nonabromodiphenyl oxide.

TABLE H3. TABULATED MASS SPECTRUM FOR NONABROMODIPHENYL OXIDE ISOMER (PEAK NO. 4)

Mass	Relative Abundance (percent of base peak)	Mass	Relative Abundance (percent of base peak)
35.36	1.09	111.14	1.68
35.41	1.68	113.12	1.13
35.46	1.72	114.95	2.77
38.98	1.44	115.95	2.05
40.00	2.94	116.95	2.28
41.02	7.81	119.04	2.56
43.06	1.54	120.00	4.07
43.99	17.43	120.99	3.67
45.04	1.44	123.95	1.23
55.08	3.15	124.61	1.10
56.10	1.44	125.14	1.29
57.10	4.19	130.95	1.10
60.04	7.19	132.02	18.69
61.04	8.87	133.03	35.43
66.02	25.17	133.95	2.40
66.52	19.82	134.05	4.23
67.03	3.82	134.94	1.46
69.01	3.51	135.08	3.34
69.09	2.73	138.94	8.80
70.09	1.28	139.95	9.87
71.10	3.07	140.94	10.12
72.03	4.53	141.95	8.95
73.04	8.46	144.94	3.43
75.06	2.18	145.44	12.08
77.07	1.28	145.94	7.69
78.97	4.21	146.44	22.65
79.98	7.24	146.97	10.68
80.55	2.99	147.44	10.90
80.97	4.23	147.95	1.95
81.11	2.20	149.05	5.21
81.98	7.23	149.91	1.20
82.12	1.09	150.05	1.29
83.13	2.80	150.25	1.69
84.05	2.93	150.94	8.97
84.14	1.24	151.59	1.62
85.06	2.21	151.95	14.28
85.16	2.06	152.95	6.92
87.09	1.41	153.95	13.58
89.09	2.74	154.95	1.19
95.12	2.05	161.00	1.16
76.04	4.30	164.94	1.22
96.12	1.11	166.97	1.36
97.02	4.52	169.00	9.28
97.13	2.66	177.17	2.30
98.10	1.16	177.95	1.83
99.12	1.04	184.95	6.69
105.09	1.30	185.45	2.08
105.49	4.23	185.95	17.01
106.00	45.74	186.44	4.62
106.49	8.91	186.61	1.25
106.99	45.52	186.95	20.04
107.50	5.84	187.27	1.38
108.03	2.39	187.45	2.89
108.95	1.68	187.95	7.24
109.06	3.50	188.97	1.37
109.95	3.46	189.95	1.37
110.95	1.45	193.91	1.45

TABLE H3. TABULATED MASS SPECTRUM FOR NONABROMODIPHENYL OXIDE ISOMER (PEAK NO. 4) (Continued)

Mass	Relative Abundance (percent of base peak)	Mass	Relative Abundance (percent of base peak)
195.91	1.62	281.34	4.18
196.91	1.75	281.84	15.55
198.94	2.70	282.34	1.82
199.95	5.62	282.84	3.17
200.94	5.93	285.00	1.32
201.95	2.35	290.87	10.97
210.94	1.09	291.87	2.31
211.95	9.87	292.87	22.20
212.95	3.39	293.87	3.20
213.94	10.01	294.87	11.22
214.95	1.75	295.87	1.37
217.86	5.98	296.81	4.97
218.87	9.95	297.81	1.58
219.86	13.38	298.78	13.34
220.87	16.17	299.81	4.54
221.86	7.41	300.78	13.61
222.87	7.51	301.81	4.34
224.37	5.27	302.78	4.32
224.86	1.33	303.78	1.55
225.37	23.01	304.31	6.05
225.87	4.01	304.81	1.02
226.37	34.19	305.28	13.47
226.87	4.89	305.78	1.62
227.37	22.28	306.28	16.96
227.87	3.07	306.78	1.19
228.37	5.23	307.28	12.57
229.86	8.48	307.78	1.30
230.87	4.58	308.28	4.76
231.86	18.16	308.78	2.77
232.87	9.28	309.81	2.22
233.86	9.30	310.78	6.61
234.91	5.91	311.81	6.72
239.28	3.29	312.81	7.60
239.86	4.37	318.81	6.59
240.34	2.73	314.78	2.50
240.52	2.34	315.81	2.16
240.87	1.65	318.31	1.98
241.19	2.02	318.84	1.42
241.39	1.48	319.28	4.33
241.87	2.05	319.78	2.15
263.84	1.07	320.28	5.96
264.84	5.57	320.81	3.87
265.34	1.59	321.28	4.15
265.84	11.98	321.81	2.05
266.34	2.62	322.28	1.70
266.84	11.83	322.81	1.17
267.31	2.29	325.81	1.30
267.84	6.47	327.81	3.56
268.31	1.10	329.81	3.34
268.87	1.62	331.78	1.01
274.78	2.20	335.03	1.45
276.78	1.93	356.78	2.00
277.84	2.97	357.78	15.58
278.84	15.70	358.28	2.12
279.34	2.08	358.78	44.51
279.84	29.26	359.28	5.86
280.34	3.83	359.78	72.53
280.84	28.42	360.28	9.16

TABLE H3. TABULATED MASS SPECTRUM FOR NONABROMODIPHENYL OXIDE ISOMER (PEAK NO. 4) (Continued)

Mass	Relative Abundance (percent of base peak)	Mass	Relative Abundance (percent of base peak)
360.78	69.06	533.69	3.71
361.25	9.09	535.69	2.05
361.78	41.37	555.69	1.59
362.28	5.40	557.69	8.03
362.75	14.00	558.69	1.14
363.28	1.73	559.69	15.53
363.78	1.85	560.69	2.40
369.81	1.51	561.69	15.47
371.81	4.27	562.62	2.10
372.81	1.57	563.69	7.79
373.81	4.60	564.69	1.08
374.81	1.31	565.69	1.62
375.78	2.24	608.62	4.18
376.72	2.21	610.62	9.75
377.72	2.01	611.62	1.44
378.72	7.60	612.62	12.99
379.72	3.21	613.62	1.54
380.72	11.59	614.56	9.71
381.72	2.12	616.56	3.90
382.72	7.32	636.62	2.11
384.72	1.88	637.62	1.21
387.37	1.16	638.62	4.74
389.72	4.49	639.62	2.19
391.72	6.68	640.56	6.88
392.72	1.28	641.62	3.24
393.72	3.82	642.56	5.17
397.78	1.50	643.56	2.61
399.25	1.81	644.62	2.10
399.81	4.78	613.56	3.15
400.22	1.44	715.56	20.74
400.78	1.39	716.50	3.07
401.22	1.31	717.50	60.31
401.81	4.72	718.50	8.17
403.78	2.04	719.50	100.00
405.72	2.67	720.50	12.67
406.75	1.56	721.50	98.65
407.75	3.58	722.50	13.33
408.75	2.01	723.50	57.17
409.72	2.52	724.50	7.65
410.75	1.30	725.50	18.61
448.75	4.07	726.50	2.60
450.75	14.28	727.50	2.11
451.75	1.94	799.44	1.44
452.75	21.38	801.44	1.33
453.75	2.80	873.37	2.62
454.72	14.57	875.37	10.66
455.75	1.95	876.37	1.42
456.69	6.95	877.37	25.62
458.66	6.94	878.37	3.23
460.66	6.57	879.37	36.94
462.62	2.90	880.37	5.11
478.75	3.93	881.37	35.82
480.75	4.83	882.37	4.59
481.75	1.10	883.37	24.10
482.72	3.66	884.37	3.32
484.75	1.08	885.37	9.82
531.69	4.17	886.37	1.44
532.69	1.12	887.37	2.53

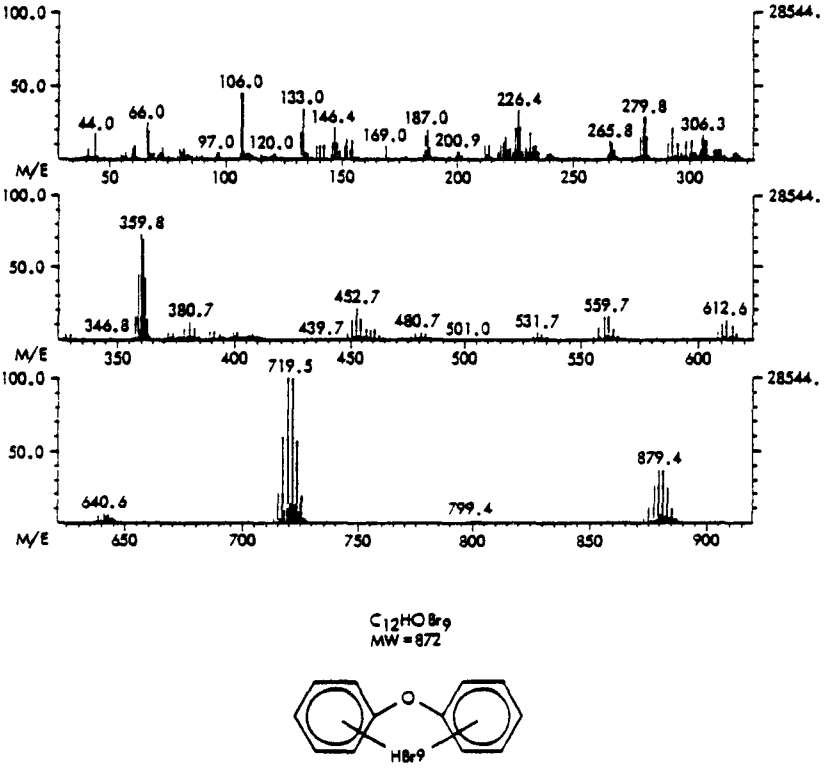


FIGURE 13. MASS SPECTRUM OF NONABROMODIPHENYL OXIDE ISOMER (PEAK NO. 3)

APPENDIX I

PREPARATION AND CHARACTERIZATION OF FORMULATED DIETS

APPENDIX I. PREPARATION AND CHARACTERIZATION

I. Studies Conducted at the Analytical Chemistry Laboratory

A. Preparation procedure

1. **Premix:** Decabromodiphenyl oxide (309.9 ± 0.1 mg) was added directly to 200 g of Wayne Lab Blox® rodent feed. This premix was homogenized by rotation in a 1-quart, large-mouth, glass jar for 15 minutes on a ball-mill-type tumbler apparatus.

2. **Bulk mixing:** The above premix and 1,300 g more feed were mixed in a Patterson-Kelly® twin-shell blender with pin-type intensifier bar for a total of 15 minutes. The blender was loaded from the top of the shells as follows: 650 g of feed was poured in and allowed to settle and level at the bottom (vertex of the "V"); then the dry premix was poured in on top of the feed from each side; this layer was covered with the remaining 650 g of feed poured in from each side. After elapsed mixing times of 10 and 15 minutes, duplicate 5-g samples were removed from the top of each shell and the bottom trap of the blender for subsequent analysis.

3. **Extraction and analysis:** Each sample was placed in a 200-ml centrifuge bottle and triturated with 50 ml of nonstabilized tetrahydrofuran (high-performance liquid chromatography grade) for 30 seconds in a Brinkmann Polytron® high-speed blender. The mixture was placed in an ultrasonic vibratory bath for 2 minutes and centrifuged for 15 minutes. The supernatant solution was pipetted into a 100-ml volumetric flask. The feed residue was mixed with an additional 50 ml of tetrahydrofuran and treated again as described above. The combined supernatant solutions were brought to volume (100 ml) with additional tetrahydrofuran. After filtration through Millipore® (0.5 µ) filters, the sample extract solutions were analyzed by the high-performance liquid chromatographic system described below.

   Instrument: Waters Programmable Component System
   Column: µBondapak C_{18}, 300 mm × 4 mm, ID
   Column temperature: Ambient
   Solvent: 100% Methanol, 1 ml/min
   Detection: Ultraviolet, 254 nm
   Retention time: 6.5 min

4. **Quality control:** Two blank (undosed) feed samples and three individually spiked mixtures (at the 200-ppm concentration) were extracted and prepared for analysis in the manner described above for the test samples. No interference from feed was found at the retention time of decabromodiphenyl oxide in the chromatograms. Chromatographic detector linearity was determined with standard solutions of the study chemical in tetrahydrofuran. A standard curve, from which the decabromodiphenyl oxide content of the test sample extracts was determined, was also constructed from these standard solutions. The stability of the test solutions and the chromatographic system was monitored throughout the analysis by periodic injections of the 11 µg/ml standard solution.

B. Homogeneity

1. Results

Sample Location	Sampling Time (min)	Average Concentration (ppm) Found in Formulated Diet (a,b)
Right	10	229 ± 12
Left	10	245 ± 14
Bottom	10	209 ± 11
Right	15	198 ± 11
Left	15	225 ± 12
Bottom	15	205 ± 11

(a) Corrected for a spiked recovery yield of 88% ± 3(δ)%. The target concentration of chemical in feed was 206.6 ± 0.6 ppm.
(b) Error values are average deviations obtained in the instrumental measurements of the test solutions.

2. **Conclusion:** Decabromodiphenyl oxide mixed with stock rodent feed at the 200-ppm concentration was found more homogenous when mixed for 15 minutes (rather than 10 minutes) in a Patterson-Kelly®, 4-quart, twin-shell blender with a pin-type intensifier bar.

C. Stability

1. **Sample mixing and storage:** A stock solution of decabromodiphenyl oxide in nonstabilized high-performance liquid chromatography grade tetrahydrofuran (0.2418 mg/ml) was prepared, and 5 ml of this solution was added to individual 5-g samples of Wayne Lab-Blox® rodent feed. The tetrahydrofuran was then removed from the samples on a rotary evaporator (30 minutes, 25° C water bath temperature). The dried samples were stored, in duplicate, at −20°, 5°, 25°, and 45° C for 2 weeks.

2. **Extraction and analysis:** Each stability sample was quantitatively transferred to a 200-ml centrifuge bottle and extracted according to the procedure described in section I.A.3. An aliquot (5 ml) of each extract solution was filtered through a 0.5-μ Millipore® filter and then analyzed by the same high-performance liquid chromatographic system described in section I.A.3.

3. **Quality control:** Undosed feed samples and individual samples (at the 200-ppm concentration) were extracted and prepared for analysis in the manner described for the test samples. The blank showed no feed interference.

4. **Results**

Storage Temperature	Average Concentration (ppm) Chemical Found in Formulated Diet (a,b)
−20° C	249 ± 14
5° C	244 ± 14
25° C	242 ± 13
45° C	221 ± 12

(a) Corrected for a spiked recovery yield of 88% ± 3(δ)%. The target concentration of chemical in feed was 242 ± 5 ppm.
(b) Error values are average deviations obtained in the instrumental measurements of the test solutions

5. **Conclusion:** Decabromodiphenyl oxide mixed with stock rodent feed at 240 ppm was found to be stable over a 2-week storage period at temperatures of 25° C and below. Samples stored for 2 weeks at 45° C showed slight but significant loss of major component.

II. Studies Conducted at the Study Laboratory

A. Preparation: Decabromodiphenyl oxide was weighed and mixed with a small amount of feed for 2 minutes. The premix was transferred to a Hobart® mixer with 5 kg of NIH 07 Rat and Mouse Ration and mixed for 1 minute/kg of feed. This mixture was transferred to a Patterson-Kelley® twin-shell blender with the required amount of feed and mixed for 1 min/kg of feed.

B. Homogeneity

A 5-g sample in a 50-ml test tube was extracted with 40 ml of tetrahydrofuran for 10 minutes on a horizontal shaker. The sample was centrifuged at 2,500 rpm for 15 minutes, and the supernatant was transferred to a 125-ml Erlenmeyer flask. The feed residue was extracted again with 40 ml of tetrahydrofuran. The combined extracts were filtered through Whatman #1 filter paper into a 100-ml volumetric flask. The solutions were brought to volume with tetrahydrofuran. Dilutions from 1:2 to 1:10 were made in order to inject 10-µl aliquots into the high-performance liquid chromatograph under the following conditions:

Instrument: Waters Model 6000A high-performance liquid chromatograph with U6K injector linked to a Waters Data Module System
Column: µBondapak C_{18}, 300 mm × 25 mm
Solvent: Water:acetonitrile (90:10), 1 ml/minute
Detection: Waters 440 model, ultraviolet, 254 nm
Retention time: 15.29 min for major peak

All feed samples were analyzed in duplicate, including control feed. Samples were quantitated against a standard of decabromodiphenyl oxide by the Data Module Integration System.

2. **Results**

Sample Location	Target Concentration (ppm)	Determined Concentration (ppm)	Determined Concentration as Percent of Target Concentration (wt/wt)
Top left	25,000	24,600	98.4
Top right	25,000	24,500	98.0
Bottom	25,000	23,800	95.2
Top left	50,000	47,900	95.8
Top right	50,000	51,300	102.6
Bottom	50,000	48,700	97.4

C. **Conclusion:** The homogeneity of both mixes was excellent. All results were within specifications (±10%).

APPENDIX J

METHODS OF ANALYSIS OF FORMULATED DIETS

APPENDIX J. METHODS OF ANALYSIS

I. Study Laboratory

A. Preparation and analysis of dosed feed samples:

A 5-g sample of feed was weighed in duplicate and transferred into 50-ml test tubes containing 40 ml of tetrahydrofuran. The test tubes were shaken on a horizontal shaker for 10 minutes or ultrasonicated for 2 minutes. The samples were centrifuged at 2,500 rpm for 15 minutes, and the supernatant was transferred to a 125-ml Erlenmeyer flask. The feed was reextracted with 40 ml of tetrahydrofuran, shaken, and centrifuged as above. The extracts were combined and filtered through Whatman #1 filter paper into a 100-ml volumetric flask. The samples were diluted to 1:50 or 1:100 for injection.

Instrument parameters

Instrument: Waters Data Module System, equipped with 6000A pump and U6K injector
Detector: Waters Model 440, ultraviolet, 254 nm
Column: Waters μBondapak C_{18}, 300 mm × 3.9 mm
Solvent: 10% water:90% acetonitrile, isocratic, 1 ml/min
Retention time: 14 min for major peak

B. Preparation and analysis of spiked feed samples: Appropriate amounts of decabromodiphenyl oxide were weighed into 5-g aliquots of feed to obtain final concentrations similar to the levels to be analyzed. The spiked feed samples were processed simultaneously with the dosed feed samples.

II. Analytical Chemistry Laboratory

A. Preparation of spiked feed standards: Two standard solutions of decabromodiphenyl oxide were prepared independently in high-performance liquid chromatography (HPLC) grade tetrahydrofuran. These solutions were diluted with tetrahydrofuran to make six standards. Aliquots (100 ml) of the six standard solutions were pipetted into individual 200-ml centrifuge bottles containing 10 g of undosed feed to make spiked feed standards bracketing the specified concentration range of the referee sample. One 200-ml centrifuge bottle containing 10 g of undosed feed was treated with 100 ml of tetrahydrofuran for use as a blank. The spiked feeds and the feed blank were sealed and allowed to stand overnight at room temperature before analysis.

B. Preparation of the referee sample: Triplicate weights of the referee feed sample (~10 g weighed to the nearest 0.01 g) were transferred to individual 200-ml centrifuge bottles. HPLC-grade tetrahydrofuran (100 ml) was pipetted into each sample; then the bottles were sealed and allowed to stand overnight at room temperature before analysis.

C. Analysis: Feed samples (10 g treated with 100 ml of tetrahydrofuran in 200-ml centrifuge bottles) were placed on a Burrell Model 75 Wrist-Action® shaker and were shaken at maximum stroke for 20 minutes. The extraction mixtures were centrifuged for 10 minutes; then 3-ml aliquots of the supernatant solutions were diluted to 50 ml with tetrahydrofuran and thoroughly mixed. The solutions were filtered through a 0.5-μ Millipore® filter, and the decabromodiphenyl oxide content of the filtrate was determined by the high-performance liquid chromatography analysis described below.

Instrument parameters

Instrument: Waters Data Module System, equipped with 6000A pump and U6K injector
Detector: Waters Model 440, ultraviolet, 254 nm, 0.5 AUFS
Column: Waters μBondapak C_{18} (3.9 mm × 300 mm, ID)
Solvent: 100% methanol, 1 ml/min
Volume injected: 15 μl
Retention time: 3.6 min

The amount of decabromodiphenyl oxide in the referee sample was determined from the linear regression equation computed for the standard data, using peak area measurements and the amount of decabromodiphenyl oxide added to the spiked feed standards.

D. **Quality Assurance:** The referee feed sample was analyzed in triplicate, and the undosed feed sample was analyzed once. For calibration, six spiked feed standards bracketing the specified concentration range of the referee sample were made from two independently prepared standard solutions. Triplicate injections of each standard and sample solution were made into the liquid chromatograph in a randomized order.

APPENDIX K

RESULTS OF ANALYSIS OF FORMULATED DIETS

TABLE K1. RESULTS OF ANALYSIS OF FORMULATED DIETS IN THE THIRTEEN-WEEK FEED STUDIES OF DECABROMODIPHENYL OXIDE (a)

Date Mixed	Concentration of Decabromodiphenyl Oxide in Feed (ppm) Target	Determined
02/06/79	3,100	2,850
	3,100	2,850
	3,100	3,140
	6,300	(b) 5,440
	12,500	(b) 14,180
	25,000	(c) 27,590
	50,000	59,800
	50,000	52,490
	50,000	52,000
02/27/79	6,300	(d) 6,890
	6,300	(d) 6,450
	12,500	(d) 12,500
	12,500	(d) 12,500

(a) Results of duplicate analysis
(b) Sample out of specification; remixed.
(c) Sample out of specification; not remixed.
(d) Remix

TABLE K2. RESULTS OF ANALYSIS OF FORMULATED DIETS IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE (a)

Date Mixed	Determined Concentration for Target Concentration of 25,000 ppm	50,000 ppm
07/08/80	24,300	50,000
07/24/80	24,655	51,600
07/31/80		46,050
08/21/80	22,550	
11/06/80	25,000	49,200
12/31/80	23,300	46,800
01/29/81	22,270	46,500
04/02/81	22,750	48,050
10/08/81	26,050	48,050
12/10/81	24,600	50,950
01/28/82	23,150	48,250
03/18/82	24,350	51,300
05/06/82	26,450	53,600
06/24/82	26,000	50,600
08/19/82	22,650	47,950
Experimental mean	24,148	49,207
Standard deviation	1,403	2,206
Coefficent of variation (percent)	5.8	4.5
Range	22,270-26,450	46,050-53,600
Number of samples	14	14

(a) Results of duplicate analysis

TABLE K3. RESULTS OF REFEREE ANALYSIS OF FORMULATED DIETS IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

Date Mixed	Target Concentration (ppm)	Determined Concentration	
		Study Laboratory	Analytical Laboratory
07/24/80	50,000	51,600	49,660
04/02/81	25,000	22,750	25,200
12/10/81	50,000	50,950	51,900
06/24/82	50,000	50,600	50,200
08/19/82	25,000	22,650	25,800

APPENDIX L

SENTINEL ANIMAL PROGRAM

APPENDIX L. SENTINEL ANIMAL PROGRAM

I. 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 viral serology on sera from extra (sentinel) animals in the study rooms. These animals are untreated, and these animals and the study animals are both 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.

Fifteen $B6C3F_1$ mice and 15 F344/N rats of each sex are selected at the time of randomization and allocation of the animals to the various study groups. Five animals of each designated sentinel group are killed at 6, 12, and 18 months on study. Data from animals surviving 24 months are collected from 5/50 randomly selected control animals of each sex and species. The blood from each animal is collected and clotted, and the serum is separated. The serum is cooled on ice and shipped to Microbiological Associates' Comprehensive Animal Diagnostic Service for determination of the viral antibody titers. The following tests are performed:

	Hemagglutination Inhibition	Complement Fixation	ELISA
Mice	PVM (pneumonia virus of mice) Reo 3 (reovirus type 3) GDVII (Theiler's encephalomyelitis virus) Poly (polyoma virus) MVM (minute virus of mice) Ectro (infectious ectromelia) Sendai (6, 12, 18 mo)	M.Ad. (mouse adenovirus) LCM (lymphocytic choriomeningitis virus) MHV (6,12 mo) Sendai (24 mo)	MHV (mouse hepatitis virus) (18, 24 mo)
Rats	PVM KRV (Kilham rat virus) H-1 (Toolan's H-1 virus) Sendai (6, 12, 18 mo)	RCV (rat coronavirus) Sendai (24 mo)	

II. Results

Results are presented in Table L1.

TABLE L1. MURINE VIRUS ANTIBODY DETERMINATIONS FOR RATS AND MICE IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE (a)

	Interval (months)	No. of Animals	Positive Serologic Reaction for
Rats	6	--	None positive
	12	9/10	RCV
	18	2/3	RCV
		5/10	KRV
	24	4/10	Sendai
Mice	6	--	None positive
	12	--	None positive
	18	--	None positive
	24	--	None positive

(a) Blood samples were taken from sentinel animals at 6, 12, and 18 months after the start of dosing and from the control animals just before they were killed; samples were sent to Microbiological Associates, Inc. (Bethesda, MD) for the Animal Disease Screening Program.

APPENDIX M

FEED AND COMPOUND CONSUMPTION BY RATS AND MICE IN THE TWO-YEAR FEED STUDIES OF DECABROMODIPHENYL OXIDE

TABLE M1. FEED AND COMPOUND CONSUMPTION BY MALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

Week	Control		25,000 ppm				50,000 ppm			
	Grams Feed/ Day (a)	Body Weight (grams)	Grams Feed/ Day (a)	Body Weight (grams)	Low/ Control (b)	Dose/ Day (c)	Grams Feed/ Day (a)	Body Weight (grams)	High/ Control (b)	Dose/ Day (c)
1	15	208	18	209	1.2	2,153	16	207	1.1	3,865
2	17	236	17	236	1.0	1,801	17	238	1.0	3,571
3	17	259	18	260	1.1	1,731	18	259	1.1	3,475
4	17	276	18	281	1.1	1,601	19	279	1.1	3,405
5	16	291	17	295	1.1	1,441	17	294	1.1	2,891
6	17	305	17	308	1.0	1,380	17	307	1.0	2,769
7	16	317	19	320	1.2	1,484	17	317	1.1	2,681
8	16	329	19	331	1.2	1,435	17	328	1.1	2,591
9	15	339	16	344	1.1	1,163	16	339	1.1	2,360
10	15	347	16	352	1.1	1,136	16	348	1.1	2,299
11	16	354	16	359	1.0	1,114	16	353	1.0	2,266
12	15	361	16	372	1.1	1,075	16	361	1.1	2,216
17	19	389	18	400	0.9	1,125	18	392	0.9	2,296
21	16	412	17	416	1.1	1,022	18	413	1.1	2,179
25	14	424	15	431	1.1	870	15	422	1.1	1,777
29	17	431	17	440	1.0	966	17	429	1.0	1,981
33	16	438	17	450	1.1	944	18	441	1.1	2,041
37	17	447	18	447	1.1	1,007	18	438	1.1	2,055
41	18	435	18	438	1.0	1,027	20	426	1.1	2,347
45	16	447	18	449	1.1	1,002	17	441	1.1	1,927
49	15	444	16	443	1.1	903	17	441	1.1	1,927
53	15	452	16	456	1.1	877	17	448	1.1	1,897
57	15	449	16	451	1.1	887	16	444	1.1	1,802
61	17	452	18	453	1.1	993	16	445	0.9	1,798
65	16	456	18	449	1.1	1,002	18	452	1.1	1,991
69	12	449	17	440	1.4	966	18	443	1.5	2,032
73	15	452	15	449	1.0	835	16	448	1.1	1,786
77	14	449	16	449	1.1	891	17	451	1.2	1,885
81	14	449	19	442	1.4	1,075	15	441	1.1	1,701
85	16	445	16	440	1.0	909	15	434	0.9	1,728
89	13	436	15	436	1.2	860	15	429	1.2	1,748
93	12	423	17	430	1.4	988	16	419	1.3	1,909
97	12	413	13	412	1.1	789	13	408	1.1	1,593
101	14	413	15	400	1.1	938	16	395	1.1	2,025
103	13	404	16	396	1.2	1,010	16	395	1.2	2,025
104	13	402	14	397	1.1	882	13	389	1.0	1,671
Mean	15.3	390	16.7	391	1.1	1,119	16.6	387	1.1	2,236
SD (d)	1.7		1.4		0.1	311	1.4		0.1	575
CV (e)	11.1		8.4		9.1	27.8	8.4		9.1	25.7

(a) Grams of feed removed from feed hopper per animal per day. Not corrected for scatter.
(b) Grams of feed per day for the dosed group divided by that for the controls
(c) Estimated milligrams of decabromodiphenyl oxide consumed per day per kilogram of body weight
(d) Standard deviation
(e) Coefficient of variation = (standard deviation/mean) × 100

TABLE M2. FEED AND COMPOUND CONSUMPTION BY FEMALE RATS IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

	Control		25,000 ppm				50,000 ppm			
Week	Grams Feed/ Day (a)	Body Weight (grams)	Grams Feed/ Day (a)	Body Weight (grams)	Low/ Control (b)	Dose/ Day (c)	Grams Feed/ Day (a)	Body Weight (grams)	High/ Control (b)	Dose/ Day (c)
1	10	139	11	139	1.1	1,978	11	138	1.1	3,986
2	11	150	11	151	1.0	1,821	11	150	1.0	3,667
3	10	159	11	159	1.1	1,730	11	157	1.1	3,503
4	11	168	13	169	1.2	1,923	14	167	1.3	4,192
5	10	173	10	174	1.0	1,437	11	173	1.1	3,179
6	10	179	11	182	1.1	1,511	12	177	1.2	3,390
7	10	185	11	186	1.1	1,478	11	184	1.1	2,989
8	10	191	10	191	1.0	1,309	11	188	1.1	2,926
9	10	195	10	196	1.0	1,276	10	192	1.0	2,604
10	10	199	10	198	1.0	1,263	11	198	1.1	2,778
11	11	202	10	199	0.9	1,256	11	198	1.0	2,778
12	9	204	10	205	1.1	1,220	11	203	1.2	2,709
17	10	217	10	214	1.0	1,168	10	209	1.0	2,392
21	10	223	10	219	1.0	1,142	11	217	1.1	2,535
25	9	228	10	227	1.1	1,101	10	223	1.1	2,242
29	11	233	10	229	0.9	1,092	11	227	1.0	2,423
33	10	238	10	234	1.0	1,068	11	234	1.1	2,350
37	11	244	12	240	1.1	1,250	12	239	1.1	2,510
41	11	246	11	240	1.0	1,146	12	240	1.1	2,500
45	11	252	12	251	1.1	1,195	12	247	1.1	2,429
49	12	256	12	255	1.0	1,176	12	254	1.0	2,362
53	12	269	12	268	1.0	1,119	13	268	1.1	2,425
57	12	278	12	276	1.0	1,087	12	272	1.0	2,206
61	12	288	15	286	1.3	1,311	13	283	1.1	2,297
65	13	299	12	297	0.9	1,010	13	294	1.0	2,211
69	12	307	12	303	1.0	990	13	297	1.1	2,189
73	12	315	12	315	1.0	952	13	309	1.1	2,104
77	13	327	12	324	0.9	926	13	314	1.0	2,070
81	12	331	12	327	1.0	917	13	324	1.1	2,006
85	12	337	13	332	1.1	979	13	327	1.1	1,988
89	11	341	12	335	1.1	896	13	329	1.2	1,976
93	11	338	11	334	1.0	823	13	322	1.2	2,019
97	11	338	12	330	1.1	909	12	319	1.1	1,881
101	12	333	11	328	0.9	838	13	318	1.1	2,044
103	11	329	13	334	1.2	973	14	322	1.3	2,174
104	9	333	12	336	1.3	893	12	320	1.3	1,875
Mean	10.9	251	11.3	250	1.0	1,199	11.9	245	1.1	2,553
SD (d)	1.1		1.2		0.1	296	1.1		0.1	588
CV (e)	10.1		10.6		10.0	24.7	9.2		9.1	23.0

(a) Grams of feed removed from feed hopper per animal per day. Not corrected for scatter.
(b) Grams of feed per day for the dosed group divided by that for the controls
(c) Estimated milligrams of decabromodiphenyl oxide consumed per day per kilogram of body weight
(d) Standard deviation
(e) Coefficient of variation = (standard deviation/mean) × 100

TABLE M3. FEED AND COMPOUND CONSUMPTION BY MALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

Week	Control		25,000 ppm				50,000 ppm			
	Grams Feed/ Day (a)	Body Weight (grams)	Grams Feed/ Day (a)	Body Weight (grams)	Low/ Control (b)	Dose/ Day (c)	Grams Feed/ Day (a)	Body Weight (grams)	High/ Control (b)	Dose/ Day (c)
1	4	29.4	5	27.9	1.3	4,480	5	29.3	1.3	8,532
2	4	30.6	4	29.7	1.0	3,367	4	29.7	1.0	6,734
3	4	30.9	5	30.2	1.3	4,139	5	30.6	1.3	8,170
4	4	32.0	5	31.6	1.3	3,956	4	32.1	1.0	6,231
5	5	31.8	4	31.5	0.8	3,175	5	31.5	1.0	7,937
6	4	33.2	4	32.3	1.0	3,096	4	31.6	1.0	6,329
7	4	34.0	5	33.3	1.3	3,754	4	33.4	1.0	5,988
8	4	34.8	2	33.6	0.5	1,488	4	34.1	1.0	5,865
9	4	34.7	4	35.1	1.0	2,849	4	34.0	1.0	5,882
10	5	35.4	5	34.1	1.0	3,666	5	34.2	1.0	7,310
11	4	35.2	4	34.5	1.0	2,899	5	34.7	1.3	7,205
12	4	35.6	4	35.2	1.0	2,841	5	35.1	1.3	7,123
16	4	36.5	4	36.5	1.0	2,740	4	35.9	1.0	5,571
20	4	36.9	4	36.4	1.0	2,747	4	35.9	1.0	5,571
24	5	37.0	5	36.4	1.0	3,434	5	36.2	1.0	6,906
28	5	38.5	5	38.4	1.0	3,255	5	37.3	1.0	6,702
32	5	39.9	5	40.1	1.0	3,117	5	39.0	1.0	6,410
36	4	39.0	4	41.0	1.0	2,439	5	40.0	1.3	6,250
40	6	40.4	4	41.1	0.7	2,433	5	39.6	0.8	6,313
42	5	41.0	5	41.0	1.0	3,049	5	40.0	1.0	6,250
44	5	40.2	5	41.7	1.0	2,998	5	40.8	1.0	6,127
46	5	41.5	4	41.7	0.8	2,398	6	40.8	1.2	7,353
48	6	41.0	4	43.0	0.7	2,326	5	42.0	0.8	5,952
50	5	40.0	4	41.0	0.8	2,439	5	41.0	1.0	6,098
52	4	39.6	5	41.1	1.3	3,041	5	41.1	1.3	6,083
54	6	41.2	4	41.3	0.7	2,421	5	39.8	0.8	6,281
56	5	40.0	5	41.4	1.0	3,019	4	40.4	0.8	4,950
58	5	40.1	6	41.5	1.2	3,614	4	41.5	0.8	4,819
60	5	40.7	5	42.1	1.0	2,969	4	41.2	0.8	4,854
62	5	40.1	4	41.3	0.8	2,421	5	41.1	1.0	6,083
64	4	40.9	4	41.6	1.0	2,404	4	41.1	1.0	4,866
66	5	40.0	6	39.0	1.2	3,846	5	40.0	1.0	6,250
68	5	40.0	6	39.7	1.2	3,778	6	39.6	1.2	7,576
70	5	39.0	6	39.0	1.2	3,846	6	39.0	1.2	7,692
72	6	38.6	7	39.9	1.2	4,386	6	38.8	1.0	7,732
74	7	39.3	6	39.7	0.9	3,778	6	39.3	0.9	7,634
76	6	38.3	6	39.5	1.0	3,797	6	38.9	1.0	7,712
80	6	40.0	6	39.0	1.0	3,846	6	39.0	1.0	7,692
84	6	39.0	6	39.0	1.0	3,846	6	38.0	1.0	7,895
88	5	39.1	5	38.8	1.0	3,222	5	39.5	1.0	6,329
92	5	40.0	6	40.0	1.2	3,750	5	39.0	1.0	6,410
96	5	40.0	5	39.0	1.0	3,205	5	38.0	1.0	6,579
100	5	38.0	5	38.0	1.0	3,289	6	37.0	1.2	8,108
102	5	37.0	5	38.0	1.0	3,289	5	37.0	1.0	6,757
103	9	37.0	5	38.0	0.6	3,289	6	38.0	0.7	7,895
Mean	5.0	37.7	4.8	37.8	1.0	3,203	5.0	37.5	1.0	6,645
SD (d)	1.0		0.9		0.2	625	0.7		0.1	955
CV (e)	20.0		18.8		20.0	19.5	14.0		10.0	14.4

(a) Grams of feed removed from feed hopper per animal per day. Not corrected for scatter.
(b) Grams of feed per day for the dosed group divided by that for the controls
(c) Estimated milligrams of decabromodiphenyl oxide consumed per day per kilogram of body weight
(d) Standard deviation
(e) Coefficient of variation = (standard deviation/mean) × 100

TABLE M4. FEED AND COMPOUND CONSUMPTION BY FEMALE MICE IN THE TWO-YEAR FEED STUDY OF DECABROMODIPHENYL OXIDE

Week	Control		125 ppm				500 ppm			
	Grams Feed/ Day (a)	Body Weight (grams)	Grams Feed/ Day (a)	Body Weight (grams)	Low/ Control (b)	Dose/ Day (c)	Grams Feed/ Day (a)	Body Weight (grams)	High/ Control (b)	Dose/ Day (c)
1	6	21.7	6	21.7	1.0	6,912	6	21.6	1.0	13,889
2	6	22.7	5	22.5	0.8	5,556	5	22.6	0.8	11,062
3	6	23.4	5	23.1	0.8	5,411	5	22.7	0.8	11,013
4	5	23.8	5	24.0	1.0	5,208	5	23.7	1.0	10,549
5	6	24.2	5	24.4	0.8	5,123	5	24.0	0.8	10,417
6	5	25.1	5	24.9	1.0	5,020	5	24.5	1.0	10,204
7	6	25.9	5	25.8	0.8	4,845	6	24.7	1.0	12,146
8	5	25.7	6	25.9	1.2	5,792	6	25.2	1.2	11,905
9	5	26.5	5	26.6	1.0	4,699	5	26.0	1.0	9,615
10	5	27.7	5	27.0	1.0	4,630	5	26.7	1.0	9,363
11	6	27.3	5	27.2	0.8	4,596	5	26.7	0.8	9,363
12	5	28.1	5	27.4	1.0	4,562	5	27.0	1.0	9,259
16	5	28.9	5	28.4	1.0	4,401	5	28.6	1.0	8,741
20	5	30.1	5	30.4	1.0	4,112	5	30.5	1.0	8,197
24	6	30.3	5	30.7	0.8	4,072	5	30.9	0.8	8,091
28	5	32.7	5	32.5	1.0	3,846	5	32.8	1.0	7,622
32	5	34.6	5	34.8	1.0	3,592	5	34.9	1.0	7,163
36	6	36.0	5	37.0	0.8	3,378	6	37.0	1.0	8,108
40	5	35.7	5	37.6	1.0	3,324	5	37.7	1.0	6,631
42	5	38.0	5	36.0	1.0	3,472	5	39.0	1.0	6,410
44	5	37.5	5	38.0	1.0	3,289	4	39.9	0.8	5,013
46	5	38.9	5	39.0	1.0	3,205	5	39.0	1.0	6,410
48	5	38.0	5	39.0	1.0	3,205	5	40.0	1.0	6,250
50	5	38.0	5	39.0	1.0	3,205	5	38.0	1.0	6,579
52	5	38.9	4	40.3	0.8	2,481	5	37.9	1.0	6,596
54	5	39.4	5	40.4	1.0	3,094	5	39.4	1.0	6,345
56	5	39.7	5	39.9	1.0	3,133	5	40.1	1.0	6,234
58	5	40.4	5	39.9	1.0	3,133	5	40.1	1.0	6,234
62	5	40.7	4	40.2	0.8	2,488	4	40.4	0.8	4,950
64	5	40.1	4	40.7	0.8	2,457	5	39.6	1.0	6,313
66	5	39.0	4	41.0	0.8	2,439	5	40.0	1.0	6,250
72	5	39.2	5	40.7	1.0	3,071	5	38.3	1.0	6,527
74	5	39.0	5	40.9	1.0	3,056	5	38.7	1.0	6,460
76	5	39.3	5	40.8	1.0	3,064	6	38.5	1.2	7,792
80	5	41.0	5	41.0	1.0	3,049	5	39.0	1.0	6,410
84	5	41.0	5	42.0	1.0	2,976	4	40.0	0.8	5,000
88	5	42.6	4	42.7	0.8	2,342	5	40.9	1.0	6,112
92	4	41.0	4	43.0	1.0	2,326	5	40.0	1.3	6,250
96	6	41.0	5	44.1	0.8	2,834	5	41.0	0.8	6,098
100	7	40.0	8	42.0	1.1	4,762	5	38.0	0.7	6,579
102	6	42.0	5	43.0	0.8	2,907	5	43.0	0.8	5,814
103	7	41.0	6	43.0	0.9	3,488	7	43.0	1.0	8,140
Mean	5.3	34.6	5.0	35.1	0.9	3,758	5.1	34.5	1.0	7,776
SD (d)	0.6		0.7		0.1	1,088	0.5		0.1	2,145
CV (e)	11.3		14.0		11.1	29.0	9.8		10.0	27.6

(a) Grams of feed removed from feed hopper per animal per day. Not corrected for scatter.
(b) Grams of feed per day for the dosed group divided by that for the controls
(c) Estimated milligrams of decabromodiphenyl oxide consumed per day per kilogram of body weight
(d) Standard deviation
(e) Coefficient of variation = (standard deviation/mean) × 100

APPENDIX N

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

Meal Diet: June 1980 to July 1982

(Manufactured by Zeigler Bros., Inc., Gardners, PA)

TABLE N1. 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
Brewer's dried 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) NIH, 1978; NCI, 1976
(b) Ingredients should be ground to pass through a U.S. Standard Screen No. 16 before being mixed.

TABLE N2. 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
d-α-Tocopheryl acetate	20,000 IU	
Riboflavin	3.4 g	
Thiamine	10.0 g	Thiamine mononitrate
Niacin	30.0 g	
d-Pantothenic acid	18.0 g	*d*-Calcium pantothenate
Folic acid	2.2 g	
Pyridoxine	1.7 g	Pyridoxine hydrochloride
B_{12}	4,000.0 mcg	
Biotin	140.0 mg	*d*-Biotin
K_3	2.8 g	Menadione activity
Choline	560.0 g	Choline chloride
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 N3. NUTRIENT COMPOSITION OF NIH 07 RAT AND MOUSE RATION (a)

Nutrient	Mean ± Standard Deviation	Range	Number of Samples
Crude protein (percent by weight)	24.20 ± 1.00	22.6-26.3	24
Crude fat (percent by weight)	5.02 ± 0.46	4.2-6.0	24
Crude fiber (percent by weight)	3.48 ± 0.41	2.4-4.3	24
Ash (percent by weight)	6.66 ± 0.41	5.97-7.42	24
Essential amino acids (percent of total diet)			
Arginine	1.260	1.21-1.31	2
Cystine	0.395	0.39-0.40	2
Glycine	1.175	1.15-1.20	2
Histidine	0.553	0.530-0.576	2
Isoleucine	0.908	0.881-0.934	2
Leucine	1.905	1.85-1.96	2
Lysine	1.250	1.20-1.30	2
Methionine	0.310	0.306-0.314	2
Phenylalanine	0.967	0.960-0.974	2
Threonine	0.834	0.827-0.840	2
Tryptophan	0.175	0.171-0.178	2
Tyrosine	0.587	0.566-0.607	2
Valine	1.085	1.05-1.12	2
Essential fatty acids (percent of total diet)			
Linoleic	2.37		1
Linolenic	0.308		1
Arachidonic	0.008		1
Vitamins			
Vitamin A (IU/kg)	11,087 ± 1,723	7,200-17,000	24
Vitamin D (IU/kg)	6,300		1
α-Tocopherol (ppm)	37.6	31.1-44.0	2
Thiamine (ppm)	18.8 ± 0.36	7.4-26.0	(b) 23
Riboflavin (ppm)	6.9	6.1-7.4	2
Niacin (ppm)	75	65-85	2
Pantothenic acid (ppm)	30.2	29.8-30.5	2
Pyridoxine (ppm)	7.2	5.6-8.8	2
Folic acid (ppm)	2.1	1.8-2.4	2
Biotin (ppm)	0.24	0.21-0.27	2
Vitamin B_{12} (ppb)	12.8	10.6-15.0	2
Choline (ppm)	3,315	3,200-3,430	2
Minerals			
Calcium (percent)	1.27 ± 0.19	0.81-1.6	24
Phosphorus (percent)	1.00 ± 0.08	0.84-1.10	24
Potassium (percent)	0.809	0.772-0.846	2
Chloride (percent)	0.557	0.479-0.635	2
Sodium (percent)	0.304	0.258-0.349	2
Magnesium (percent)	0.172	0.166-0.177	2
Sulfur (percent)	0.278	0.270-0.285	2
Iron (ppm)	418	409-426	2
Manganese (ppm)	90.8	86.0-95.5	2
Zinc (ppm)	55.1	54.2-56.0	2
Copper (ppm)	12.68	9.65-15.70	2
Iodine (ppm)	2.58	1.52-3.64	2
Chromium (ppm)	1.86	1.79-1.93	2
Cobalt (ppm)	0.57	0.49-0.65	2

(a) One or two batches of feed analyzed were manufactured in January and/or April 1983.
(b) One batch (7/22/81) not analyzed for thiamine.

TABLE N4. CONTAMINANT LEVELS IN NIH 07 RAT AND MOUSE RATION

Contaminant	Mean ± Standard Deviation	Range	Number of Samples
Arsenic (ppm)	0.39 ± 0.17	0.13-0.93	24
Cadmium (ppm) (a)	<0.1		24
Lead (ppm)	1.09 ± 0.72	0.33-2.93	24
Mercury (ppm) (a)	<0.05		
Selenium (ppm)	0.30 ± 0.07	0.16-0.48	24
Aflatoxins (ppb) (a, b)	<10		24
Nitrate nitrogen (ppm) (c)	8.50 ± 4.39	0.6-18.0	24
Nitrite nitrogen (ppm) (c)	2.05 ± 1.28	0.4-5.3	24
BHA (ppm) (d, e)	3.68 ± 2.71	0.4-11.0	24
BHT (ppm) (d)	2.65 ± 1.13	1.2-4.9	24
Aerobic plate count (CFU/g)	70,729 ± 49,351	7,000-210,000	21
Coliform (MPN/g) (f)	731 ± 880	<3-2,400	24
E. coli (MPN/g)	7.50 ± 7.68	<3-23	24
Total nitrosamines (ppb) (g, h)	7.24 ± 6.70	1.8-24.5	22
Total nitrosamines (ppb) (g, i)	17.03 ± 28.20	1.8-101.6	24
N-Nitrosodimethylamine (ppb) (g, j)	5.55 ± 6.07	0.7-20.0	22
N-Nitrosodimethylamine (ppb) (g, k)	13.29 ± 26.86	0.7-99	24
N-Nitrosopyrrolidine (ppb)	1.32 ± 0.81	0.3-3.5	24
Pesticides (ppm)			
α-BHC (a, l)	<0.01		24
β-BHC (a)	<0.02		24
γ-BHC-Lindane (a)	<0.01		24
δ-BHC (a)	<0.01		24
Heptachlor (a)	<0.01		24
Aldrin (a)	<0.01		24
Heptachlor epoxide (a)	<0.01		24
DDE (a, m)	<0.01	0.05 (7/14/81)	24
DDD (a)	<0.01		24
DDT (a)	<0.01		24
HCB (a)	<0.01		24
Mirex (a)	<0.01		24
Methoxychlor (a, m)	<0.05	0.13 (8/25/81)	24
Dieldrin (a)	<0.01		24
Endrin (a)	<0.01		24
Telodrin (a)	<0.01		24
Chlordane (a)	<0.05		24
Toxaphene (a)	<0.1		24
Estimated PCB's (a)	<0.2		24
Ronnel (a)	<0.01		24
Ethion (a)	<0.02		24
Trithion (a)	<0.05		24
Diazinon (a)	<0.1		24
Methyl parathion (a)	<0.02		24
Ethyl parathion (a)	<0.02		24
Malathion (n)	0.08 ± 0.05	<0.05-0.25	24
Endosulfan I (a)	<0.01		24
Endosulfan II (a)	<0.01		24
Endosulfan sulfate (a)	<0.03		24

TABLE N4. CONTAMINANT LEVELS IN NIH 07 RAT AND MOUSE RATION (Continued)

(a) All values were less than the detection limit, given in the table as the mean.
(b) Detection limit was reduced from 10 ppb to 5 ppb after 7/81.
(c) Source of contamination: Alfalfa, grains, and fish meal
(d) Source of contamination: Soy oil and fish meal
(e) Two batches contained less than 0.5 ppm.
(f) MPN = most probable number
(g) All values were corrected for percent recovery.
(h) Mean, standard deviation, and range exclude two very high values of 101.6 and 100.3 ppb in batches produced on 1/26/81 and 4/27/81.
(i) Mean, standard deviation, and range include the very high values given in footnote h.
(j) Mean, standard deviation, and range exclude two very high values of 97.9 and 99 ppb in batches produced on 1/26/81 and 4/27/81.
(k) Mean, standard deviation, and range include the high values given in footnote j.
(l) BHC = hexachlorocyclohexane or benzene hexachloride
(m) One observation was above the detection limit. The value and the date it was obtained are listed under the range.
(n) Nine batches contained more than 0.05 ppm.

APPENDIX O

DISPOSITION OF DECABROMODIPHENYL OXIDE IN F344/N RATS

APPENDIX O. CHEMICAL DISPOSITION

I. Materials and Methods

A. Chemicals: Unlabeled decabromodiphenyl oxide was obtained from Fluka Chemical Corporation, Hauppauge, New York. No purity was specified. [U-^{14}C]decabromodiphenyl oxide (lot no. 83-127-22-25), with a stated specific activity of 16.9 mCi/mmol (0.0176 mCi/mg), was supplied by Midwest Research Institute. No radiochemical purity was indicated.

The radiochemical purity of the ^{14}C-decabromodiphenyl oxide used in the dosing solutions and formulated diets was assessed by high-performance liquid chromatography (HPLC) with a Waters Chromatograph equipped with a model 6000A pump, a model U6K injector, a model 440 absorbance detector, and a model 730 data module. The following conditions were used:

Sample: 0.010-0.020 ml of solution of ^{14}C-decabromodiphenyl oxide in tetrahydrofuran (THF)
Column: Nova-Pak C_{18}
Solvent: 93% methanol, 1 ml/min
UV wavelength: 254 nm

The effluent was collected in vials, as a series of 1-ml samples, starting immediately after injection of the sample and continuing for 30 minutes. Samples were diluted with 15 ml of ScintiVerse I solution and assayed for radioactivity in a Packard Tricarb Scintillation counter. In this chromatographic system, decabromodiphenyl oxide had a retention time of 20-22 minutes. The percent purity was determined by dividing the disintegrations per minute (dpm) present in the major eluted peak by the total dpm eluted from the column. The radiochemical purity of ^{14}C-decabromodiphenyl oxide was 97.9%-99.2%. Unlabeled decabromodiphenyl oxide was assayed similarly, except that the purity was calculated by dividing the area of the major UV peak by the total area of all peaks not in the chromatogram of the blank. Unlabeled decabromodiphenyl oxide was 92% pure, with other components eluting at 12.9 minutes (1%), 17.5 minutes (2%), and 22.5 minutes (5%).

To allow calculation of the specific activity of the ^{14}C-decabromodiphenyl oxide in the dosing solutions and formulated diets, portions were added to the ScintiVerse I scintillation solution and assayed for radioactivity in a Packard Tri-Carb counter. Feed samples were combusted in a Packard 301 sample oxidizer before assay.

Solutions for intravenous injection were prepared at room temperature, with sonication as necessary, and used immediately after preparation. Rats were injected intravenously in the tail vein with 0.1 ml/100 g of body weight. To determine whether the preparations were homogenous and stable, the concentrations of decabromodiphenyl oxide in the dosing solutions and in the formulated diets were determined, before and after dosing, by HPLC analysis with the system described above, except that amounts of 0.003-0.020 ml were injected. The amount present in each sample was calculated from the area under the major UV-absorbing peaks by relating these values to those of a standard curve. To determine the amounts of decabromodiphenyl oxide in the batches of feed, the compound was extracted with THF before HPLC analysis.

B. Study animals: Seven- to eight-week old F344/N rats were purchased from Charles River Laboratories, Stoneridge, New York. The rats, housed five per cage in suspended, solid-bottom, polycarbonate cages lined with hardwood chips, were quarantined for 3-13 days. Food and water were provided at all times, unless otherwise indicated. Before initiation of each feed study, three to six rats were killed, examined and found to have no evidence of ectoparasites or endoparasites and to have no gross abnormalities. For acclimation to the powdered diet, rats to be exposed by feeding were fed powdered chow for 3 days before day 1 of the feeding studies. On study day 1, rats in studies involving more than three animals were randomized by use of a table of random numbers and were identified by inscribing numbers with a felt-tip marker on the dorsal side of the tail. After exposure, the rats, except those in experiment E, were placed in metabolism cages for the duration of the studies and were killed by exsanguination after anesthetization. Those in experiment E were restrained and, at the end of the experiment, killed by an overdose of ether.

C. Procedures

1. **Experiment A--Uptake and disposition of ^{14}C-decabromodiphenyl oxide in F344/N male rats after exposure in the diet:** Formulated diets containing decabromodiphenyl oxide were prepared by mixing decabromodiphenyl oxide and ^{14}C-decabromodiphenyl oxide, in various proportions, with pulverized Wayne Lab-Blox® feed. Mixing was accomplished by placing bottles containing the chemical, feed, and mixing stones on automatic rollers. Each preparation of feed was mixed until homogeneity was attained. Analysis of each was accomplished by extracting samples with THF and assaying by HPLC. The amounts present were calculated by comparison to a standard curve. The feed preparations were determined to be homogenous and stable by assay of quadruplicate samples before and after the feeding periods. Rats were assigned to six groups of three rats each. The rats, 8 weeks old, weighed 156-184 g on study day 1. The feed was provided to the rats in glass beakers inside porcelain jars. The jars had metal screw caps with a center opening 2.5 cm in diameter. Feed consumption was measured daily, beginning with the acclimation period. Fresh feed was supplied each day. Each group of rats was fed the standard diet, which contained unlabeled decabromodiphenyl oxide, on days 1-7 and 9-11 and the study diet, containing ^{14}C-decabromodiphenyl oxide, on day 8. Group I received feed containing the highest concentration of decabromodiphenyl oxide (5.11%) and group VI, the lowest (0.0238%).

   Urine and feces were collected separately each day on study days 9-12. On day 12, tissues were collected separately from each rat. A portion of the collected blood was centrifuged to obtain plasma. The following tissues were collected, blotted on filter paper (if appropriate), wrapped in foil, frozen on dry ice, and stored frozen until analysis: liver, kidney, lung, voluntary muscle, fat, skin (ear), brain, gut contents, and gut tissue.

   For assay of radioactivity, the total collection of feces from each rat was dried at room temperature for 3 days, weighed, and pulverized in a Salton Quick Mill grinder (Salton, Inc., Bronx, New York). Quadruplicate portions of each collection were combusted in the sample oxidizer before assay. Portions of urine, plasma, and whole blood were placed in combustion cups and allowed to dry overnight before combustion and assay for radioactivity. Portions of fat were combusted and assayed without drying. No other types of collected samples were assayed.

2. **Experiment B--Disposition of ^{14}C-decabromodiphenyl oxide after intravenous injection in F344/N male rats:** Five rats, 8.5 weeks old and weighing 150-171 g on study day 1, were used. They were injected intravenously in the tail vein with ^{14}C-decabromodiphenyl oxide in THF:Emulphor:water (1:1:2, v/v/v). Analysis of the dosing solution by HPLC revealed that it was not stable. Before dosing, the concentration was 0.533 ± 0.019 mg/ml (8,150 nCi/ml) and after dosing, 0.429 ± 0.010 mg/ml (6,580 nCi/ml). Although a few tissues were collected and analyzed as described in experiment A, the results were compromised by the instability of the dosing solution.

3. **Experiment C--Uptake and disposition of ^{14}C-decabromodiphenyl oxide in F344/N male rats at 24, 48, and 72 hours after exposure:** Rats were assigned to six groups of three rats each. The 8-week-old rats weighed 149-165 g on study day 1. Feed containing high (4.80%) and low (0.0277%) concentrations of labeled or unlabeled decabromodiphenyl oxide were prepared and characterized as described for experiment A. The preparations were determined to be homogenous and stable. Groups I-III were fed a diet containing the higher amount of decabromodiphenyl oxide, and groups IV-VI were fed a diet containing the lower amount. Rats were killed as follows: group I and IV, on day 10; groups II and V, on day 11; and groups III and VI, on day 12. Tissue and other samples were collected as described in experiment A; in addition, the spleen was collected.

   Samples of whole blood, plasma, urine, and feces were assayed as described for experiment A. Portions of other tissues and gut contents were assayed after homogenization in 9 volumes of water after combustion.

   To determine the extractability of ^{14}C-decabromodiphenyl oxide from feces, a solution (THF:Emulphor:water, 2:1:2, v/v/v) containing this compound was added to feces from F344/N rats, and the feces were dried and pulverized. To quadruplicate 0.5-g portions, 5 ml of water was added, and the preparations were sonicated for 15 minutes. THF (10 ml) and benzene (10 ml) were added, and the preparations were shaken for 60 minutes and centrifuged. The solid material was further extracted, twice with 10 ml of benzene and three times with 10 ml of THF. The pooled benzene extracts were washed with 5 ml of water. The upper phase, the benzene extract, was retained for analysis. The lower phase was added to the combined THF extracts, and 5 ml of benzene was added. The resulting upper layer was retained as the THF extract. The percent extractability was calculated by dividing the amounts in the benzene and THF extracts by the total amount present in all fractions and multiplying by 100. The value derived was 99.7% ± 0.2%.

   To determine the extent of metabolism of ^{14}C-decabromodiphenyl oxide by rats fed decabromodiphenyl oxide and ^{14}C-decabromodiphenyl oxide, pulverized fecal samples collected on days 9-11 were pooled for all rats within a dose group. (There was no appreciable radioactivity in the feces for day 12.) Each of the pooled fecal samples was mixed on a roller apparatus, and portions (0.5 g) were extracted as described above. Of the total radioactivity present, 99.4% ± 0.2% was in the benzene and THF extracts. The extracts were evaporated to dryness. The benzene extracts were dissolved (or suspended) in 4 ml of THF/benzene (1:1, v/v), and the THF extracts in 1 ml of THF. The benzene extracts from rats fed the two highest doses were cloudy with a white substance. Both types of extracts were exposed to the HPLC procedure described above.

To determine the extractability of ^{14}C-decabromodiphenyl oxide from liver, a portion of liver from an F344/N rat was homogenized in 9 volumes of water, ^{14}C-decabromodiphenyl oxide was added, and the preparation was homogenized again and lyophilized to dryness. For each of four portions, extractions were performed with three separate 5-ml portions of THF. The extracts were allowed to evaporate to dryness before radioassay. The remaining pellets were also subjected to radioassay. The percent extractability was calculated by dividing the amount in the extracts by this amount plus the amount in the pellet and multiplying by 100. The value derived was 86.4% ± 1.9%.

In some experiments, a model 1040A photodiode assay spectrophotometric detector (Hewlett-Packard, Palo Alto, California) was used to obtain UV spectra of components eluting from the HPLC column.

4. **Experiment D--Disposition of ^{14}C-decabromodiphenyl oxide in male F344/N rats 72 hours after intravenous injection:** Rats weighed 134-137 g and were 7.5 weeks old. Three rats were injected intravenously with ^{14}C-decabromodiphenyl oxide (1.07 mg/kg, 0.0173 mCi/kg) in THF:Emulphor:water (2:1:2, v/v/v). As determined by the HPLC assay described in I.A., the dosing solution was found to be stable and homogeneous. Urine and feces were collected daily for 3 days. At 72 hours after dosing, tissue and other samples, including spleen and tail, were collected as described in experiment A. Feces (0-48 h and 48-72 h) were pooled separately, extracted, and assayed.

5. **Experiment E--Biliary excretion of ^{14}C-decabromodiphenyl oxide after intravenous administration to F344/N rats:** Six rats (165-181 g, 8.5 weeks old) were anesthetized with pentobarbital (30 mg/kg, intraperitoneally), and their bile ducts were cannulated. The rats were allowed to recover from the anesthesia before ^{14}C-decabromodiphenyl oxide (0.947 mg/kg, 0.016 mCi/kg) in THF:Emulphor:water (2:1:2, v/v/v) was injected intravenously. As determined by the HPLC assay described in I.A., the dosing solution was found to be stable and homogeneous. Bile was collected at designated times over a 4-hour period. During bile collection, each rat was provided water from a bottle placed within reach of the animal. The rats were killed 4 hours after dosing, and their tails were collected and homogenized in 9 volumes of water. Measured portions of each bile sample and portions of the tail homogenates were assayed for radioactivity after combustion.

D. Results

Experiment A: Rats were fed, on days 1-7 and 9-11, unlabeled decabromodiphenyl oxide in amounts ranging from 238 to 51,100 ppm in the diet and on day 8 with ^{14}C-decabromodiphenyl oxide in similar amounts (Table O1). Over the entire period, rats in group I (51,100 ppm) consumed significantly less food ($P < 0.025$) than those in groups III, IV, V, and VI (238 ppm). For day 8, however, the difference in consumption was not significant ($0.10 < P < 0.25$) by a one-way analysis of variance.

In the 72 hours after the diet containing ^{14}C-decabromodiphenyl oxide was removed, recovery of radiolabel in the feces ranged from 91.3% ± 4.0% to 101% ± 4% of the amount ingested (Table O2). Recovery was not related to the dose of decabromodiphenyl oxide. Although the liver contained only small amounts of radioactivity, rats fed the smaller amounts of unlabeled decabromodiphenyl oxide had a greater percentage of radioactivity in this organ. The amounts ranged from 0.008% of the dose for group I to 0.064% for group VI. Although the amount of radioactivity in fat was also low, there was a tendency for rats fed the smaller amounts of unlabeled decabromodiphenyl oxide to have more radioactivity in this tissue. The amounts ranged from 0.072% for group I to 0.157% for group VI, with the value for Group IV (0.090%) being out of line.

A notable result of exposure to decabromodiphenyl oxide was that the liver weights of rats were significantly greater ($P < 0.001$) for those consuming diets with large concentrations of decabromodiphenyl oxide (Figure 14). For the two lowest concentrations, the weights were 9.65 ± 0.92 g and 9.80 ± 0.19 g and, for the two highest concentrations, 13.8 ± 0.9 g and 13.7 ± 1.3 g.

Experiment B: As noted above, the results from this experiment were compromised by the instability of the dosing solution. The only results of note were that 15.8% ± 4.3% of the dose (based on the predosing value) was found in the lungs of these rats 72 hours after dosing. Such a large amount in this tissue, which collects particulate material injected into the bloodstream, tends to confirm that precipitation of ^{14}C-decabromodiphenyl oxide in the dosing solution had occurred. This experiment was repeated with a different dosing formulation (experiment D).

TABLE O1. FEED CONSUMPTION, DECABROMODIPHENYL OXIDE CONCENTRATION IN THE DIET, AND DECABROMODIPHENYL OXIDE CONSUMED BY F344/N RATS

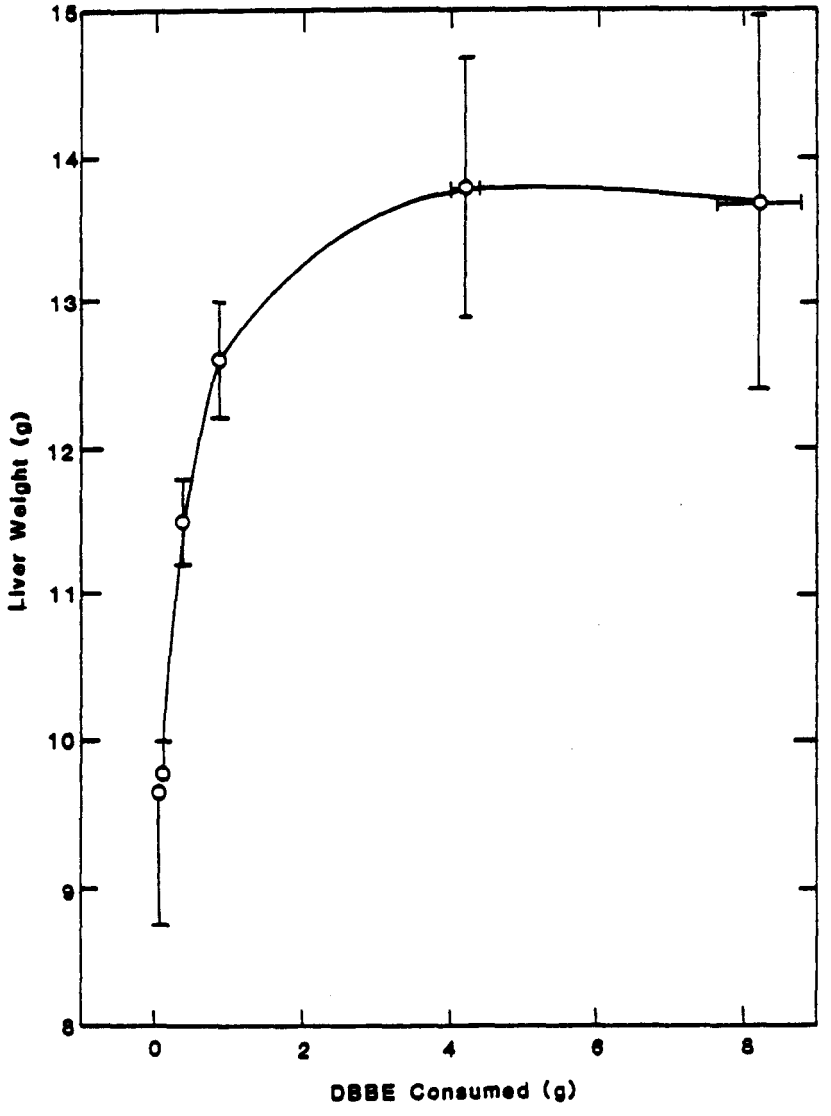
Rat Group	Feed Consumed (g/day)	Concentration of Decabromodiphenyl Oxide in Feed (ppm)			Decabromodiphenyl Oxide Consumed on Day 8	
		Unlabeled (a)	Labeled (b)	nCi/g (b)	mg	nCi[^{14}C]
I	(c,d) 14.4 ± 1.0	51,100	48,600	214 ± 5	716 ± 58	3,150 ± 250
II	15.1 ± 1.1	25,400	24,400	219 ± 28	370 ± 10	3,320 ± 90
III	16.5 ± 0.7	4,730	5,000	232 ± 23	78.0 ± 5.1	3,620 ± 240
IV	17.1 ± 0.3	2,510	2,490	212 ± 19	43.9 ± 2.4	3,740 ± 200
V	16.9 ± 0.5	496	521	206 ± 8	8.72 ± 0.40	3,460 ± 160
VI	17.0 ± 1.5	238	261	215 ± 23	4.37 ± 0.68	3,610 ± 560

(a) Concentration of unlabeled decabromodiphenyl oxide in feed, fed on days 1-7 and 9-11; the values are the averages of those derived by analysis before and after feeding.
(b) Concentration of ^{14}C-decabromodiphenyl oxide in feed, fed on day 8; the values are the averages of those derived by analysis before and after feeding.
(c) Mean ± standard deviation for three rats
(d) Significantly less than ($P < 0.025$) values for groups III, IV, V, and VI

TABLE O2. DISPOSITION OF RADIOACTIVITY IN F344/N RATS 72 HOURS AFTER EXPOSURE TO ^{14}C-DECABROMODIPHENYL OXIDE IN THE DIET ON DAY 8

Rat Group	Feces (days 8-12) (percent of dose)	Liver (day 12) (percent of dose)	Fat (a) (day 12) (percent of dose)
I	(b) 95.5 ± 9.9	0.008 ± 0.002	0.072 ± 0.041
II	93.0 ± 5.0	0.006 ± 0.001	0.088 ± 0.022
III	91.3 ± 4.0	0.011 ± 0.003	0.126 ± 0.017
IV	101 ± 4	0.016 ± 0.003	0.090 ± 0.027
V	100 ± 1	0.043 ± 0.010	0.161 ± 0.026
VI	97.7 ± 5.8	0.064 ± 0.003	0.157 ± 0.007

(a) Considered to be 7% of total body weight
(b) The values are means ± standard deviation for three rats.



The values on the horizontal axis are the total amounts of decabromodiphenyl oxide and ^{14}C-decabromodiphenyl oxide consumed (days 1-12). The points represent the means, and the vertical and horizontal bars, the standard deviations.

FIGURE 14. EFFECT OF EXPOSURE TO DECABROMODIPHENYL OXIDE ON LIVER WEIGHTS OF F344/N RATS

Experiment C: These rats were fed a diet containing unlabeled decabromodiphenyl oxide on days 1-7 and day 9 (groups I and IV), days 1-7 and days 9-10 (groups II and V), or days 1-7 and days 9-11 (groups II and VI) (Table O3). For groups I-III, unlabeled decabromodiphenyl oxide concentration was 48,000 ppm, and for groups IV-VI, 277 ppm unlabeled decabromodiphenyl oxide. A diet containing correspondingly similar amounts of ^{14}C-decabromodiphenyl oxide was fed on day 8. Although for groups I-II the mean values for feed consumption were lower than those for groups IV-VI, the difference was not significantly different. The amount of ^{14}C-decabromodiphenyl oxide consumed was in proportion to the content of the diet. The radioactivity ingested ranged from 3,070 ± 60 nCi to 3,590 ± 140 nCi, but the amounts were not related to the concentrations of decabromodiphenyl oxide in formulated diets.

Recovery of radioactivity in the feces ranged from 82.5% ± 4.7% to 86.4% ± 8.5% and was not related to the dietary concentration of decabromodiphenyl oxide or to the time the rats were killed (24, 48, or 72 hours) after consumption of ^{14}C-decabromodiphenyl oxide (Table O4). For both doses, the percent of the dose remaining in the gut contents (less than 4%) decreased with time the rats were killed after exposure to ^{14}C-decabromodiphenyl oxide. A similar observation was noted for gut tissue, which contained less than 0.04% of the dose.

At 72 hours, the liver contents of radioactivity in rats exposed to decabromodiphenyl oxide in the diet were low (0.016% of the dose for rats fed 48,000 ppm decabromodiphenyl oxide and 0.109% for rats fed 277 ppm decabromodiphenyl oxide). These values are consistent with the values derived in experiment A. For rats fed the low amount of decabromodiphenyl oxide, the liver contained 0.449% ± 0.010% of the dose of ^{14}C-decabromodiphenyl oxide at 24 hours after feeding and 0.213% ± 0.016% at 48 hours. Also consistent with results for experiment A, liver weights for rats receiving the high dose were 12.5 ± 0.7 g; those from rats given the low dose were 8.68 ± 0.69 g.

The maximum percent of dose in other organs and tissues was as follows: kidney, 0.016%; spleen, 0.003%; lungs, 0.011%; brain, less than 0.001%; muscle (considered to be 50% of body weight), 0.248%; fat (considered to be 7% of body weight), 0.077%; and skin (considered to be 16% of body weight), 0.252% (Table O4). For all of these tissues, the maximum value were for rats in groups fed the smaller dose.

The remaining portions of the liver homogenates from rats in group IV were lyophilized to dryness and extracted three times with 5 ml of THF. The extract containing the most radioactivity was purified on a Sep-Pak C_{18} cartridge and analyzed by HPLC under the conditions described above, except that 0.05 ml of sample was injected. Fractions of 1 ml were collected and assayed for radioactivity, revealing that 81% of the radioactivity eluted at the retention time of decabromodiphenyl oxide (23 minutes). The remainder of the sample was further purified by HPLC and passage through a Sep-Pak cartridge. A final HPLC analysis allowed a UV spectrum to be determined for the radioactive material. The spectrum was identical to that for decabromodiphenyl oxide (Figure 15).

In extracts of feces, three main metabolite peaks, eluting at 3-6 minutes, 6-12 minutes, and 12-17 minutes, were evident; decabromodiphenyl oxide eluted at 17-25 min (Table O5). The percent of metabolites present tended to increase as the concentration of decabromodiphenyl oxide in the diet increased. For samples derived from rats fed larger amounts, however, the results are equivocal due to the low recovery of injected radioactivity. Such low recovery was probably due to precipitation of decabromodiphenyl oxide and possibly decabromodiphenyl oxide metabolites when solutions approaching saturation were injected into the HPLC instrument.

TABLE O3. FEED CONSUMPTION, DECABROMODIPHENYL OXIDE CONCENTRATION IN THE DIET, AND DECABROMODIPHENYL OXIDE CONSUMED BY F344/N RATS 24, 48, OR 72 HOURS AFTER EXPOSURE

Rat Group	Food Consumed (g/day)	Concentration of Decabromodiphenyl Oxide in Feed			Decabromodiphenyl Oxide Consumed on Day 8	
		Unlabeled (a)	Labeled (b)	nCi/g (b)	mg	nCi [^{14}C]
I	(c) 12.6 ± 2.3	48,000	48,500	219 ± 9	(c) 755 ± 129	(c) 3,410 ± 580
II	12.9 ± 2.7	48,000	48,500	219 ± 9	794 ± 32	3,590 ± 140
III	13.8 ± 2.5	48,000	48,500	219 ± 9	744 ± 250	3,360 ± 1,130
IV	14.3 ± 2.3	277	259	215 ± 5	3.70 ± 0.07	3,070 ± 60
V	15.7 ± 2.0	277	259	215 ± 5	4.27 ± 0.51	3,540 ± 420
VI	15.8 ± 2.4	277	259	215 ± 5	4.06 ± 1.15	3,370 ± 960

(a) Concentration (ppm) of unlabeled decabromodiphenyl oxide in the feed on days 1-7 and 9 (groups I and IV), days 1-7, and days 9-10 (groups II and V), or days 1-7 and days 9-11 (groups III and VI). Values are the averages of those derived by analysis before and after feeding.
(b) Concentration (ppm) of ^{14}C-decabromodiphenyl oxide in the feed for day 8. Values for ppm decabromodiphenyl oxide are averages of those derived by analysis before and after feeding. The values for nCi/g are the mean ± standard deviation for four separate determinations.
(c) Mean ± standard deviation for three rats

TABLE O4. DISPOSITION OF RADIOACTIVITY IN RATS 24, 48, OR 72 HOURS AFTER EXPOSURE TO ^{14}C-DECABROMODIPHENYL OXIDE IN THE DIET ON DAY 8 (a)

Tissue or Sample	Group I (kill day = 10) Percent of Dose	nCi/g or ml	Group II (kill day = 11) Percent of Dose	nCi/g or ml	Group III (kill day = 12) Percent of Dose	nCi/g or ml
Urine	(b) 0.004 ± 0.002	(c)	0.007 ± 0.003	(c)	0.008 ± 0.005	(c)
Feces	85.3 ± 7.1	(c)	85.6 ± 4.5	(c)	85.1 ± 5.5	(c)
Gut contents	3.32 ± 1.65	(c)	0.552 ± 0.873	(c)	0.059 ± 0.039	(c)
Gut tissue	0.031 ± 0.016	0.255 ± 0.132	0.012 ± 0.011	0.095 ± 0.086	0.001 ± 0.001	0.013 ± 0.011
Liver	0.007 ± 0.001	0.019 ± 0.005	0.007 ± 0.006	0.019 ± 0.015	0.016 ± 0.006	0.040 ± 0.004
Kidneys	<0.001	0.007 ± 0.004	<0.001	0.009 ± 0.003	<0.001	0.009 ± 0.005
Lungs	<0.001	0.015 ± 0.006	<0.001	0.010 ± 0.006	0.001 ± 0.001	0.022 ± 0.005
Spleen	<0.001	0.031 ± 0.018	<0.001	0.038 ± 0.025	<0.001	0.022 ± 0.011
Brain	<0.001	<0.01	<0.001	<0.01	<0.001	<0.01
Muscle (d)	0.015 ± 0.014	0.005 ± 0.005	0.014 ± 0.005	0.006 ± 0.002	0.008 ± 0.012	0.004 ± 0.006
Skin (e)	0.099 ± 0.018	0.115 ± 0.024	0.049 ± 0.017	0.061 ± 0.023	0.036 ± 0.013	0.038 ± 0.008
Fat (f)	0.040 ± 0.015	0.107 ± 0.036	0.018 ± 0.004	0.049 ± 0.010	0.012 ± 0.012	0.025 ± 0.022
Blood (g)	0.003 ± 0.001	0.006 ± 0.002	0.001 ± 0.002	0.003 ± 0.004	0.014 ± 0.011	0.023 ± 0.009
Plasma (h)	0.001 ± 0.001	0.003 ± 0.003	0.001 ± 0.001	0.002 ± 0.002	0.006 ± 0.002	0.019 ± 0.003
Total recovery (percent of dose)	88.8		86.3		85.3	

Tissue or Sample	Group IV (kill day = 10) Percent of Dose	nCi/g or ml	Group V (kill day = 11) Percent of Dose	nCi/g or ml	Group VI (kill day = 12) Percent of Dose	nCi/g or ml
Urine	0.012 ± 0.005	(c)	0.011 ± 0.003	(c)	0.012 ± 0.007	(c)
Feces	86.4 ± 8.5	(c)	83.9 ± 0.9	(c)	82.5 ± 4.7	(c)
Gut contents	1.82 ± 0.36	(c)	0.518 ± 0.413	(c)	0.093 ± 0.029	(c)
Gut tissue	0.038 ± 0.004	0.302 ± 0.023	0.021 ± 0.000	0.181 ± 0.023	0.011 ± 0.001	0.107 ± 0.024
Liver	0.449 ± 0.010	1.62 ± 0.012	0.213 ± 0.016	0.846 ± 0.057	0.109 ± 0.029	0.440 ± 0.203
Kidneys	0.016 ± 0.002	0.407 ± 0.015	0.016 ± 0.000	0.430 ± 0.066	0.013 ± 0.001	0.295 ± 0.059
Lungs	0.011 ± 0.001	0.457 ± 0.022	0.007 ± 0.000	0.321 ± 0.051	0.004 ± 0.001	0.167 ± 0.055
Spleen	0.003 ± 0.001	0.273 ± 0.030	0.002 ± 0.000	0.160 ± 0.017	0.001 ± 0.000	0.074 ± 0.028
Brain	<0.001	<0.01	<0.001	<0.01	<0.001	<0.01
Muscle (d)	0.198 ± 0.024	0.006 ± 0.001	0.244 ± 0.016	0.009 ± 0.001	0.248 ± 0.007	0.008 ± 0.002
Skin (e)	0.252 ± 0.018	0.257 ± 0.022	0.207 ± 0.031	0.232 ± 0.062	0.136 ± 0.018	0.144 ± 0.042
Fat (f)	0.062 ± 0.033	0.145 ± 0.073	0.077 ± 0.022	0.196 ± 0.073	0.048 ± 0.001	0.115 ± 0.026
Blood (g)	0.043 ± 0.006	0.077 ± 0.009	0.024 ± 0.010	0.048 ± 0.023	0.026 ± 0.008	0.050 ± 0.024
Plasma (h)	0.035 ± 0.004	0.112 ± 0.010	0.019 ± 0.006	0.067 ± 0.019	0.021 ± 0.004	0.068 ± 0.007
Total recovery (percent of dose)	89.3		85.3		83.2	

(a) Rats were fed unlabeled decabromodiphenyl oxide in the diet on days 1-7, ^{14}C-decabromodiphenyl oxide in the diet on day 8, and unlabeled decabromodiphenyl oxide in the diet through the kill day.
(b) Tetrahydrofuran extract mean ± standard deviation for three rats
(c) Not calculated
(d) Considered to be 50% of body weight
(e) Considered to be 16% of body weight
(f) Considered to be 7% of body weight
(g) Considered to be 9% of body weight
(h) Considered to be 5% of body weight

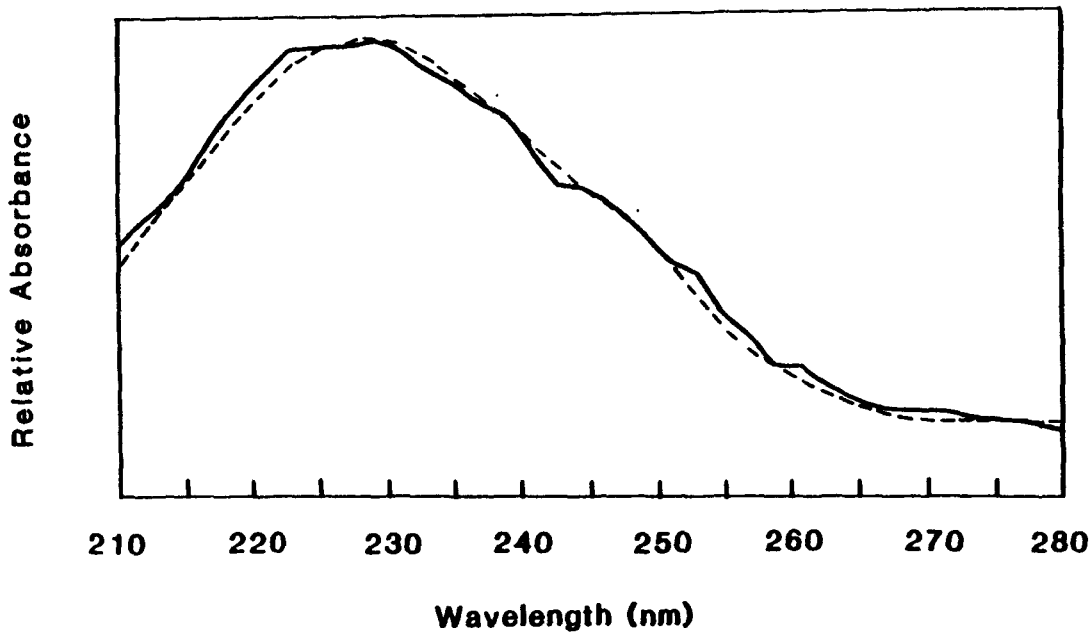


FIGURE 15. ULTRAVIOLET SPECTRA OF REFERENCE DECABROMODIPHENYL OXIDE (——) AND OF THE ISOLATE FROM THE LIVERS (-------) OF F344/N RATS EXPOSED TO DECABROMODIPHENYL OXIDE IN THE DIET

TABLE O5. RECOVERY OF DECABROMODIPHENYL OXIDE AND METABOLITES IN EXTRACTS OF FECES OF RATS FED DIETS CONTAINING DECABROMODIPHENYL OXIDE

Concentration of Decabromodiphenyl Oxide in Diet (ppm)	Extract	Retention Time (a)				Radioactivity (nCi)	
		Metabolites			Decabromodiphenyl Oxide		
		3-6 min	6-12 min	12-17 min	17-25 min	Injected	Recovered
50,000	Benzene (b)	5.47 (4.57)	5.34 (6.04)	9.87 (3.31)	62.2 (69.0)	0.93 (0.37)	0.16 (0.22)
	(c) THF	1.82 (2.50)	2.64 (2.40)	1.80 (2.58)	9.81 (9.52)	0.78 (0.15)	0.11 (0.18)
Total recovery		7.29 (7.07)	7.98 (8.44)	11.7 (5.89)	72.0 (78.5)		
25,000	Benzene	11.7 (8.90)	7.51 (4.65)	5.38 (9.15)	57.8 (59.7)	1.16 (0.46)	0.41 (0.27)
	THF	3.40 (2.11)	1.87 (1.00)	2.08 (2.09)	10.3 (12.4)	0.99 (0.20)	0.29 (0.15)
Total recovery		15.1 (11.0)	9.38 (5.65)	7.46 (11.2)	68.1 (72.1)		
5,000	Benzene	3.26	2.57	2.54	80.4	2.80	1.57
	THF	0.36	0.05	0.17	10.6	0.71	0.44
Total recovery		3.62	2.62	2.71	91.0		
2,500	Benzene	5.28	3.47	2.86	75.5	2.33	2.23
	THF	0.74	0.65	0.54	11.0	0.69	0.67
Total recovery		6.02	4.12	3.40	86.5		
500	Benzene	2.70	2.27	1.55	74.2	4.08	3.78
	THF	0.72	0.56	0.69	16.8	0.95	1.07
Total recovery		3.42	2.83	2.24	91.0		
250	Benzene	0.00	0.00	0.00	86.6	4.51	3.61
	THF	0.67	0.31	0.52	11.8	0.69	0.71
Total recovery		0.67	0.31	0.52	98.4		

(a) High-performance liquid chromatographic analysis
(b) Percent radioactivity in sample; the numbers in parentheses represent values obtained after dilution and reassay of the extracts.
(c) Tetrahydrofuran

To determine if the loss was associated only with decabromodiphenyl oxide or with decabromodiphenyl oxide and its metabolites, the benzene and THF extracts for samples from feces of rats exposed to diets containing 50,000 and 25,000 ppm decabromodiphenyl oxide were diluted by 2.5-fold and fivefold, respectively. The previously insoluble material in the benzene extracts, presumably decabromodiphenyl oxide, went into solution. Although recovery of radioactivity from injected portions of the benzene extracts was higher than the previous recovery, it was still incomplete (Table O5). No further dilutions were possible due to the reduced amount of radioactivity present. The relative amounts of decabromodiphenyl oxide and decabromodiphenyl oxide metabolites did not change drastically, an indication that, on injection of these extracts, both decabromodiphenyl oxide and its metabolites were being lost in equal proportions.

Experiment D: At 72 hours after an intravenous dose of ^{14}C-decabromodiphenyl oxide (1.07 mg/kg), feces plus gut contents contained 74% of the dose (Table O6). The radioactivity appeared to be present in relatively high and approximately equal concentrations in the liver, kidney, and lung. Only traces of radioactivity were in the urine, spleen, and brain. Although the tails contained an average of 9.5% of the dose, there was little difference for the three individual rats, an indication that all three received equivalent amounts in the bloodstream. Muscle and skin retained 12.9% and 7.25% of the dose, respectively. Relative to tissues other than brain and spleen, the concentration of radioactivity in blood was low (1.36 nCi/ml); most of that present was in the plasma (1.97 nCi/ml).

Extraction of the feces of these rats showed that most of the excreted material was decabromodiphenyl oxide metabolites (Table O7). Unchanged decabromodiphenyl oxide constituted 36.5% of the total for the 0- to 48-hour collection period and 40.4% for the 48- to 72-hour period.

Experiment E: Although two of the three rats examined in the initial health check for this experiment had in their livers a single scar-like focus, three additional rats examined had no such defects. Examination of the livers of rats used in the experiment revealed no abnormalities.

As determined by assay of the tail, one of the six rats with biliary cannulas was improperly injected. The values derived for bile from this rat were not used in further calculations. For the remaining five rats, the rate of excretion and the cumulative excretion in the bile of radioactivity from ^{14}C-decabromodiphenyl oxide is shown in Figure 16. Of the dose administered, 7.17% $\pm$ 1.01% appeared in the bile in 4 hours. From 1.5 to 4 hours, the rate of excretion was the same, 2.2% of the dose per hour. Tails of the five rats contained 5.38% $\pm$ 2.11% of the administered dose, an indication that each received an adequate dose.

TABLE O6. DISTRIBUTION OF RADIOACTIVITY IN F344/N RATS ADMINISTERED ^{14}C-DECABROMODIPHENYL OXIDE BY INTRAVENOUS INJECTION

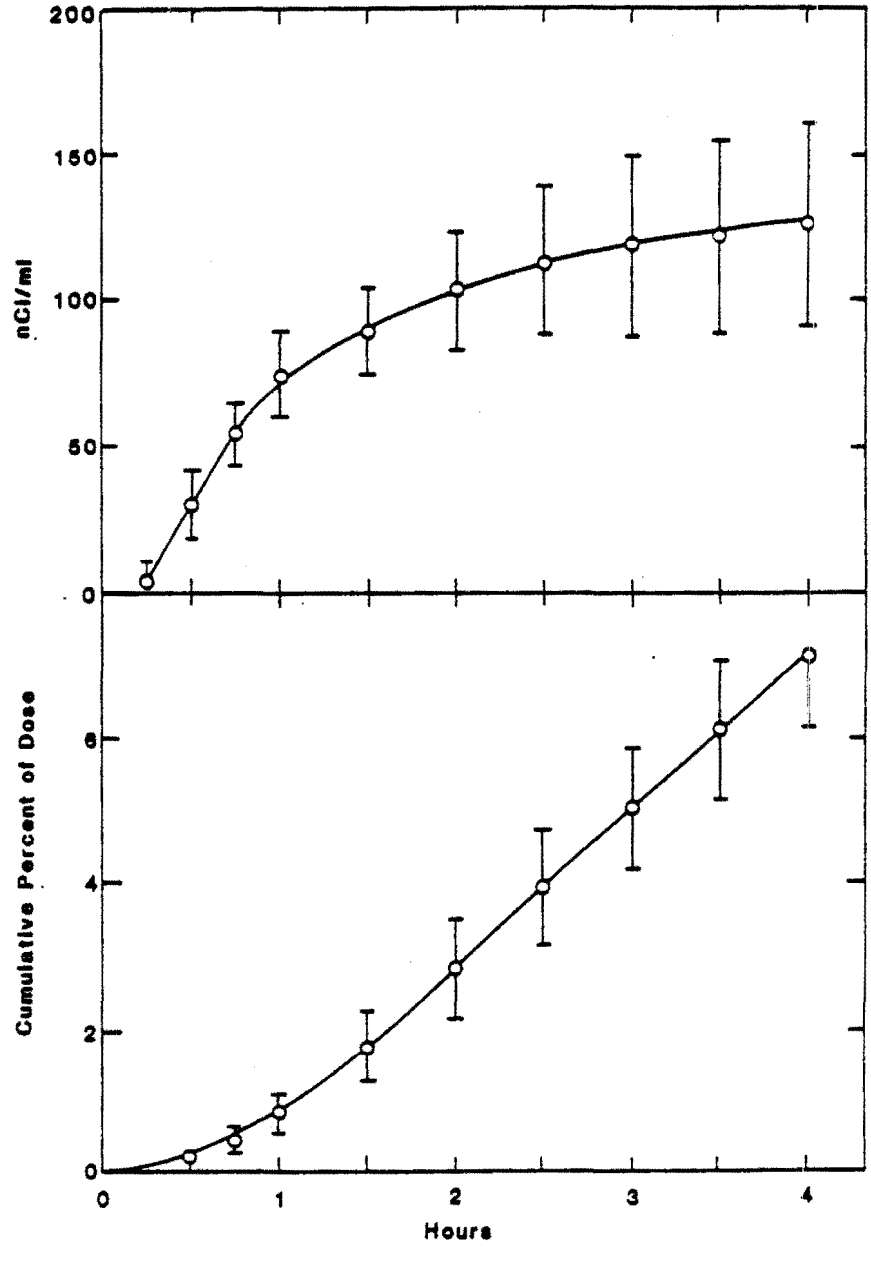
Tissue or Sample	Percent of Dose (a)	nCi/g or ml
Urine	(b) 0.129 ± 0.007	(c) --
Feces	70.0 ± 2.5	--
Gut contents	4.21 ± 1.71	--
Gut tissue	0.853 ± 0.127	--
Tail	9.50 ± 0.89	--
Liver	4.27 ± 1.05	15.1 ± 3.9
Kidney	0.697 ± 0.073	13.7 ± 1.4
Lung	0.361 ± 0.030	13.3 ± 1.4
Spleen	0.027 ± 0.004	1.78 ± 0.42
Brain	0.047 ± 0.003	0.69 ± 0.04
Muscle (d)	12.9 ± 1.1	4.32 ± 0.68
Skin (e)	7.25 ± 0.76	7.53 ± 0.41
Fat (f)	2.99 ± 1.94	7.33 ± 5.25
Blood (g)	0.732 ± 0.053	1.36 ± 0.17
Plasma (h)	0.589 ± 0.068	1.97 ± 0.35

(a) 72 hours after intravenous injection
(b) The numbers are the means ± standard deviation for three rats.
(c) Not calculated
(d) Considered to be 50% of body weight
(e) Considered to be 16% of body weight
(f) Considered to be 7% of body weight
(g) Considered to be 9% of body weight
(h) Considered to be 5% of body weight

TABLE O7. RECOVERY OF DECABROMODIPHENYL OXIDE AND METABOLITES FROM FECES OF F344/N RATS ADMININISTERED DECABROMODIPHENYL OXIDE BY INTRAVENOUS INJECTION

Collection Time	Extract	Retention Time (a)			
		Metabolites			Decabromodiphenyl Oxide
		3-6 min	6-12 min	12-17 min	17-25 min
(b) 0-48	Benzene	4.9 ± 1.6	0.5 ± 0.1	2.1 ± 0.6	28.5 ± 8.2
	(c) THF	(c) 19.7 ± 4.2	1.7 ± 0.5	2.5 ± 0.9	8.0 ± 2.4
	Total	24.6	2.2	4.6	36.5
(b) 48-72	Benzene	10.4	6.9	7.0	36.3
	THF	18.7	4.3	2.5	4.1
	Total	29.1	11.2	9.5	40.4

(a) From HPLC analysis
(b) The 0-48 hour fecal collections for the three rats were assayed separately. The 48-72 hour fecal collections were combined before assay.
(c) The numbers are the means ± standard deviation of the percent of radioactivity in the samples for three rats.



The points represent the means and the vertical bars, the standard deviations. For one point, the standard deviation was too small to be displayed.

FIGURE 16. BILIARY EXCRETION OF RADIOACTIVITY IN F344/N RATS ADMINISTERED DECABROMODIPHENYL OXIDE BY INTRAVENOUS INJECTION

APPENDIX P

DATA AUDIT SUMMARY

APPENDIX P. DATA AUDIT SUMMARY

An audit was conducted on the archival data and pathology materials for the toxicology and carcinogenesis studies of decabromodiphenyl oxide in rats and mice. This study was performed at Hazleton Laboratories America, Vienna, Virginia, under a subcontract with Tracor Jitco, Inc., from the National Cancer Institute. The studies were conducted from July 1980 to July 1982 for mice and from September 1980 to September 1982 for rats and was initiated before the requirement of compliance to Good Laboratory Practice standards by NTP in October 1980. The audit was conducted at Dynamac Corporation and at the NTP Archives in Research Triangle Park, North Carolina. The audit involved the following Dynamac personnel: L. Keifer, Ph.D.; J. Konz, M.S.P.H.; R. Schueler, D.V.M.; M. Perrault, B.S.; C. Sexsmith, B.S.; and Eva Zurek. An additional participant was C. Veigle (Pathology Associates, Inc.).

The full audit report has been reviewed and approved by NTP personnel and is on file at the National Institute of Environmental Sciences, Research Triangle Park, North Carolina. The audit consisted of an indepth review of the data and pathology materials collected during the conduct of these studies as well as review of the correspondence. For the inlife toxicology data, this review involved examination of 100% of the records on animal receipt and husbandry, mortality, environmental conditions, and dosing and examination of body weight and clinical observation data for 10% of the animals. In the review of the chemistry data, all of the available records associated with initial analysis and stability testing by Midwest Research Institute were examined. Records pertaining to bulk chemical analysis and diet preparation and analysis by the study laboratory were examined. The audit of the pathology materials included review of 100% of the Individual Animal Data Records (IADR's) for gross observation to microscopic diagnosis correlation and clerical errors, examination of the wet tissues of 10% of the animals for unidentified lesions, correct animal identification, correlation of slides and tissue blocks for all control and high dose groups, and verification of the reported pathology on a 10% sample of the animals.

Review of the toxicologic data found no problems that affected interpretation of the study. Temperature and humidity readings outside the range specified in the protocol were recorded frequently during several months of the study. No relationship was found between the periods of poor environmental control and mortality. A review of the available chemistry data found no discrepancies.

Although several discrepancies were noted between gross observation and microscopic diagnosis records, these were adequately resolved by subsequent examination of wet tissues and slides.

Overall, the items identified during the audit did not substantially reduce confidence in the data reported. Some problems and discrepancies were identified and discussed in the audit report; most of these were adequately resolved.

* U.S. GOVERNMENT PRINTING OFFICE: 1986-491-292:41087