NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 410

TOXICOLOGY AND CARCINOGENESIS STUDIES OF NAPHTHALENE

(CAS NO. 91-20-3)

IN B6C3F$_1$ MICE

(INHALATION STUDIES)

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

FOREWORD

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

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

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

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

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NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS

STUDIES OF NAPHTHALENE

(CAS NO. 91-20-3)

IN B6C3F$_1$ MICE

(INHALATION STUDIES)

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
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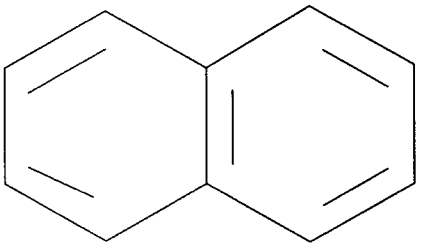
ABSTRACT



NAPHTHALENE

CAS No. 91-20-3

Chemical Formula: $C_{10}H_8$ Molecular Weight: 128.16

Synonyms: Naphthalin, Naphthene, Tar Camphor

Naphthalene, a white, crystalline powder, is used as a moth repellent and in the manufacture of phthalic and anthranilic acids, naphthylamines, and synthetic resins. The 2-year studies were conducted by exposing groups of male and female B6C3F$_1$ mice to naphthalene (>99% pure) vapor for 6 hours daily, 5 days per week, for 104 weeks. Genetic toxicology studies were conducted in *Salmonella typhimurium* and Chinese hamster ovary cells.

2-Year Studies

Groups of male and female mice were exposed to atmospheres containing 0 (75 mice per group), 10 (75 mice per group), or 30 ppm (150 mice per group) naphthalene. Mice from each group were included for 14-day hematology evaluations (male: 0 ppm, 5 animals; 10 ppm, 4; 30 ppm, 10; female: 0 ppm, 4; 10 ppm, 5; 30 ppm, 10). Mean body weights of exposed mice were slightly lower than those of controls throughout the studies. Survival of male control mice was significantly less than that of exposed mice; the lower survival was the result of wound trauma and secondary infections related to fighting among the group-housed mice (0 ppm, 26/70, 37%; 10 ppm, 52/69, 75%; 30 ppm, 118/133, 89%). Survival of exposed female mice was similar to that of controls (59/69, 86%; 57/65, 88%; 102/135, 76%).

Neoplastic and Nonneoplastic Effects in the 2-Year Studies

No increase in tumor incidence related to naphthalene administration was observed in male mice. In females, the incidence of pulmonary alveolar/bronchiolar adenomas was significantly greater in the high-dose group than in the controls (5/69, 7%; 2/65, 3%; 28/135, 21%). One other high-dose female had an alveolar/bronchiolar carcinoma. The combined incidence of alveolar/bronchiolar adenomas and carcinomas in the high-dose females was above those for control female B6C3F$_1$ mice from NTP feed, water, and inhalation studies (91/1,166, 7.8%, range 0%-16%). These lung tumors were attributed to naphthalene exposure.

Nonneoplastic lesions attributed to naphthalene exposure were observed in the nose and lungs of mice of both sexes. In the nose, naphthalene exposure was associated with an increase in the incidence and severity of chronic inflammation, metaplasia of the olfactory epithelium, and hyperplasia of respiratory epithelium. Chronic inflammation in the lung was associated with chemical exposure.

Genetic Toxicology

Naphthalene was negative for the induction of gene mutations in *Salmonella typhimurium* strains TA100, TA1535, TA1537, and TA98 with and without exogenous metabolic activation (S9). In cytogenetic tests with Chinese hamster ovary cells, naphthalene induced sister chromatid exchanges with and without S9 activation. Exposure to naphthalene induced a significant increase in chromosomal aberrations in Chinese hamster ovary cells in the presence of S9.

Conclusions

Under the conditions of these 2-year inhalation studies, there was *no evidence of carcinogenic activity** of naphthalene in male B6C3F$_1$ mice exposed to 10 or 30 ppm. There was *some evidence of carcinogenic activity* of naphthalene in female B6C3F$_1$ mice, based on increased incidences of pulmonary alveolar/bronchiolar adenomas.

In both male and female mice, naphthalene caused increased incidences and severity of chronic inflammation, metaplasia of the olfactory epithelium, and hyperplasia of the respiratory epithelium in the nose and chronic inflammation in the lungs.

* Explanation of Levels of Evidence of Carcinogenic Activity appears on page 8. A summary of peer review comments and the public discussion on this Technical Report appears on page 10.

Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of Naphthalene

	Male B6C3F$_1$ Mice	Female B6C3F$_1$ Mice
Doses	0, 10, or 30 ppm in the air for 6 hours daily, 5 days a week, for 104 weeks	0, 10, or 30 ppm in the air for 6 hours daily, 5 days a week, for 104 weeks
Body weights	Exposed slightly lower than controls	Exposed slightly lower than controls
2-Year survival rates	26/70, 37%; 52/69, 75%; 118/135, 87%	59/69, 86%; 57/65, 88%; 102/135, 76%
Nonneoplastic effects	Nose: chronic inflammation (0/70, 67/69, 133/135), metaplasia of the olfactory epithelium (0/70, 66/69, 134/135), hyperplasia of respiratory epithelium (0/70, 66/69, 134/135)	Nose: chronic inflammation (1/69, 65/65, 135/135), metaplasia of the olfactory epithelium (0/69, 65/65, 135/135), hyperplasia of respiratory epithelium (0/69, 65/65, 135/135)
	Lung: chronic inflammation (0/70, 21/69, 56/135)	Lung: chronic inflammation (3/69, 13/65, 52/135)
Neoplastic effects	None	Lung: alveolar/bronchiolar adenomas (5/69, 2/65, 28/135) and alveolar/bronchiolar carcinomas (0/69, 0/65, 1/135)
Level of evidence of carcinogenic activity	No evidence	Some evidence
Genetic toxicology		
Salmonella typhimurium gene mutation:	Negative with and without S9 in strains TA100, TA1535, TA1537, and TA98	
Sister chromatid exchange		
Chinese hamster ovary cells *in vitro*:	Positive with and without S9	
Chromosomal aberrations		
Chinese hamster ovary cells *in vitro*:	Positive with S9	

EXPLANATION OF LEVELS OF EVIDENCE OF CARCINOGENIC ACTIVITY

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

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

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

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

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

PEER REVIEW PANEL

The members of the Peer Review Panel who evaluated the draft Technical Report on the inhalation studies on naphthalene on March 11, 1991, 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:

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

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SUMMARY OF PEER REVIEW COMMENTS

On March 11, 1991, the draft Technical Report on the toxicology and carcinogenesis studies of naphthalene received public review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Committee and associated Panel of Experts. The review meeting was held at the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Dr. K.M. Abdo, NIEHS, introduced the toxicology and carcinogenesis studies of naphthalene by discussing the chemical and rationale for the study, describing the experimental design, reporting on survival and body weight effects, and commenting on compound-related neoplasms and nonneoplastic lesions in mice. The proposed conclusions were *no evidence of carcinogenic activity* in male $B6C3F_1$ mice and *some evidence of carcinogenic activity* in female $B6C3F_1$ mice.

Dr. Carlson, a principal reviewer, agreed with the conclusions. He asked for clarification of the incidence of inflammation. Dr. M.M. McDonald, NIEHS, explained that there were animals with inflammation and other animals characterized with a more extensive inflammatory response called granulomatous inflammation; therefore, there was no real overlap. Dr. Carlson suggested that the extensive work of Alan Buckpitt and coworkers on naphthalene metabolism and toxicity should be reviewed and mentioned since these studies may help in understanding any tie between metabolism and inflammation in the lung. Dr. Abdo said he was familiar with some of this work and would cite it (page 12).

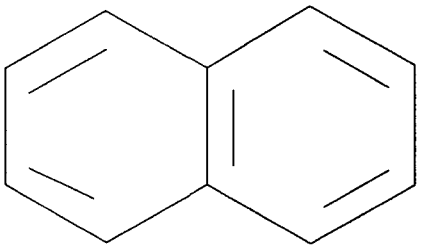
Dr. Davis, the second principal reviewer, agreed with the conclusions, but asked why the conclusion in female mice was not *clear evidence*. Dr. Abdo said the level of *some evidence* was chosen in part because all but one of the lung tumors were benign. Dr. Davis asked whether there was information on metabolites of naphthalene in humans. Dr. Abdo said he would cite information on human metabolism in the report (page 12).

Dr. Bailey, the third principal reviewer, agreed with the conclusions. He said that an explanation should be given for the absence of cataractogenesis in view of background information indicating such effects in mice. Dr. G.N. Rao, NIEHS, said $B6C3F_1$ mice were responsive at the Ah locus. (A report in the literature with nine inbred mouse strains exposed to naphthalene indicated cataracts developed only in responsive strains.) Dr. Rao commented that in the current studies exposure may not have been adequate for a cataractogenic effect since the animals often closed their eyes during exposure periods.

Dr. Hayden said inhalation exposure seemed to be appropriate based on types of human exposure. Thus, since previous studies with naphthalene in rats have been by other routes of administration, he proposed that a future study in rats by inhalation could be useful. Dr. Zeise said she disagreed with discounting the relationship of hemangiosarcomas in females to naphthalene exposure because they occurred at various sites. Dr. J.K. Haseman, NIEHS, noted that the main reason for discounting them was that the incidence in the high-dose group (4%) was similar to the mean historical control value.

Dr. Carlson moved that the Technical Report on naphthalene be accepted with the revisions discussed and the conclusions as written for male mice, *no evidence of carcinogenic activity*, and for female mice, *some evidence of carcinogenic activity*. Dr. Davis seconded the motion, which was accepted unanimously with 10 votes.

INTRODUCTION



NAPHTHALENE

CAS No. 91-20-3

Chemical Formula: $C_{10}H_8$ Molecular Weight: 128.16

Synonyms: Naphthalin, Naphthene, Tar Camphor

PHYSICAL AND CHEMICAL PROPERTIES

Naphthalene is a white, crystalline powder with a characteristic odor. Naphthalene has a boiling point of 217.9° C, a melting point of 80.2° C, a specific gravity of 1.14 at 4° C, a vapor pressure of 1 mm at 52.5° C, and vapor density of 4.4. It is insoluble in water (3 mg/100 mL), slightly soluble in methanol and ethanol (4.2 g/100 mL), soluble in benzene (40.2 g/100 mL), and very soluble in ether, chloroform, and carbon disulfide (50 g/100 mL). Naphthalene is commercially prepared from coal tar by fractional distillation or by sublimation (*Merck Index*, 1983).

PRODUCTION, USE, AND HUMAN EXPOSURE

United States production of naphthalene in 1984 was 280 million pounds (RTECS, 1990). Naphthalene is used in the manufacture of phthalic and anthranilic acids, naphthols, naphthylamines, sulfonic acid, synthetic resins, celluloid, lampblack, smokeless powder, and hydronaphthalenes. It is used as an insecticide, antiseptic, and vermicide (*Merck Index*, 1983). It is also an ingredient in various commercial moth repellents and toilet bowl cleaners (Gosselin *et al.*, 1976). A 0.2% solution in combination veterinary topical antiseptic is used for irrigating wounds; 1% solutions are used on neglected wounds. Naphthalene is also used externally on livestock and poultry to control lice (Rossoff, 1974).

From a survey conducted between 1981-1983, NIOSH estimated 112,696 workers, about 4.6% females, in 31 major industrial groups were potentially exposed to naphthalene. The top six industries, by total workers, accounted for over 50% of the total workers potentially exposed to naphthalene. Also, the petroleum and coal products and oil and gas extraction industries were among the top three industries and comprised about 21.4% of the workers potentially exposed to naphthalene. An estimated 1,838 agricultural services workers were exposed to naphthalene; over 87% were females (NIOSH, 1990).

ENVIRONMENTAL OCCURRENCE

Naphthalene has frequently been detected in water samples from the United States (Shackelford and Keith, 1976). A concentration of 1 ng/L was detected in tap water from the District of Columbia in 1974 (Scheiman *et al.*, 1974). The highest concentration detected in potable water by the Environmental Protection Agency was 1 μg/L (EPA, 1975). Naphthalene has also been detected in tap water from Waterloo, Iowa, although no levels were reported (Burnham *et al.*, 1973). The EPA has detected naphthalene in industrial effluent discharges from pesticide manufacture, petroleum refining, and nylon production; the level detected in petroleum refining effluent was 53 μg/L (Keith and Hercules, 1973; Webb *et al.*, 1973). Concentrations from 0.1 to 3.4 μg/kg were detected in tissue of fish from the Charles River in Boston (Hites and Biemann, 1972) and an unspecified concentration was detected in fish tissue from the Escambra River in Florida (Keith and Hercules, 1973).

The current Occupational Health and Safety Administration (OSHA) limit for naphthalene is 10 ppm in the air per 8-hour work shift (NIOSH, 1981). The American Conference of Governmental Hygienists reports that the odor threshold for naphthalene is at least as low as 0.3 ppm (ACGIH, 1989).

ABSORPTION AND METABOLISM

Naphthalene is readily absorbed when inhaled (Clayton and Clayton, 1982); it is also absorbed orally. This compound was readily absorbed by tissues of laying pullets (0.443 mg), swine (2.46 mg), and dairy cattle (30.69 mg) after oral intubation of a single dose or 31 daily doses (0.036, 0.112, and 5.115 mg). The adipose tissue, kidney, liver, and lung of pullets had the highest naphthalene levels after a single dose, and the kidney had the highest level after 31 daily doses. In swine, adipose tissue had the highest level of naphthalene after a single dose and lung tissue had the highest level after 31 daily doses. In cattle, the liver had the highest levels after both treatments (Eisele, 1985).

Thirty minutes after instillation of 100 nmol of ^{14}C-naphthalene into a closed rat intestinal loop, 84% was recovered unmetabolized from portal blood and only 1% was found in the luminal contents (Bock *et al.*, 1979). After an intraperitoneal injection of 100 mg/kg of naphthalene in rats, 20% to 30% was excreted in the urine and 5% to 10% in the bile. Of these excretions, 70% to 90% were in the form of acid conjugates (Clayton and Clayton, 1982). Naphthalene was not detected in fecal excretion of rats given 535 or 770 mg of the compound in the feed or 100 mg by stomach tube (Chang, 1943), suggesting that the compound was readily absorbed by rats.

An epoxide intermediate was postulated as the initial metabolite, with subsequent conversion to the trans-1,2-diol and other products (Sims and Grover, 1974). Support for this mechanism was first provided by Jerina *et al.* (1970) who demonstrated the formation of 1,2-naphthalene oxide from naphthalene in a microsomal system. Naphthalene was shown to be bioactivated by cytochrome P_{450} to electrophilic intermediates, which were subsequently metabolized to naphthoquinones and possibly to free radical intermediates (Buckpitt and Warren, 1983; Doherty *et al.*, 1985). In more recent studies, naphthalene was found to be biotransformed to dihydrodiol and 3-glutathinone conjugates by a human lung microsomal fraction in the presence of glutathiase and glutathione transferase (Buckpitt and Bahnson, 1986). Table 1 shows some of the metabolites identified in the urine of various species (Williams, 1959). The metabolic pathway for naphthalene suggested by Bock *et al.* (1976) is presented in Figure 1.

TABLE 1
Metabolites of Naphthalene Identified in the Urine of Various Species[a]

	Rat	Mouse	Rabbit	Guinea Pig
1-Naphthol	+	+	+	+
1-Naphthylsulfuric acid	+	+	+	+
1-Naphthylglucuronide	+	-	+	+
2-Naphthol	+	+	+	+
1,2-Dihydroxynaphthalene	+	-	-	+
2-Hydroxy-1-naphthyl-sulfuric acid	NT	NT	+	NT
1:2-Dihydronaphthalene-1:2-diol	+	+	+	+
1,2-Dihydro-2-hydroxy-1-naphthylglucuronide	+	-	+	-
1:2-Dihydro-1-naphthyl-glucuronide	+	NT	+	NT
1-Naphthylmercapturic acid	+	-	+	-

[a] + = metabolite present; - = metabolite not present; NT = species not tested for this metabolite; Williams, 1959

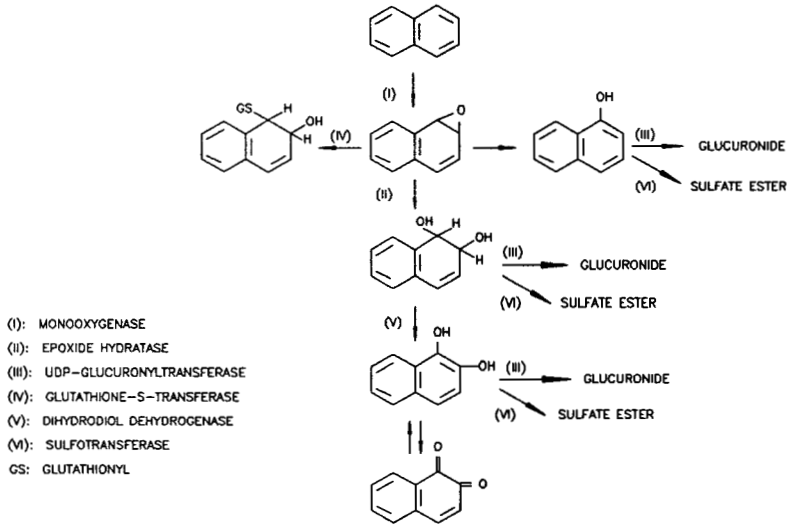


FIGURE 1
Metabolism of Naphthalene in Hepatocytes (from Bock *et al.*, 1976)

TOXICITY

Human Toxicity

Effects of naphthalene inhalation in humans include headache, confusion, eye irritation, nausea, profuse perspiration with vomiting, optic neuritis, hematuria, and edema. Naphthalene ingestion has resulted in abdominal pain, nausea, vomiting, diarrhea, darkening of the urine, irritation of the bladder, jaundice, anemia, and hyperthermia (Gerarde, 1960).

A pharmacist ingesting 5 g of naphthalene developed blindness and bilateral cataracts (Lezenius, 1902). Occupational exposure to powdered naphthalene resulted in cataracts, retinal hemorrhage, and chorioretinitis in two workers (Van der Hoeve, 1906). Cataracts were diagnosed in 8 of 29 chemical plant workers exposed to naphthalene for 5 years, with a greater incidence noted among younger workers (Ghetti and Mariani, 1956).

Naphthalene poisoning has produced hemolytic anemia in children (Zuelzer and Apt, 1949; Dawson *et al.*, 1958; Zinkham and Childs, 1958; Santhanakrishnan *et al.*, 1973) and adults (Taylor and Russell, 1932; Konar *et al.*, 1939). Individuals with decreased glucose-6-phosphate dehydrogenase activity are particularly susceptible to this effect (Haddad and Winchester, 1983; Melzer-Lange and Walsh-Kelly, 1989). Notable features of the hemolytic anemia included Heinz-body formation, hemoglobinuria, and decreases in hemoglobin, hematocrit, and red blood cell count. The hemolytic anemia was followed by renal failure (MacGregor, 1954; Gidron and Leurer, 1956). A case of aplastic anemia was reported in a woman exposed to vapors of dichlorobenzene and naphthalene, but the association is uncertain due to the lack of other substantiating reports (Harden and Baetjer, 1978).

Animal Toxicity

The oral LD_{50} value for naphthalene is 490 mg/kg for rats. LD_{50} values for mice are 533 mg/kg (oral), 969 mg/kg (subcutaneous), 100 mg/kg (intravenous), and 100 mg/kg (inhalation) (Union Carbide, 1969; RTECS, 1983).

Daily oral administration of 1 g/kg to rabbits led to degenerative changes in the lens of the eye, initially observed as swelling of the peripheral portion of the lens. Within 2 weeks the whole lens became cataractous (Potts, 1986). Van Heyningen and Pirie (1976) reviewed cataract formation in rats and rabbits resulting from naphthalene administration and concluded that, although the toxic agent in both species is the liver metabolite 1,2-dihydroxynaphthalene, different metabolic routes are involved: phenol oxidase in rats and catechol oxidase in rabbits. This is consistent with the observations that the pigmented strain of rats was more susceptible to cataract formation than the albino strain since polyphenol oxidase is found only in the pigmented strain. Albino and pigmented rabbits responded similarly to naphthalene (Koch and Doldi, 1975). The strain difference observed in rats also appears to occur in mice. Shichi *et al.* (1980) have reported correlations between the Ah^b allele and cataract formation in nine inbred mouse strains (four responsive at the Ah locus and five nonresponsive), with cataracts developing only in the responsive strains. Animals were exposed concomitantly to β-naphthoflavone for the induction of total body cytochrome P_{450} during daily administration of 60 to 120 mg/kg in a 60-day study. A study conducted with biochemical probes on male C57BL/6J mice suggests naphthalene cataractogenesis requires P_{450} bioactivation to a reactive metabolite (possibly a naphthoquinone), a free radical derivative, or a combination of both (Wells *et al.*, 1989). In these studies, a pretreatment of mice with SKF-525A or α-phenyl-N-butylnitrone in addition to treatment with vitamin E or caffeic acid inhibited naphthalene cataractogenicity, while pretreatment with phenobarbital or with diethyl-maleate enhanced naphthalene cataractogenicity.

Hemolytic anemia was observed in dogs given oral doses of 3 to 9 g of naphthalene (Zuelzer and Apt, 1949). All hematological values returned to normal 50 days after administration.

Pulmonary necrosis was observed in rats and mice given intraperitoneal injections of naphthalene. Naphthalene accumulated in the lungs of rats and mice after a single intraperitoneal injection (Reid *et al.*, 1973). Mice given a single intraperitoneal injection of 0.5, 1, or 2 mmol/kg showed dose-related necrosis of the bronchiolar epithelium (Mahvi *et al.*, 1977). This lesion was reversible and regeneration occurred after 7 days. Necrosis of the bronchial epithelial (Clara) cells occurred in the lungs of mice given a single intraperitoneal injection of 125 or 250 mg/kg naphthalene (Tong *et al.*, 1981).

Rats are more tolerant to naphthalene toxicity than mice. An intraperitoneal injection of 400 or 600 mg/kg in mice damaged the Clara cells in the lung and proximal tubule epithelial cells of the kidney. In contrast, an intraperitoneal injection of 1,600 mg/kg to rats did not produce any damage in the lung or the kidney (O'Brien *et al.*, 1985). The difference in susceptibility was attributed to the variation in the metabolic rate of the two species. It was found that the covalent binding and metabolism of naphthalene were 10% greater in microsomes prepared from mouse lung than those prepared from rats.

In vivo studies with target cell explants from sensitive species (mice) and nonsensitive species (rats and hamsters) showed that the cells obtained from mice contain a unique P_{450} enzyme capable of stereospecific metabolism of naphthalene to 1R,2S-naphthalene oxide; 1R,2S-naphthalene epoxide was not detected. Cells from rats and hamsters metabolized naphthalene to these two metabolites with the latter metabolite predominant (Chang *et al.*, 1991). Tolerance to pulmonary toxicity was observed in mice upon repeated dosing with naphthalene. Mice given a single intraperitoneal injection of 50, 100, or 200 mg/kg showed swelling of Clara cells with some exfoliation of epithelial cells, necrosis, and swollen cells with pyknotic nuclei. The severity of these lesions was dose dependent. Airways of mice receiving the same doses once a day for 7 days were essentially similar to controls. The increased tolerance resulting from multiple dosing was attributed to the selective decrease in the formation of 1R,2S-naphthalene oxide by mouse lung but not liver microsomal enzymes (O'Brien *et al.*, 1989).

Other Effects

A single intraperitoneal injection of naphthalene (1 g/kg) caused ammonia accumulation in the brains of rats. The accumulation of ammonia correlated positively with the lethality of the compound (Bolonova, 1967). Brain ammonia reacts with glutamic acid, with glutamine dehydrogenase as a catalyst, to form glutamine (DeBruin, 1976). This suggests glutamine dehydrogenase activity is inhibited by naphthalene. Naphthalene inhibited aryl hydrocarbon hydroxylase activity in liver homogenates and microsomal preparations obtained from rats given 40 mg/kg intraperitoneal injections for 3 days (Alexandrov and Frayssinet, 1973). A single 250 mg/kg intraperitoneal dose of naphthalene to C57BL/6J mice depressed the enzyme activity of microsomal monooxygenase in the lung by 30% to 70%; enzyme activity was not affected in the liver (Tong *et al.*, 1982).

Carcinogenic Activity

Possible Evidence in Humans

In East Germany, four cases of laryngeal carcinoma, a case of gastric carcinoma, a case of colon carcinoma, and a case of lupus erythematosus of the cheek were reported among 7 of 15 employees involved in naphthalene manufacture (Wolf, 1976). Seven tumor-free workers suffered various degrees of rhinopharyngo-laryngitis, an inflammation possibly conducive to prodromal carcinogenesis. Laryngeal cancer developed in 4 of 15 naphthalene distillation workers (Wolf, 1978). The incidence of laryngeal cancer in these distillation workers is approximately four thousand times greater than the general incidence of laryngeal cancer in East Germany. Kup (1978) studied 15 patients: 12 with laryngeal carcinomas, two with epipharyngeal cancer, and one with nasal carcinoma. He observed that four of the laryngeal cancer patients were exposed to naphthalene, but suggested that most of the cancers were not work related; most of the workers were smokers as well.

Possible Evidence in Animals

Daily 6-hour exposures to atmospheres of 30 ppm naphthalene for 6 months did not elicit a significant increase in lung adenomas among Strain A/J mice. Histopathologic examination of lungs from the animals, however, revealed an increased incidence of multiple alveolar adenomas relative to concurrent controls. However, the number of tumors per tumor-bearing lung in the concurrent controls was significantly lower than that observed in unexposed controls for this strain of mice (Adkins *et al.*, 1986). Negative results were reported in early naphthalene dermal studies, but experimental details were unavailable (Kennaway, 1930). A rat dermal study with 1,4-naphthoquinone, a naphthalene metabolite, resulted in skin papilloma incidences of 15% to 20%, with some leading to malignant epitheliomas (Takizawa, 1940). Levels of naphthalene producing systemic toxicity in a rabbit dermal study did not cause any carcinogenic activity (Bogdat'eva and Bid, 1955). Tumors occurred in 9 of 25 black mice

receiving naphthalene in benzene and in 3 of 21 black mice receiving the benzene control in a lifetime (5 days/week) dermal study (Knake, 1956). In the exposed mice, four had lymphocytic leukemia, three had lung adenomas, one had lymphosarcoma, and one had a nonspecified tumor; in the benzene controls, one had lymphosarcoma, one had lung adenoma, and one had a nonspecified tumor. A group of 40 rats administered seven subcutaneous biweekly doses of 500 mg/kg of naphthalene in benzene and then observed for 18 months had a tumor incidence of 15% (five animals with lymphosarcomas and one with fibroadenoma), while tumor incidences of 5% and 2% occurred in vehicle controls and unexposed controls, respectively (Knake, 1956). No carcinogenic activity or toxic effects were observed either in rats given a total of 10 g of naphthalene orally over a 700-day period or in rats given 820 mg subcutaneously or intraperitoneally over a 40-week period (Schmal, 1955). No controls were used in these studies, but a concurrent study with anthracene administered subcutaneously did produce tumors. Boyland *et al.* (1964) examined the effects of implanting naphthalene in the urinary bladder of mice and found a 4% incidence of carcinomas after 30 weeks which was similar to the effect of implanting inert substances such as glass.

Genetic Toxicology

Data from numerous genotoxicity studies indicate that naphthalene is nonmutagenic in *Salmonella typhimurium*, with or without metabolic activation (Anderson and Styles, 1978; Connor *et al.*, 1985; Nohmi *et al.*, 1985; Sakai *et al.*, 1985; Mortelmans *et al.*, 1986; Narbonne *et al.*, 1987; Bos *et al.*, 1988). In addition, the halogenated structural analogue 1-chloronaphthalene and the metabolites 1-naphthol and 2-naphthol showed no mutagenic activity in *S. typhimurium*, with or without metabolic activation (Anderson and Styles, 1978; Florin *et al.*, 1980; De Flora, 1981; Gocke *et al.*, 1981; Probst *et al.*, 1981; Lofroth *et al.*, 1985; Narbonne *et al.*, 1987). Testing of viscosity changes *in vitro* showed little binding of naphthalene to bacterial DNA (Lerman, 1965). Naphthalene can be bound, but only weakly, to nucleic acid (denatured and native calf thymus DNA) *in vitro* (Ts'o and Lu, 1964). Naphthalene was reported to be negative for the induction of single-strand breaks in rat hepatocytes *in vitro* when assayed by alkaline elution (Sina *et al.*, 1983). Brookes and Lawley (1964) found no binding to mouse skin proteins *in vivo* and noted that binding of naphthalene to DNA and RNA was insignificant.

Although the metabolite 1-naphthol was negative in several *S. typhimurium* gene mutation studies, it did cause differential growth inhibition in some strains of *Escherichia coli* (Suter and Jaeger, 1982) and *Bacillus subtilis* (Tanooka, 1977; Kawachi *et al.*, 1980), presumably as a result of DNA damage. It was negative in a variety of other genotoxicity tests, including assays for induction of sex-linked recessive lethal mutations in male Berlin K *Drosophila melanogaster* (Gocke *et al.*, 1981), unscheduled DNA synthesis in rat hepatocytes *in vitro* (Probst and Hill, 1980), and gene mutations in mouse L5178Y cells (Amacher and Turner, 1982). 1-Naphthol was also reported to be negative for induction of micronuclei in rat (Hossack and Richardson, 1977) and mouse (Gocke *et al.*, 1981) bone marrow cells following acute exposure *in vivo*.

Study Rationale

Naphthalene was nominated by NIOSH, OSHA, and EPA for carcinogenic evaluation because evidence in the literature was inadequate for reaching a regulatory decision, and because of the potential for chronic exposure to humans through the use of mothballs in the home. Potential chronic exposure can also occur on the job or through cigarette smoke (3 μg naphthalene/cigarette; Schweltz *et al.*, 1978). The inhalation route of administration was chosen because it is the primary route of human exposure. The decision to conduct the chronic studies in mice instead of rats was based on the negative results obtained by Schmal (1955) in a gavage study of naphthalene in rats. In that study, 28 animals were dosed once daily, 6 times per week, until each rat was administered a total of 10 g over 700 days. The study alone would be considered inadequate as a full carcinogenicity bioassay by today's standards.

MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF NAPHTHALENE

Naphthalene (scintillation grade) was obtained from Fisher Scientific Company (Fair Lawn, NJ) in two lots (lot numbers 775379 and 735773). Identity, purity, and stability analyses were performed by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO). The methods and results of these studies are detailed in Appendix E.

The study chemical, a white, crystalline powder, was identified as naphthalene by appearance, melting point determination, and infrared, ultraviolet/visible, and nuclear magnetic resonance spectroscopy. The purity of lot number 775379 was found to be greater than 99% by elemental analysis, Karl Fischer water analysis, thin-layer chromatography, and gas chromatography. Stability studies indicated that naphthalene was stable as a bulk chemical for 2 weeks at temperatures up to 60° C.

GENERATION AND MONITORING OF CHAMBER CONCENTRATIONS

In each of three Hinners-type inhalation chambers, naphthalene vapor was generated by direct sublimation from a 500 mL flask and was delivered through metering valves using nitrogen. Naphthalene chamber concentrations were monitored with a Miran Model 80 infrared analyzer and computer-adjusted to the desired concentration by a software feedback arrangement. Individual monitors were used for each of the exposure chambers. Calibration was performed daily using a closed loop system.

During the 2-year studies, weekly average concentrations in the 10 ppm chamber were within 20% of the target concentration except for one week when the mean was 5.5 ppm. Concentrations in the two 30 ppm chambers were within 20% of the target concentration throughout the studies. A summary of weekly average exposure concentrations for the 2-year studies is presented in Table E1.

Study Design

Groups of 75 mice of each sex were exposed by inhalation to naphthalene at target concentrations of 0 (chamber controls), 10, or 30 ppm. These dose levels were equivalent to 0, 50, or 150 mg/m^3. Two additional groups of 75 male mice and 75 female mice were exposed to 30 ppm in a fourth chamber. Twice as many animals received the high dose because of the lack of information on the long-term toxicity of inhaled naphthalene and to ensure that a sufficient number of animals lived to study termination. Exposures were for 6 hours daily, 5 days weekly, for 104 weeks.

In each chamber, 50 animals per sex were designated for the 2-year studies; 5 animals per sex were designated for 14-day and 3, 6, 12, and 18-month interim hematology evaluations. However, because of the high mortality in the male control group, the 3-, 6-, 12-, and 18-month interim evaluations were cancelled and all surviving interim animals were incorporated into the 2-year studies.

The high dose, 30 ppm, is equal to approximately one half of the saturating concentration for naphthalene at 20° C. Higher levels were not selected to ensure that condensation did not occur in the exposure chambers. The low dose, 10 ppm, is the threshold limit value established for the compound by the American Conference of Governmental Industrial Hygienists (ACGIH, 1989).

Source and Specification of Animals

Male and female B6C3F$_1$ mice were obtained from Simonsen Labs (Gilroy, CA). Mice were held 28 or 35 days before study initiation. The study began when the mice were 10 to 11 weeks old. Animal health was to be monitored by serologic analyses performed at 6-month intervals according to the protocols of the NTP Sentinel Animal Program; these were not conducted due to deaths among study animals. All mice were vaccinated for Sendai virus before study initiation and at week 31.

Animal Maintenance

Mice were housed five per cage with feed and water available *ad libitum* during nonexposure periods. All exposure cages were rotated weekly in the exposure chambers during the studies. Further details of animal maintenance are given in Table 2.

Clinical Examinations and Pathology

All animals were observed twice daily, 7 days a week. Each group of five mice was weighed by cage initially, weekly for the first 13 weeks of the study, and monthly thereafter. Hematology parameters were measured on up to five mice of each sex from each chamber 14 days after study initiation. Serial slit-lamp biomicroscopy and indirect ophthalmoscopic examinations were performed on five animals of each sex from each dose group at 6-month intervals during the studies. Table 2 contains the complete list of the analyses and studies performed on animals in the 2-year inhalation studies of naphthalene.

A necropsy was performed on all animals. During necropsy, all organs and tissues were examined for grossly visible lesions. A complete histopathologic examination inclusive of gross lesions was performed on all control and high-dose animals and on all animals dying or killed moribund prior to 21 months. Histopathologic examinations of the lungs and nasal cavities were performed on all low-dose mice. Tissues for microscopic examination were fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned to a thickness of 4 to 6 μm, and stained with hematoxylin and eosin.

Pathology evaluations were completed by the study laboratory pathologist and the pathology data were entered into the Toxicology Data Management System (TDMS). The slides, paraffin blocks, and residual wet tissues were sent to the NTP Archives for inventory, slide/block match, and wet tissue audit for accuracy of labeling and animal identification and for thoroughness of tissue trimming. The slides, individual animal data records, and pathology tables were evaluated by an independent quality assessment laboratory. The individual animal records and tables were compared for accuracy, slides and tissue counts were verified, and histotechnique was evaluated. A quality assessment pathologist reviewed all lung and nose sections from all male and female mice for accuracy and consistency of neoplastic and nonneoplastic lesion diagnosis.

The quality assessment report and slides were submitted to the Pathology Working Group (PWG), which reviewed tissues for which there was a disagreement in diagnosis between the laboratory and quality assessment pathologists. Representative examples of potential chemical-related nonneoplastic lesions and neoplasms of the nose and lungs and examples of disagreements in diagnosis between the laboratory and quality assessment pathologists were selected by the PWG chair for review by the PWG. The PWG included the quality assessment pathologist as well as other pathologists experienced in rodent toxicologic pathology, who examined these tissues without knowledge of dose group or previously rendered diagnoses. When the consensus diagnosis of the PWG differed from that of the laboratory pathologist, the final diagnosis was changed to reflect the opinion of the PWG. Details of these review procedures have been described, in part, by Maronpot and Boorman (1982) and Boorman *et al.* (1985). For subsequent analysis of pathology data, the diagnosed lesions for each tissue type are evaluated separately or combined according to the guidelines of McConnell *et al.* (1986).

Statistical Methods

Survival Analyses

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

Calculation of Incidence

The incidence of neoplasms 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) before tissue

sampling for histopathology, or when lesions could have appeared at multiple sites (e.g., mononuclear cell leukemia), the denominators consist of the number of animals on which a necropsy was performed.

Analysis of Tumor Incidence

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

In addition to logistic regression, alternative methods of statistical analysis were used, and the results of these tests are summarized in the appendixes. These include the life table test (Cox, 1972; Tarone, 1975), appropriate for rapidly lethal tumors, and the Fisher exact test and the Cochran-Armitage trend test (Armitage, 1971; Gart *et al.*, 1979), procedures based on the overall proportion of tumor-bearing animals. Tests of significance include pairwise comparisons of each dosed group with controls and a test for an overall dose-response trend. Continuity-corrected tests were used in the analysis of tumor incidence, and reported P values are one sided. The procedures described above also were used to evaluate selected nonneoplastic lesions. For further discussion of these methods, see Haseman (1984).

Historical Control Data

Although the concurrent control group is always the first and most appropriate control group used for evaluation, historical control data can be helpful in the overall assessment of tumor incidence. NTP historical control database (Haseman *et al.*, 1984, 1985) are included in the NTP reports for tumors appearing to show compound-related effects.

Analysis of Continuous Variables

Hematology data, which typically have skewed distributions, were analyzed using the multiple comparison methods of Dunn (1964) or Shirley (1977). Jonckheere's test (Jonckheere, 1954) was used to assess the significance of the dose-response trends and to determine whether a trend-sensitive test (Shirley's test) was more appropriate for pairwise comparisons than a test that does not assume a monotonic dose-response trend (Dunn's test).

Quality Assurance Methods

Study records were submitted to the NTP Archives and audited by an independent quality assurance contractor. Separate audits covering completeness and accuracy of the pathology data, pathology specimens, final pathology tables, and preliminary review draft of this NTP Technical Report were conducted. Audit procedures are presented in the reports, which are on file at the NIEHS. The audit findings were reviewed and assessed by the NTP staff so that all had been resolved or were otherwise addressed during the preparation of this Technical Report.

GENETIC TOXICOLOGY

The genetic toxicity of naphthalene was assessed by testing its ability to induce mutations in *Salmonella typhimurium* (strains TA100, TA1535, TA1537, and TA98) and sister chromatid exchanges and chromosomal aberrations in Chinese hamster ovary cells. The protocols and results for these studies are given in Appendix C.

TABLE 2
Experimental Design and Materials and Methods in the 2-Year Inhalation Studies of Naphthalene

Study Laboratory
Northrop Services, Incorporated (Research Triangle Park, NC)

Strain and Species
B6C3F$_1$ Mice

Animal Source
Simonsen Labs (Gilroy, CA)

Time Held Before Study Initiation
28 and 35 days

Age When Placed on Studies
10-11 weeks

Date of First Dose
31 August 1982

Duration of Dosing
6 hours daily, 5 days a week, for 104 weeks

Date of Last Dose
24 August 1984

Age When Killed
116-118 weeks

Size of Study Groups
75 males and 75 females in 0 and 10 ppm groups; 150 males and 150 females in 30 ppm dose group

Animals per Cage
5

Method of Animal Identification
Ear punch

Diet
NIH-31 diet (Zeigler Brothers, Gardners, PA), available *ad libitum* during nonexposure periods

Maximum Storage Time for Feed
90 days

Water
Deionized water, available *ad libitum* during nonexposure periods, in new polypropylene/polyethylene bottles (Girton Manufacturing, Millville, PA), changed weekly

Cages
Stainless steel wire mesh cages (Lab Products, Inc., Maywood, NJ), changed weekly

Chambers
Stainless steel and glass Rochester-type chambers (Young and Bertke Company, Cincinnati, OH)

TABLE 2
Experimental Design and Materials and Methods in the 2-Year Inhalation Studies of Naphthalene
(continued)

Bedding
BetaChips®, hardwood laboratory bedding (Northeastern Products, Warrensburg, NY) and Sanichip (P.J. Murphy Forest Products Corp., Rochelle Park, NJ), changed twice weekly

Cage Filters
Semi-permanent, spun-bonded polyester (Lab Products, Inc., Maywood, NJ), changed monthly

Racks
Stainless steel, changed twice weekly

Animal Room Environment
Fluorescent light: 12 hours/day
Room air changes: 10 changes/hour

Doses
0, 10, or 30 ppm by inhalation

Type and Frequency of Observation
Observed twice daily; body weights taken initially, weekly through week 13, monthly thereafter, and at scheduled sacrifice or death

Necropsy
Necropsy performed on all animals.

Histopathology
Complete histopathologic examination performed on all mice dying early or killed moribund prior to 21 months, and all control and high-dose animals. In addition to tissue masses, gross lesions, and associated regional lymph nodes, the following organs and/or tissues were examined: adrenal gland, bone (femur including marrow), brain, epididymis, esophagus, gallbladder, heart, kidney, large intestine (cecum, colon, rectum), larynx, liver, lung, lymph node (bronchial, mandibular, mediastinal, and mesenteric), mammary gland, nasal cavity, ovary, pancreas, parathyroid gland, pituitary gland, prostate gland, salivary gland, seminal vesicle, skin, small intestine (duodenum, jejunum, ileum), spleen, stomach (glandular and forestomach), testis, thymus, thyroid gland, trachea, urinary bladder, and uterus. Low-dose animals had lungs and nasal cavities examined microscopically.

Hematology
Blood samples were collected from 5 mice of each sex from each chamber (except 4 control female mice) for hematology determinations: hematocrit, hemoglobin, erythrocytes, mean cell volume, reticulocytes, and leukocytes at day 14.

Supplemental Studies
Serial ophthalmoscopic examinations by slit-lamp biomicroscopy and indirect ophthalmoscopy were performed at 6-month intervals throughout the studies on 5 mice at each dose.

RESULTS

As detailed in the Materials and Methods section, the 30 ppm groups were housed in two chambers, each containing 75 animals of each sex. For comparative purposes, the incidences of neoplasms and nonneoplastic lesions for males and females in the two 30 ppm chambers are given separately in Appendixes A and B.

Survival and body weights of male and female mice in one 30 ppm exposure chamber were similar to those of male and female mice in the other 30 ppm chamber. With three exceptions, tumor incidences of males and females in one 30 ppm chamber were also similar to those of males and females in the other 30 ppm chamber. These exceptions were subcutaneous mesenchymal tumors in males (0/67 or 0% vs. 8/68 or 12%), hepatocellular tumors in males (7/67 or 10% vs. 16/68 or 24%), and hemangiomas and hemangiosarcomas in females (0/68 or 0% vs. 5/67 or 8%). Application of permutation tests (Farrar and Crump, 1988) revealed that the latter two tumor incidences might be due to chance, but that the difference in integumentary system mesenchymal tumors in males remained significant ($P \leq 0.05$) even after adjusting for multiple comparisons. The reason for this variation in integumentary system tumors between chambers is unknown, but since this was the only strong evidence of a difference (the incidences of most nonneoplastic lesions were similar in the two chambers), the incidences from the two chambers were pooled in subsequent statistical analyses.

BODY WEIGHTS AND CLINICAL FINDINGS

Mean body weights of female mice exposed to naphthalene were slightly lower than but within 10% of those of the controls throughout the study. Mean body weights of exposed male mice were slightly lower than but within 10% of those of the controls the first 18 months (Figure 2).

No clinical findings attributed directly to naphthalene exposure were observed. In general, exposed mice tended to huddle in the cage corners during exposure periods, therefore, fighting was observed less frequently among the exposed males than among control males. No treatment-related ocular lesions were observed in selected control and exposed mice subjected to serial slit-lamp biomicroscopy and indirect ophthalmoscopic examination at 6-month intervals throughout the studies. There were no biologically significant changes in hematology parameters for exposed mice at day 14 of the study (Table D1).

SURVIVAL

Table 3 and Figure 3 show that survival was significantly decreased in the male controls compared to the exposed males, while survival of the females did not vary significantly among groups. The lower survival in control males was related to wound trauma and secondary lesions resulting from increased fighting in the group.

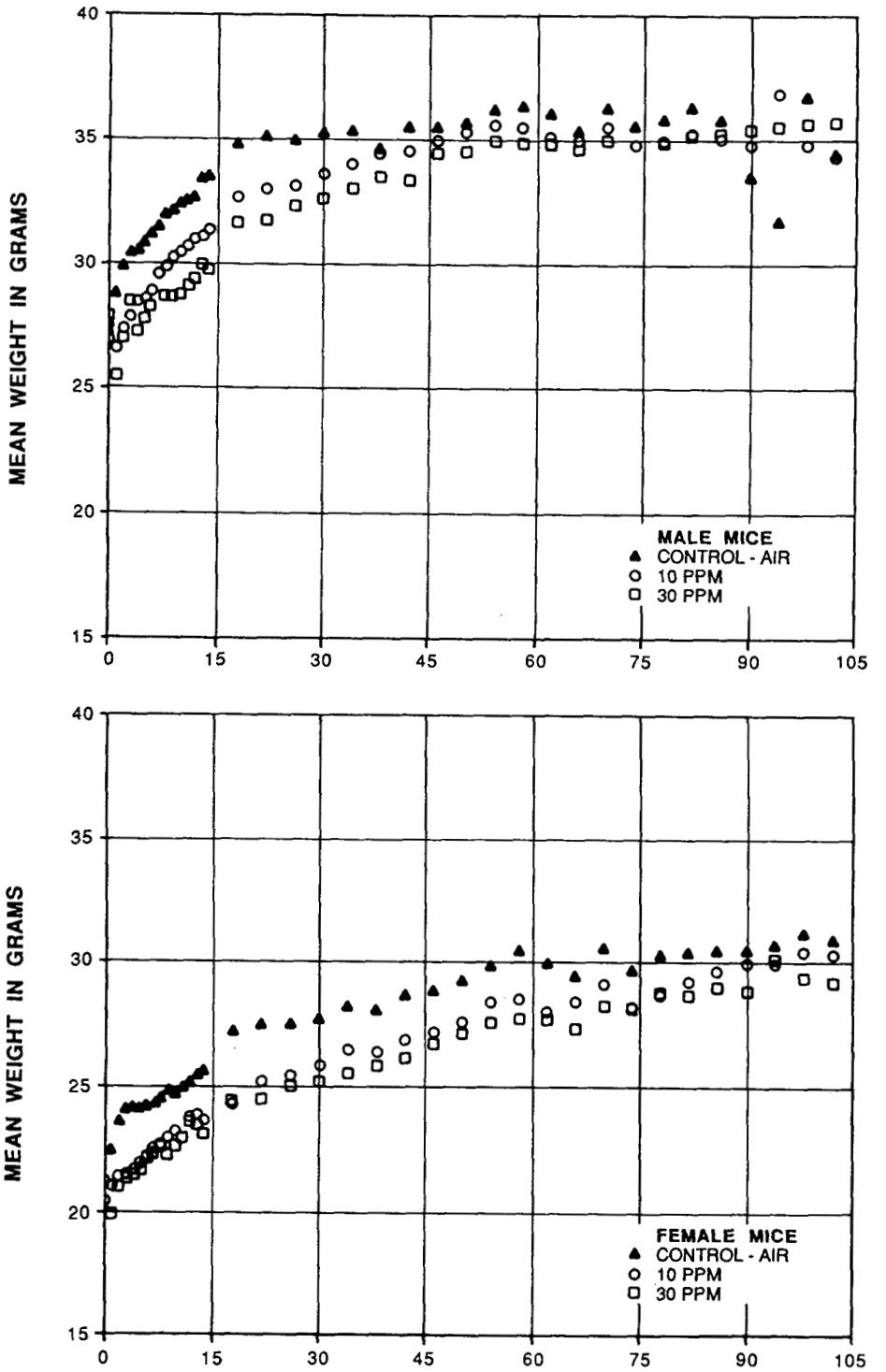


FIGURE 2
Growth Curves for Male and Female Mice Administered Naphthalene by Inhalation for 2 Years

TABLE 3
Survival of Mice in the 2-Year Inhalation Studies of Naphthalene

	0 ppm	10 ppm	30 ppm
Male			
Animals initially in study	75	75	150
Special study animals[a,b]	5	5	13
Natural deaths	31	10	7
Moribund kills	13	7	8
Accidental deaths[a]			2
Missing[a]		1	2
Animals surviving to study termination[c]	26	52	118
Percent survival at end of study[d]	37	75	89
Mean survival (days)[e]	525	648	701
Survival analysis[f]	P≤0.001N	P≤0.001N	P≤0.001N
Female			
Animals initially in study	75	75	150
Special study animals[a,b]	5	7	12
Natural deaths	8	6	17
Moribund kills	2	2	16
Accidental deaths[a]	1		
Missing[a]		3	3
Animals surviving to study termination[c]	59	57	102
Percent survival at end of study[d]	86	88	76
Mean survival (days)[e]	707	692	696
Survival analysis[f]	P=0.025	P=0.673N	P=0.125

[a] Censored from survival analysis.
[b] These mice not examined microscopically; includes mice from the 14-day interim evaluation and mice found dead or killed moribund before the study began
[c] Includes animals that died the last week of the study
[d] Kaplan-Meier determinations
[e] Mean of all deaths (uncensored, censored, and terminal sacrifice)
[f] The entry in the control column is the trend test (Tarone, 1975) result. Subsequent entries are the results of pairwise tests (Cox, 1972). A negative trend or lower mortality is indicated by N.

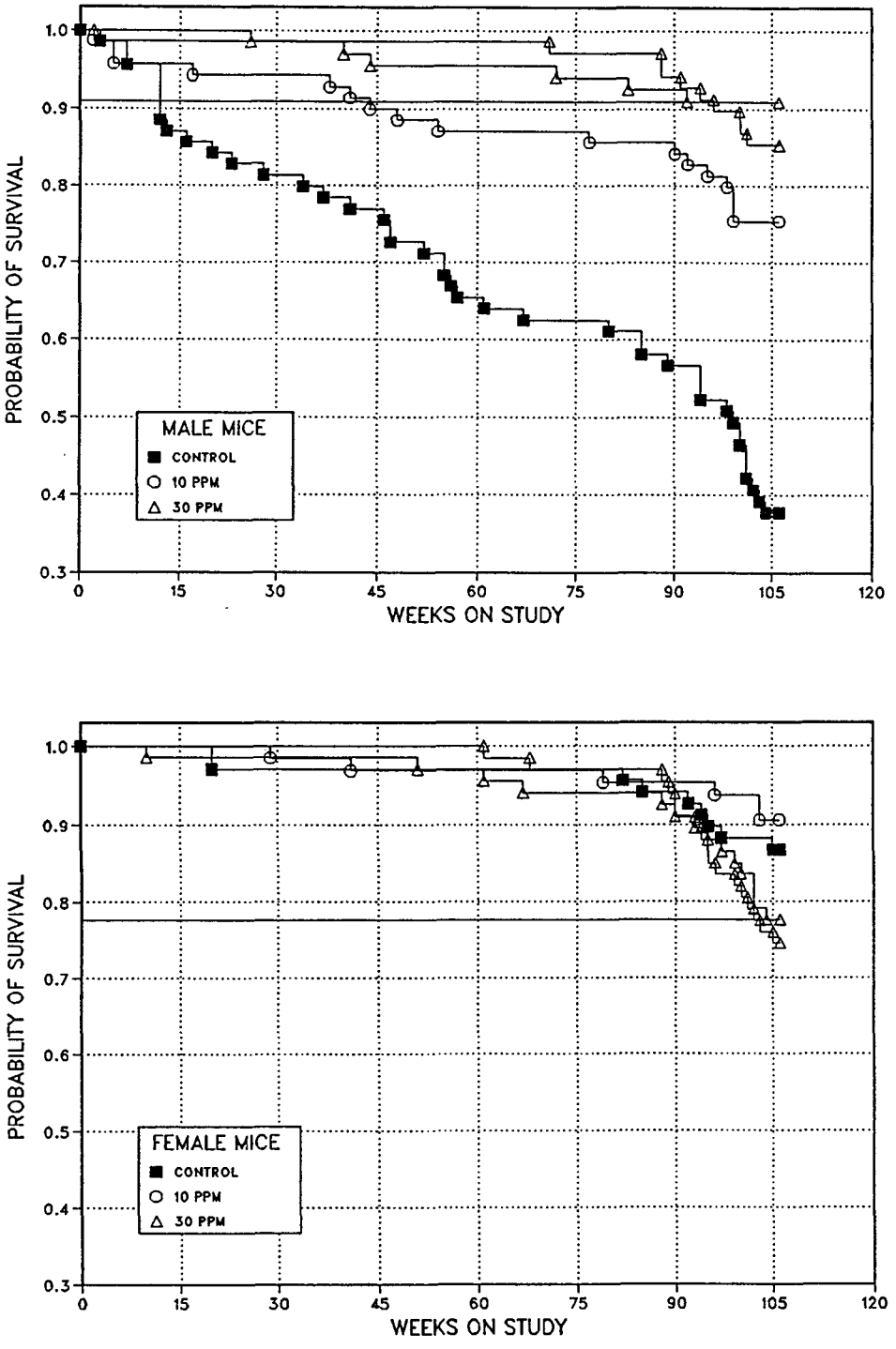


FIGURE 3
Kaplan-Meier Survival Curves for Male and Female Mice Administered Naphthalene by Inhalation for 2 Years

PATHOLOGY AND STATISTICAL ANALYSIS OF RESULTS

This section describes the statistically significant or biologically noteworthy changes in the incidences of neoplastic or nonneoplastic lesions of the lung, nose, and skin, as well as hemangiosarcomas at various hematopoietic sites (bone marrow and spleen).

Summaries of the incidences of neoplastic and nonneoplastic lesions, individual animal tumor diagnoses, statistical analyses of primary tumors that occurred at an incidence of at least 5% in at least one study group, and historical incidences for the neoplasms mentioned in this section are presented in Appendixes A and B.

Lung: The high-dose females had significantly increased incidences of alveolar/bronchiolar adenomas, and one carcinoma occurred in a high-dose female (Table 4). The combined incidence of alveolar/bronchiolar adenomas and carcinomas in control female B6C3F$_1$ mice from NTP inhalation studies is 39/466 (8.4%, range 0%-12%) (Table B4a). In control female B6C3F$_1$ mice from NTP feed, water, and inhalation studies, the combined incidence of alveolar/bronchiolar adenomas and carcinomas is 91/1,166 (7.8%, range 0%-16%). Because increased incidences of these neoplasms in exposed females were statistically significant and well above historical control ranges, they were considered to be directly related to naphthalene exposure.

Compared to control males, exposed males had marginally increased incidences of alveolar/bronchiolar adenomas and carcinomas. In control male B6C3F$_1$ mice from NTP inhalation studies, the combined incidence of alveolar/bronchiolar adenomas and carcinomas is 94/478 (19.7%, range 10%-30%) (Table A4). In control male B6C3F$_1$ mice from NTP feed, water, and inhalation studies, the combined incidence of alveolar/bronchiolar adenomas and carcinomas is 229/1,172 (19.5%, range 6%-42%). Because the incidences of these neoplasms in exposed animals were not statistically significant and were within historical control ranges, they were considered unlikely to be directly related to naphthalene exposure. The marginally increased incidences were likely related to the greater survival in the exposed groups than in the controls.

Alveolar/bronchiolar adenomas and carcinomas constitute a morphologic continuum. Adenomas were locally compressive nodular masses consisting of cords of well-differentiated epithelial cells (Plate 1), while carcinomas were composed of ribbons and/or coalescing sheets of smaller, more anaplastic, cells which sometimes extended into adjacent parenchyma.

Several spontaneous nonneoplastic lung lesions occurred in controls but were more frequent and severe in exposed mice of both sexes, while other lesions were seen only in exposed mice. Lesions were generally minimal to mild. Collectively, these were considered features of an overall inflammatory response directly related to naphthalene exposure. Accumulations of intra-alveolar foamy macrophages (histiocyte infiltration) (Plate 2) or interstitial lymphocytes (lymphocyte infiltration) were present in some controls, but were more frequent and extensive in exposed mice. Inflammation and granulomatous inflammation were diagnostic terms used to describe progressive morphologic stages of an overall response. In many exposed mice, focal intra-alveolar mixed inflammatory cell exudates and interstitial fibrosis were collectively termed "inflammation." In similar but more advanced lesions, the cellular infiltrate consisted primarily of large foamy macrophages, sometimes accompanied by multinucleated giant cells, a condition termed "granulomatous inflammation" (Plate 3). Usually only one of these terms was used to describe the overall response in any given mouse. Bronchial submucosal gland distension by mixed inflammatory cell exudates (inflammation) was in many cases also accompanied by the aforementioned lesions. Foci of alveolar epithelial hyperplasia generally occurred distant to areas of inflammation.

TABLE 4
Incidence of Lung Lesions in Mice in the 2-Year Inhalation Studies of Naphthalene

	0 ppm	10 ppm	30 ppm
Male			
Neoplasms			
Alveolar/bronchiolar Adenoma[a]			
Overall rates[b]	7/70 (10%)	15/69 (22%)	27/135 (20%)
Adjusted rates[c]	25.7%	28.8%	22.7%
Terminal rates[d]	6/26 (23%)	15/52 (29%)	26/118 (22%)
First incidence (days)	714	736 (T)	656
Logistic regression tests[e]	P=0.411N	P=0.450	P=0.541
Alveolar/bronchiolar Carcinoma[f]			
Overall rates	0/70 (0%)	3/69 (4%)	7/135 (5%)
Adjusted rates	0.0%	5.5%	5.9%
Terminal rates	0/26 (0%)	2/52 (4%)	7/118 (6%)
First incidence (days)	–[g]	629	736 (T)
Logistic regression tests	P=0.180	P=0.176	P=0.222
Alveolar/bronchiolar Adenoma or Carcinoma[h]			
Overall rates	7/70 (10%)	17/69 (25%)	31/135 (23%)
Adjusted rates	25.7%	31.9%	26.0%
Terminal rates	6/26 (23%)	16/52 (31%)	30/118 (25%)
First incidence (days)	714	629	656
Logistic regression tests	P=0.530	P=0.212	P=0.394
Nonneoplastic Lesions			
Infiltration Cellular, Lymphocyte			
Overall rates	3/70 (4%)	0/69 (0%)	8/135 (6%)
Logistic regression tests	P=0.143	P=0.201N	P=0.407
Average severity grade[i]	1.7	0	2.3
Infiltration Cellular, Histiocyte			
Overall rates	1/70 (1%)	12/69 (17%)	16/135 (12%)
Logistic regression tests	P=0.083	P=0.003	P=0.009
Average severity grade	3.0	1.8	1.6
Inflammation			
Overall rates	0/70 (0%)	21/69 (30%)	56/135 (41%)
Logistic regression tests	P≤0.001	P≤0.001	P≤0.001
Average severity grade	0	2.3	2.1
Inflammation, Granulomatous			
Overall rates	0/70 (0%)	19/69 (28%)	15/135 (11%)
Logistic regression tests	P=0.495N	P≤0.001	P=0.021
Average severity grade	0	2.2	2.6
Alveolar Epithelium, Hyperplasia			
Overall rates	2/70 (3%)	7/69 (10%)	12/135 (9%)
Logistic regression tests	P=0.482	P=0.354	P=0.323
Average severity grade	1.5	1.7	1.7
Glands, Inflammation			
Overall rates	7/70 (10%)	14/69 (20%)	22/135 (16%)
Logistic regression tests	P=0.265N	P=0.500	P=0.519N
Average severity grade	1.4	2.1	2.0

TABLE 4
Incidence of Lung Lesions in Mice in the 2-Year Inhalation Studies of Naphthalene (continued)

	0 ppm	10 ppm	30 ppm
Female			
Neoplasms			
Alveolar/bronchiolar Adenoma[j]			
Overall rates	5/69 (7%)	2/65 (3%)	28/135 (21%)
Adjusted rates	8.3%	3.5%	25.6%
Terminal rates	4/59 (7%)	2/57 (4%)	22/102 (22%)
First incidence (days)	729	736 (T)	471
Logistic regression tests	P≤0.001	P=0.233N	P=0.010
Alveolar/bronchiolar Carcinoma[k]			
Overall rates	0/69 (0%)	0/65 (0%)	1/135 (1%)
Alveolar/bronchiolar Adenoma or Carcinoma[l]			
Overall rates	5/69 (7%)	2/65 (3%)	29/135 (22%)
Adjusted rates	8.3%	3.5%	26.5%
Terminal rates	4/59 (7%)	2/57 (4%)	23/102 (23%)
First incidence (days)	729	736 (T)	471
Logistic regression tests	P≤0.001	P=0.233N	P=0.007
Nonneoplastic Lesions			
Infiltration Cellular, Lymphocyte			
Overall rates	11/69 (16%)	21/65 (33%)	46/135 (34%)
Logistic regression tests	P=0.007	P=0.024	P=0.003
Average severity grade	2.2	2.1	2.2
Infiltration Cellular, Histiocyte			
Overall rates	1/69 (1%)	5/65 (8%)	4/135 (3%)
Logistic regression tests	P=0.537N	P=0.096	P=0.430
Average severity grade	2.0	1.6	2.0
Inflammation			
Overall rates	3/69 (4%)	13/65 (20%)	52/135 (39%)
Logistic regression tests	P≤0.001	P=0.006	P≤0.001
Average severity grade	1.7	2.2	2.1
Inflammation, Granulomatous			
Overall rates	0/69 (0%)	38/65 (58%)	42/135 (31%)
Logistic regression tests	P=0.004	P≤0.001	P≤0.001
Average severity grade	0	2.1	2.3
Alveolar Epithelium, Hyperplasia			
Overall rates	3/69 (4%)	6/65 (9%)	12/135 (9%)
Logistic regression tests	P=0.222	P=0.215	P=0.187
Average severity grade	2.3	1.5	1.2
Glands, Inflammation			
Overall rates	1/69 (1%)	3/65 (5%)	15/135 (11%)
Logistic regression tests	P=0.002	P=0.294	P=0.009
Average severity grade	2.0	2.0	2.0

TABLE 4
Incidence of Lung Lesions in Mice in the 2-Year Inhalation Studies of Naphthalene (continued)

(T)Terminal sacrifice
[a] Historical incidence for 2-year NTP inhalation studies with unexposed control groups (mean ± standard deviation): 69/478 (14% ± 5.5%); range 6%-24%
[b] Incidence expressed as number of animals with lesion/total number of animals examined microscopically
[c] Kaplan-Meier estimated tumor incidence at the end of the studies after adjustment for intercurrent mortality
[d] Observed incidence at terminal kill
[e] Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The logistic regression tests regard these lesions as nonfatal. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.
[f] Historical incidence: 30/478 (6% ± 5.5%); range 0%-14%
[g] Not applicable; no tumors in animal group
[h] Historical incidence: 94/478 (20% ± 8.1%); range 10%-30%
[i] Average severity grade based on 1=minimal, 2=mild, 3=moderate, and 4=marked
[j] Historical incidence: 27/466 (6% ± 3.2%); range 0%-10%
[k] Historical incidence: 13/466 (3% ± 2.7%); range 0%-6%
[l] Historical incidence: 39/466 (8% ± 3.5%); range 0%-12%

Nose: Several nonneoplastic lesions of the nose occurred in virtually all exposed mice of each sex (Table 5). These lesions included inflammation, metaplasia of the olfactory epithelium (Plate 4), and respiratory epithelial hyperplasia. These focal or multifocal lesions occurred mainly in the posterior nasal cavity and were minimal to mild in severity. Inflammation was characterized by substantia propria edema, congestion, mixed inflammatory cell infiltrates, and occasional fibroplasia as well as intraluminal serous to fibrinopurulent exudate and necrotic debris. Respiratory epithelium hyperplasia, characterized by increased cell layers of respiratory epithelium, resulted in a thickened, folded, irregular mucosal surface. In many cases, the usual olfactory cell layer was replaced by ciliated columnar or pseudo-columnar respiratory-like epithelial cells (olfactory epithelium metaplasia). Collectively, these lesions were considered features of a generalized inflammatory and regenerative process. The dose-related increased incidences of these lesions were considered directly related to naphthalene exposure in both sexes.

Nasal adenomas occurred in the anterior nasal cavities of two females receiving 10 ppm. The incidence of nasal adenomas was not statistically significant and did not occur with a dose-related increased incidence. Therefore, it is unlikely that the occurrence of these neoplasms was directly related to naphthalene exposure.

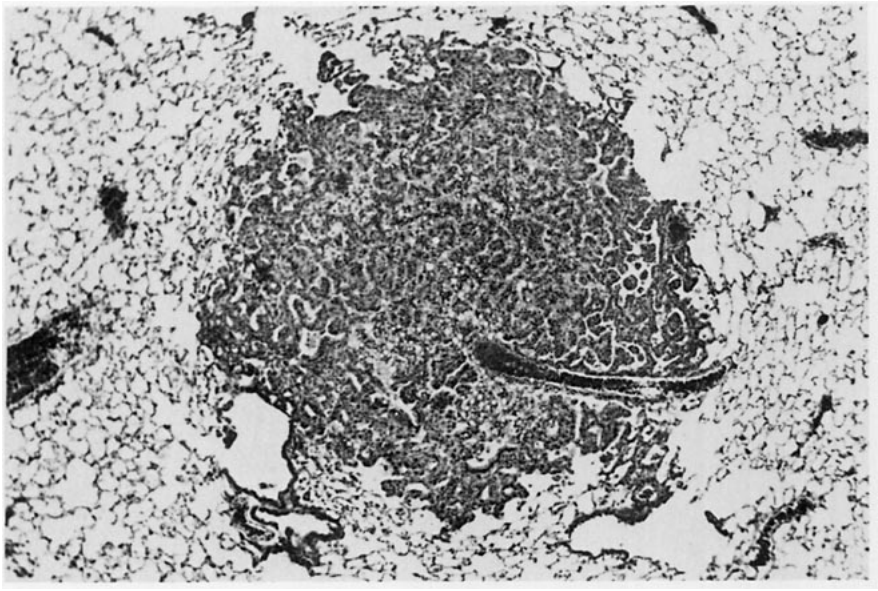


Plate 1
Lung: Alveolar/bronchiolar adenoma in the lung of a male B6C3F$_1$ mouse from 30 ppm exposure group in the 2-year inhalation studies of naphthalene. H&E, ×48

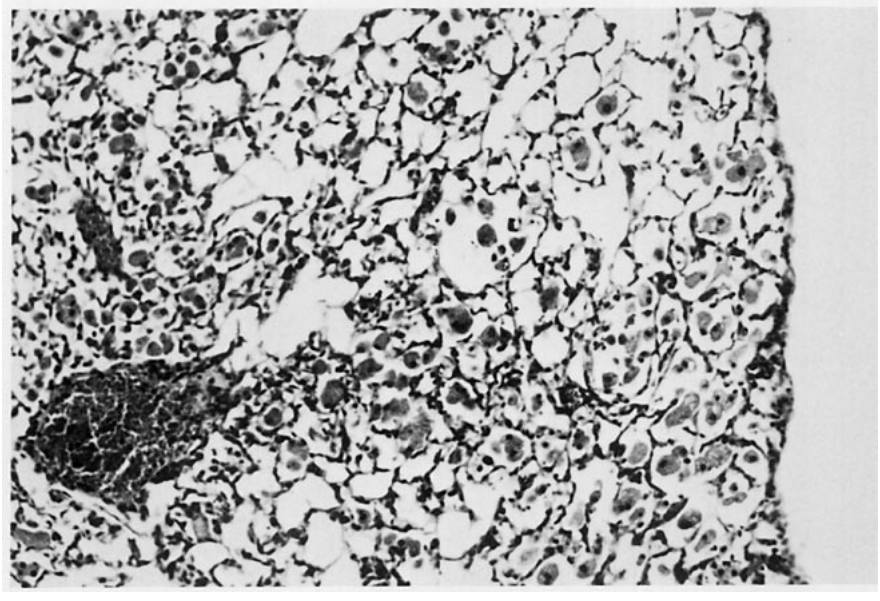


Plate 2
Lung: Mild histiocyte infiltration in alveolar lumens of the lung of a male B6C3F$_1$ mouse from the 10 ppm exposure group in the 2-year inhalation studies of naphthalene. Compare to Plate 3. H&E, ×120

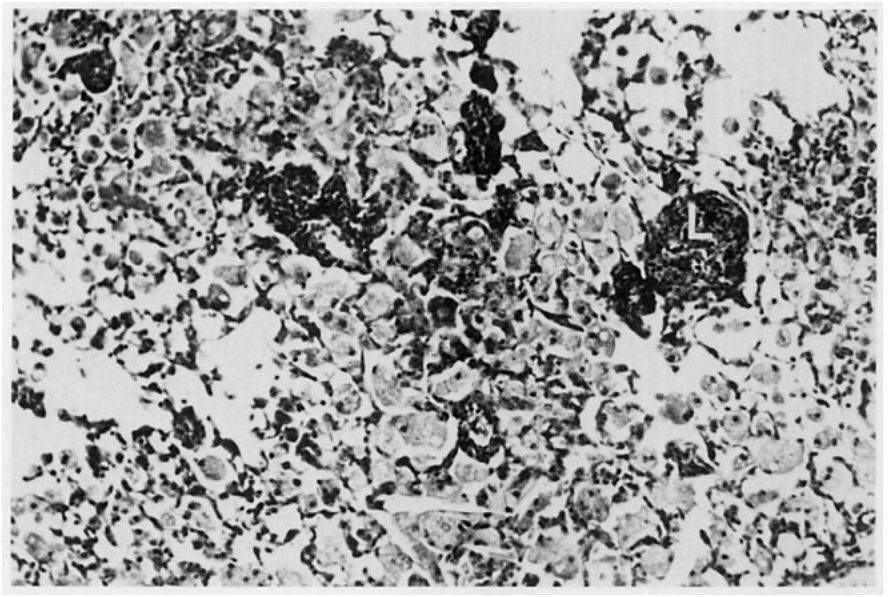


Plate 3
Lung: Moderate granulomatous inflammation in the lung of a female B6C3F$_1$ mouse from the 10 ppm exposure group in the 2-year inhalation studies of naphthalene. Abundant foamy histiocytes are present in alveolar lumens. Note lymphocytic infiltration (L). Compare to Plate 2. H&E, ×120

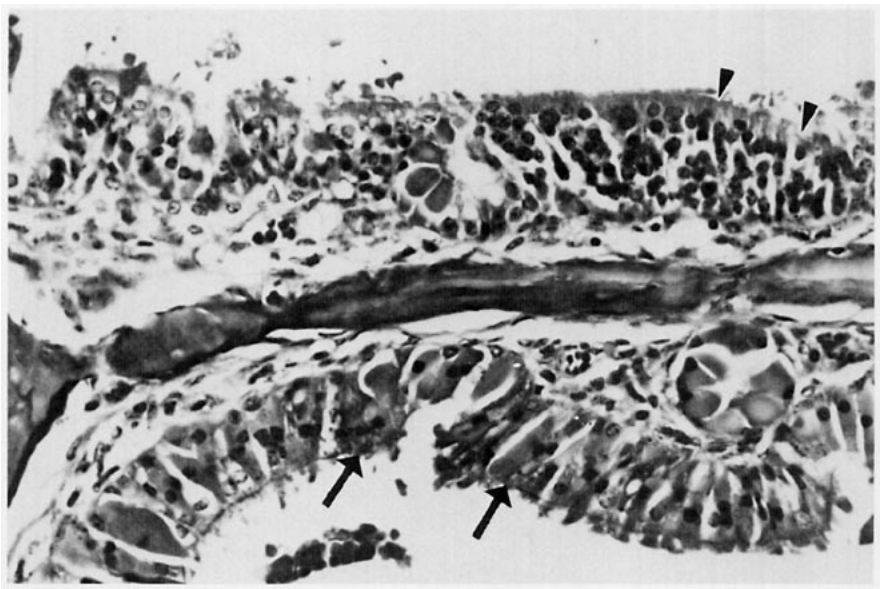


Plate 4
Nose: Nasal turbinate from a B6C3F$_1$ male mouse from the 30 ppm exposure group in the 2-year inhalation studies of naphthalene. Metaplasia of olfactory epithelium (arrows) is present; compare to adjacent relatively unaffected olfactory epithelium (arrowheads). H&E, ×30

TABLE 5
Incidence of Nonneoplastic Nasal Lesions in Mice in the 2-Year Inhalation Studies of Naphthalene

	0 ppm	10 ppm	30 ppm
Male			
Inflammation			
Overall rates[a]	0/70 (0%)	67/69 (97%)	133/135 (99%)
Logistic regression tests[b]	P≤0.001	P≤0.001	P≤0.001
Average severity grade[c]	0	2.2	2.6
Olfactory Epithelium, Metaplasia			
Overall rates	0/70 (0%)	66/69 (96%)	134/135 (99%)
Logistic regression tests	P≤0.001	P≤0.001	P≤0.001
Average severity grade	0	2.5	2.6
Respiratory Epithelium, Hyperplasia			
Overall rates	0/70 (0%)	66/69 (96%)	134/135 (99%)
Logistic regression tests	P≤0.001	P≤0.001	P≤0.001
Average severity grade	0	2.6	2.8
Female			
Inflammation			
Overall rates	1/69 (1%)	65/65 (100%)	135/135 (100%)
Logistic regression tests	P≤0.001	P≤0.001	P≤0.001
Average severity grade	2.0	2.3	2.4
Olfactory Epithelium, Metaplasia			
Overall rates	0/69 (0%)	65/65 (100%)	135/135 (100%)
Logistic regression tests	P≤0.001	P≤0.001	P≤0.001
Average severity grade	0	2.5	2.4
Respiratory Epithelium, Hyperplasia			
Overall rates	0/69 (0%)	65/65 (100%)	135/135 (100%)
Logistic regression tests	P≤0.001	P≤0.001	P≤0.001
Average severity grade	0	2.5	2.7

[a] Incidence expressed as number of animals with lesion/total number of animals examined microscopically
[b] Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The logistic regression tests regard these lesions as nonfatal.
[c] Average severity grade based on 1=minimal, 2=mild, 3=moderate, and 4=marked

Hemangiosarcomas: Hemangiosarcomas (all sites combined) occurred in five high-dose female mice (Table 6). Hemangiomas and hemangiosarcomas are neoplasms of the vascular endothelium that form a morphologic continuum and can occur in any vascularized site in the body. The combined incidence of hemangiomas and hemangiosarcomas in control female B6C3F$_1$ mice from NTP inhalation studies is 17/467 (3.6%, range 0%-8%) (Table B4b). In control female B6C3F$_1$ mice from NTP feed, water, and inhalation studies, the incidence of hemangiomas and hemangiosarcomas (combined) was 47/1,167 (4.0%, range 0%-10%). Because the incidence of these neoplasms was well within the historical control ranges and because the neoplasms occurred at various sites, they were not considered directly related to naphthalene exposure.

TABLE 6
Incidence of Hemangiosarcomas in Female Mice in the 2-Year Inhalation Study of Naphthalene[a]

	0 ppm	10 ppm	30 ppm
Overall rates[b]	0/69 (0%)	0/65 (0%)	5/135 (4%)
Adjusted rates[c]	0.0%	0.0%	4.4%
Terminal rates[d]	0/59 (0%)	0/57 (0%)	2/102 (2%)
First incidence (days)	-[e]	-	648
Logistic regression tests[f]	P=0.034	-	P=0.127

[a] Historical incidence for 2-year NTP inhalation studies with unexposed control groups (mean ± standard deviation): 12/467 (3% ± 2.2%); range 0%-6%
[b] Incidence expressed as number of animals with lesion/total number of animals necropsied
[c] Kaplan-Meier estimated tumor incidence at the end of the studies after adjustment for intercurrent mortality
[d] Observed incidence at terminal kill
[e] Not applicable; no tumors in animal group
[f] Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The logistic regression tests regard these lesions as nonfatal.

Skin: There was a decreased incidence of combined subcutaneous mesenchymal neoplasms (fibroma, fibrosarcoma, neurofibrosarcoma, sarcoma, and multiple sarcoma) in exposed males compared to controls (Table 7). Multiple fibroma occurred in a single control male. The incidence of combined subcutaneous neoplasms in control males in NTP inhalation studies is 25/479 (5.2%, range 0%-33%) (Table A4b). In control male B6C3F$_1$ mice from recent NTP feed, water, and inhalation studies, the incidence of combined subcutaneous neoplasms was 111/1,177 (9.4%, range 0%-41%). In group-housed male mice, incidences of such neoplasms are variable, and their relationship to fighting is uncertain. It is unlikely that the decreased incidence of combined subcutaneous mesenchymal neoplasms in exposed males was a direct effect of naphthalene exposure. This conclusion is supported by the fact that the two groups of male mice exposed to 30 ppm naphthalene housed in different chambers had significantly different incidences of subcutaneous mesenchymal tumors (0/67 or 0% vs. 8/68 or 12%; Table A2).

Miscellaneous lesions: In exposed male mice versus controls, there were decreased incidences of several nonneoplastic integumentary and genitourinary lesions including skin inflammation and ulcers, preputial ulcers, prostate inflammation, urinary bladder inflammation, and renal pelvis inflammation (Table A5). These lesions were probably associated with fight wound trauma and/or possible secondary ascending genitourinary bacterial infections and may have contributed to the decreased survival of male controls.

TABLE 7
Incidence of Subcutaneous Skin Tumors in Male Mice in the 2-Year Inhalation Study of Naphthalene

	0 ppm	10 ppm	30 ppm
Fibroma			
Overall rates[a]	4/70 (6%)	3/69 (4%)	1/135 (1%)
Adjusted rates[b]	15.4%	5.8%	0.8%
Terminal rates[c]	4/26 (15%)	3/52 (6%)	1/118 (1%)
First incidence (days)	736 (T)	736 (T)	736 (T)
Logistic regression tests[d]	P=0.002N	P=0.165N	P=0.001N
Fibrosarcoma			
Overall rates	11/70 (16%)	6/69 (9%)	4/135 (3%)
Adjusted rates	31.0%	10.4%	3.2%
Terminal rates	4/26 (15%)	2/52 (4%)	2/118 (2%)
First incidence (days)	558	536	611
Logistic regression tests	P≤0.001N	P=0.055N	P≤0.001N
Neurofibrosarcoma			
Overall rates	2/70 (3%)	0/69 (0%)	1/135 (1%)
Adjusted rates	5.5%	0.0%	0.8%
Terminal rates	0/26 (0%)	0/52 (0%)	0/118 (0%)
First incidence (days)	589	-[e]	493
Logistic regression tests	P=0.347N	P=0.199N	P=0.331N
Sarcoma			
Overall rates	6/70 (9%)	2/69 (3%)	3/135 (2%)
Adjusted rates	17.7%	3.7%	2.5%
Terminal rates	2/26 (8%)	1/52 (2%)	2/118 (2%)
First incidence (days)	652	692	696
Logistic regression tests	P=0.013N	P=0.054N	P=0.006N
Fibroma, Fibrosarcoma, Neurofibrosarcoma, or Sarcoma[f]			
Overall rates	23/70 (33%)	11/69 (16%)	8/135 (6%)
Adjusted rates	57.8%	19.1%	6.4%
Terminal rates	10/26 (38%)	6/52 (12%)	4/118 (3%)
First incidence (days)	558	536	493
Logistic regression tests	P≤0.001N	P≤0.001N	P≤0.001N

(T)Terminal sacrifice
[a] Incidence expressed as number of animals with lesion/total number of animals necropsied
[b] Kaplan-Meier estimated tumor incidence at the end of the studies after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The logistic regression tests regard these lesions as nonfatal. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.
[e] Not applicable; no tumors in animal group
[f] Historical incidence for 2-year NTP inhalation studies with unexposed control groups (mean ± standard deviation): 25/479 (5.2% ± 7.0%); range 0%-33%

GENETIC TOXICITY

Naphthalene (0.3-100 μg/plate) was negative for the induction of gene mutations in *Salmonella typhimurium* strains TA100, TA1535, TA1537, and TA98 when tested in a preincubation protocol in the presence and the absence of Aroclor 1254induced male Sprague-Dawley rat or Syrian hamster liver S9 (Mortelmans *et al.*, 1986) (Table C1). In cytogenetic tests with Chinese hamster ovary cells, naphthalene induced both sister chromatid exchanges and chromosomal aberrations. Sister chromatid exchanges were induced both in the presence and the absence of Aroclor 1254-induced male Sprague-Dawley rat liver S9 (Table C2). The positive responses in the chromosomal aberration test were obtained only in the presence of S9, within a dose range of 30 to 67.5 μg/mL naphthalene (Table C3); a delayed harvest protocol was employed to offset naphthalene-induced cell cycle delay and allow accumulation of sufficient metaphases for scoring.

DISCUSSION AND CONCLUSIONS

Naphthalene, a white, crystalline powder, is widely used as a moth repellant. Naphthalene is also used in the manufacture of phthalic and anthranilic acids, naphthol, naphthylamines, and synthetic resins. This chemical was nominated for toxicology and carcinogenicity studies by NIOSH, OSHA, and EPA because of the potential exposure of millions of people through its use as a moth repellant. Carcinogenicity studies were conducted in mice because no long-term information in mice was available. Inhalation studies were conducted because results of epidemiological studies showed limited evidence for laryngeal cancer in workers exposed to naphthalene (Wolf, 1978) and because human exposure usually occurs via this route. Long-term studies were not conducted in rats because the results of carcinogenicity studies conducted by Schmal (1955) were negative. In those studies, groups of 28 rats were given either 10 g orally over a 700-day period or 820 g given intraperitoneally or intravenously over a 40-week period.

The high dose used for the 2-year studies was 30 ppm. This dose is equal to approximately one-half of the saturating concentration for naphthalene at 20° C and would minimize the condensation of naphthalene in the exposure chambers. The low dose, 10 ppm, represents the threshold limit value established for this compound by the American Conference of Governmental Industrial Hygienists (ACGIH, 1989).

Mean body weights of mice receiving naphthalene were slightly lower than, but within 10% of those of the controls for 18 months of the studies. Survival of control male mice was significantly lower than the survival of the exposed groups (0 ppm, 26/70, 37%; 10 ppm, 52/69, 75%; 30 ppm, 118/133, 89%) due to fighting and wound trauma. However, since over 50% of the animals survived to week 92, a sufficient number of control animals was available for evaluation of carcinogenic potential. Thus the study was considered adequate. Because nasal hyperplasia and metaplasia were seen in virtually all exposed animals, but not in the controls, the doses chosen offered a sufficient challenge for determining the carcinogenic potential of naphthalene.

No biologically significant changes in hematologic parameters in male or female mice were attributable to naphthalene after 14 days of exposure. Naphthalene poisoning in humans was reported to cause hemolytic anemia characterized by Heinz-bodies formation, hemoglobinuria, leukocytosis, and decreases in hemoglobin, hematocrit, and red blood cell count (Melzer-Lange and Walsh-Kelly, 1989). Hemolytic anemia was also observed in dogs given oral doses of 3 to 9 g of naphthalene (Zuelzer and Apt, 1949). The contrast between the effects of naphthalene on mice and its effects on humans and dogs may be attributed to the differences in susceptibility to hemolytic agents (methemoglobin formers) by the species. Humans and dogs were reported to be the most sensitive to such agents, and rats and mice were among the least susceptible (Beard and Noe, 1981). These differences may be due to inherent differences in methemoglobin reductase activity in erythrocytes of the various species. Reductase activity in the less susceptible species was two- to four-fold greater than that of humans (Robin and Harley, 1966).

No increased incidences of neoplastic lesions were attributable to naphthalene exposure in males. The incidence of subcutaneous tissue tumors (fibroma, fibrosarcoma, neurofibrosarcoma, and sarcoma) individually or combined occurred with a negative trend. The decreased incidence in the male high-dose group was significant when compared to the incidence in the control group (Table 7). The overall NTP historical rate for these tumors (combined) in recent inhalation studies is 25/479 (5.2%, range 0%-33%). Differences in survival between the control and exposed male mice cannot be considered as a contributing factor for this negative trend, because subcutaneous tissue tumors are late-appearing tumors, and survival of controls was lower than that of exposed mice. The negative trend for subcutaneous tissue tumors observed in males may be related to the reduced fighting among males exposed to naphthalene. Exposed male mice huddled in the corners of the cages during the 6 hours of exposure and, thus, were less inclined to fight than controls. Negative trends for subcutaneous tissue tumors were not seen in females.

The incidences of pulmonary alveolar/bronchiolar adenomas (7/70, 10%; 15/69, 22%; 27/135, 20%), carcinomas (0/70, 0%; 3/69, 4%; 7/135, 5%), and combined alveolar/bronchiolar adenomas and carcinomas (7/70, 10%; 17/69, 25%; 31/135, 23%) were marginally increased in exposed male mice. The low survival rate of controls, however, accounts for the numerical increase of pulmonary tumors in the exposed males which lived longer. The marginal increase was not statistically significant. Additionally, the incidences of lung neoplasms in the exposed groups of males were within the historical range of 10% to 30%. In female mice, the incidence of these lung neoplasms (principally alveolar/bronchiolar adenoma) in the high-dose group was significantly greater than that of the control (5/69, 7%; 2/65, 3%; 29/135, 22%). The historical incidence of lung tumors in female mice in recent NTP inhalation studies is 39/466 (8.4%, range 0%-12%). These lung neoplasms have also been seen in female mice exposed to structurally related chemicals such as 1,5-naphthalenediamine (NCI, 1978a) and several other aromatic compounds including benzene (NTP, 1986), benzofuran (NTP, 1989), and phenesterin (NCI, 1978b). Accordingly, the increased incidence in lung tumors in this study was considered to be related to naphthalene exposure. Papillary adenomas of the nose were observed in two low-dose female mice. Because these lesions occurred only in the low-dose group, they were not considered to be related to naphthalene exposure.

Compound-related, minimal to mild nonneoplastic lesions were observed in the nose and lung of male and female mice. The nasal lesions observed included chronic inflammation, metaplasia of the olfactory epithelium, and hyperplasia of the respiratory epithelium (Table 5). These lesions were generally slightly more severe in the high-dose mice. Inflammation was also observed in the lung of exposed mice (Table 4). This inflammation was characterized by focal accumulation of large histiocytes and varying degrees of lymphocytic infiltration, primarily perivascular and peribronchiolar. Alveolar epithelial hyperplasia occurred primarily distant from areas of inflammation. Occasionally, multinucleated giant cells were present in the center of large foci of histiocytes. The lung has been previously identified as the site of naphthalene toxicity in mice. A single intraperitoneal injection of 125 or 250 mg/kg caused necrosis of bronchial and bronchiolar epithelium (Mahvi *et al.*, 1977; Tong *et al.*, 1981). Similar, though more severe pulmonary lesions have occurred in female $B6C3F_1$ mice administered methylnaphthalene by dermal application (Emi and Konishi, 1985).

Conclusions

Under the conditions of these 2-year inhalation studies, there was *no evidence of carcinogenic activity** of naphthalene in male $B6C3F_1$ mice exposed to 10 or 30 ppm. There was *some evidence of carcinogenic activity* of naphthalene in female $B6C3F_1$ mice, based on increased incidences of pulmonary alveolar/bronchiolar adenomas.

In both male and female mice, naphthalene caused increased incidences and severity of chronic inflammation, metaplasia of the olfactory epithelium, and hyperplasia of the respiratory epithelium in the nose and chronic inflammation in the lungs.

* Explanation of Levels of Evidence of Carcinogenic Activity appears on page 8. A summary of peer review comments and the public discussion on this Technical Report appears on page 10.

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APPENDIX A
SUMMARY OF LESIONS IN MALE MICE IN THE 2-YEAR INHALATION STUDY OF NAPHTHALENE

TABLE A1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Inhalation Study of Naphthalene[a]

	0 ppm	10 ppm	30 ppm	30 ppm
Disposition Summary				
Animals initially in study	75	75	75	75
Special study animals[b]	5	5	6	7
Early deaths				
Natural death	31	10	2	5
Moribund	13	7	3	5
Accidental deaths			2	
Survivors				
Died last week of study		2	1	
Terminal sacrifice	26	50	59	58
Missing		1	2	
Animals examined microscopically	70	69	67	68
Alimentary System				
Gallbladder	(57)	(7)	(61)	(65)
Intestine large, cecum	(56)	(5)	(65)	(65)
Intestine small, duodenum	(49)	(5)	(64)	(66)
Adenocarcinoma			1 (2%)	1 (2%)
Liver	(70)	(33)	(67)	(68)
Hemangiosarcoma				1 (1%)
Hepatocellular carcinoma	6 (9%)	4 (12%)	4 (6%)	3 (4%)
Hepatocellular adenoma	3 (4%)	8 (24%)	3 (4%)	12 (18%)
Hepatocellular adenoma, multiple		2 (6%)		1 (1%)
Mesentery	(1)			(1)
Pancreas	(67)	(10)	(66)	(68)
Salivary glands	(69)	(11)	(67)	(68)
Stomach, forestomach	(63)	(10)	(65)	(68)
Stomach, glandular	(62)	(10)	(65)	(68)
Cardiovascular System				
Heart	(70)	(10)	(67)	(68)
Endocrine System				
Adrenal gland, cortex	(66)	(9)	(65)	(68)
Adenoma			2 (3%)	
Adrenal gland, medulla	(66)	(11)	(64)	(66)
Pheochromocytoma benign	2 (3%)	1 (9%)		1 (2%)
Islets, pancreatic	(67)	(9)	(66)	(68)
Pituitary gland	(52)	(5)	(58)	(55)
Pars distalis, adenoma			1 (2%)	
Thyroid gland	(67)	(8)	(66)	(68)
Follicular cell, adenoma	1 (1%)			
General Body System				
None				

TABLE A1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Inhalation Study of Naphthalene
(continued)

	0 ppm	10 ppm	30 ppm	30 ppm
Genital System				
Epididymis	(69)	(11)	(67)	(68)
Penis	(2)	(2)		(1)
Prostate	(65)	(11)	(67)	(66)
Testes	(69)	(12)	(67)	(68)
Fibrosarcoma, metastatic, skin		1 (8%)		
Hematopoietic System				
Bone marrow	(70)	(10)	(67)	(68)
Lymph node	(67)	(14)	(67)	(68)
Lymph node, bronchial	(38)	(5)	(57)	(43)
Lymph node, mandibular	(61)	(8)	(59)	(66)
Lymph node, mediastinal	(37)	(4)	(43)	(47)
Lymph node, mesenteric	(57)	(4)	(66)	(63)
Spleen	(69)	(18)	(67)	(68)
Thymus	(47)	(1)	(63)	(63)
Integumentary System				
Skin	(69)	(21)	(67)	(68)
Subcutaneous tissue, fibroma	3 (4%)	3 (14%)		1 (1%)
Subcutaneous tissue, fibroma, multiple	1 (1%)			
Subcutaneous tissue, fibrosarcoma	11 (16%)	6 (29%)		4 (6%)
Subcutaneous tissue, fibrous histiocytoma	1 (1%)			1 (1%)
Subcutaneous tissue, neurofibrosarcoma	2 (3%)			1 (1%)
Subcutaneous tissue, sarcoma	6 (9%)	2 (10%)		2 (3%)
Subcutaneous tissue, sarcoma, multiple				1 (1%)
Musculoskeletal System				
Skeletal muscle		(4)		
Sarcoma, metastatic, skin		1 (25%)		
Nervous System				
Brain	(70)	(10)	(67)	(68)
Respiratory System				
Lung	(70)	(69)	(67)	(68)
Alveolar/bronchiolar adenoma	7 (10%)	13 (19%)	12 (18%)	7 (10%)
Alveolar/bronchiolar adenoma, multiple		2 (3%)	3 (4%)	5 (7%)
Alveolar/bronchiolar carcinoma		3 (4%)	4 (6%)	3 (4%)
Fibrosarcoma, metastatic		1 (1%)		
Fibrosarcoma, metastatic, skin		1 (1%)		
Hepatocellular carcinoma, metastatic, liver	3 (4%)			
Sarcoma, metastatic, skin	1 (1%)	1 (1%)		
Sarcoma, metastatic, uncertain primary site			1 (1%)	
Nose	(70)	(69)	(67)	(68)
Special Senses System				
Harderian gland	(1)	(1)	(1)	(1)
Adenoma	1 (100%)	1 (100%)	1 (100%)	1 (100%)

TABLE A1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Inhalation Study of Naphthalene
(continued)

	0 ppm	10 ppm	30 ppm	30 ppm
Urinary System				
Kidney	(70)	(16)	(67)	(68)
Adenoma	1 (1%)			
Carcinoma				1 (1%)
Urinary bladder	(60)	(16)	(66)	(68)
Systemic Lesions				
Multiple organs[c]	(70)	(69)	(67)	(68)
Leukemia granulocytic				1 (1%)
Lymphoma malignant histiocytic	1 (1%)	1 (1%)		
Lymphoma malignant lymphocytic	3 (4%)	2 (3%)	3 (4%)	1 (1%)
Tumor Summary				
Total animals with primary neoplasms[d]	36	36	27	39
Total primary neoplasms	49	48	34	48
Total animals with benign neoplasms	15	24	19	25
Total benign neoplasms	19	30	22	28
Total animals with malignant neoplasms	26	16	12	19
Total malignant neoplasms	30	18	12	20
Total animals with secondary neoplasms[e]	4	3	1	
Total secondary neoplasms	4	5	1	
Total animals with malignant neoplasms uncertain primary site			1	

[a] Incidences are expressed as the ratio of animals with lesions to the number of animals examined microscopically at the site.
[b] Animals from the hematology group that were sacrificed or died prior to becoming part of the 2-year studies; these animals were not examined microscopically.
[c] Number of animals with any tissues examined microscopically
[d] Primary tumors: all tumors except metastatic tumors
[e] Secondary tumors: metastatic tumors or tumors invasive to an adjacent organ

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm

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

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

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

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

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	
Carcass ID Number	0 0 0 5 1	0 0 5 2	0 0 5 5	0 0 6 4	0 0 7 1	0 0 7 5	0 0 8 2	0 0 8 5	0 0 9 1	0 0 9 2	0 0 9 3	0 0 9 4	0 0 9 5	0 1 3	0 2 3	0 2 3	0 2 4	0 2 5	0 2 5	0 2 5	**Total Tissues/ Tumors**	
Alimentary System																						
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	66	
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	57	
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	59	
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	56	
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	56	
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	58	
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	57	
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51	
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51	
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	70	
Hepatocellular carcinoma							X								X						6	
Hepatocellular adenoma															X						3	
Mesentery																					1	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67	
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69	
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	64	
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	63	
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	62	
Cardiovascular System																						
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	70	
Endocrine System																						
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	66	
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	66	
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	66	
Pheochromocytoma benign															X						2	
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67	
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	64	
Pituitary gland	+	+	+	+	+	M	M	M	+	+	+	+	+	+	+	+	M	+	+	+	52	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67	
Follicular cell, adenoma																					1	
General Body System																						
None																						

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

Number of Days on Study	0 1 5	0 4 8	0 4 8	0 8 3	0 8 3	0 8 3	0 8 3	0 8 4	0 8 8	0 8 2	1 1 4	1 3 5	1 5 8	1 8 3	1 9 6	2 3 5	2 5 5	2 8 2	3 2 0	3 2 6	3 2 7	3 6 1	3 8 2	3 8 3	3 8 9	3 9 6
Carcass ID Number	0 2 4 2	0 0 6 2	0 2 3 1	0 0 8 3	1 1 0 2	1 1 0 4	1 2 0 5	2 2 0 2	1 0 0 1	0 0 7 2	0 0 4 5	0 0 7 3	0 0 5 4	0 0 3 4	0 2 3 4	0 0 6 1	0 2 5 4	0 0 2 1	0 0 7 4	0 2 5 2	0 0 6 3	0 0 6 5	0 0 4 2	0 0 2 3	0 0 3 2	0 0 1 2
Genital System																										
Epididymis	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Penis	+																	+								
Preputial gland					+						+			+		+	M									
Prostate	+	+	+	+	+	+	M	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	M	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Testes	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																										
Blood																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Lymph node, bronchial	M	M	M	M	M	M	+	M	+	M	M	M	M	+	+	+	M	M	M	M	+	M	+	+	M	
Lymph node, mandibular	M	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	M	
Lymph node, mediastinal	+	M	M	M	M	M	M	M	M	M	M	M	+	+	+	M	+	M	+	+	+	M	M	+	M	
Lymph node, mesenteric	+	+	+	+	+	+	M	M	M	M	+	M	+	M	+	+	M	+	+	M	+	+	M	+	M	
Spleen	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Thymus	+	+	M	M	M	M	+	M	M	M	M	+	+	M	+	M	+	M	+	+	+	+	M	+	M	
Integumentary System																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibroma																										
Subcutaneous tissue, fibroma, multiple																										
Subcutaneous tissue, fibrosarcoma																										
Subcutaneous tissue, fibrous histiocytoma																										
Subcutaneous tissue, neurofibrosarcoma																										
Subcutaneous tissue, sarcoma																										
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

Number of Days on Study	4 2 1	4 6 5	5 5 8	5 8 9	5 9 0	6 2 0	6 5 2	6 5 4	6 5 5	6 5 1	6 8 8	6 8 7	6 9 0	7 0 4	7 0 6	7 0 6	7 1 4	7 1 5	7 2 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6
Carcass ID Number	0 0 8 1	0 0 8 1	0 0 1 3	0 2 2 4	0 2 2 1	0 0 4 3	0 0 1 1	0 2 4 4	0 2 3 2	0 2 4 3	0 0 4 1	0 0 2 5	0 0 4 4	0 2 2 5	0 0 1 5	0 0 5 3	0 0 3 1	0 2 3 5	0 2 4 1	0 0 1 4	0 0 2 2	0 0 0 4	0 0 3 3	0 0 3 4	0 0 3 5
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Penis																									
Preputial gland																									
Prostate	+	+	+	M	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Blood								+					+				+								
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Lymph node, bronchial	+	M	M	M	+	+	M	+	+	+	M	+	+	+	M	M	+	M	+	M	+	+	M	+	M
Lymph node, mandibular	+	+	+	M	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Lymph node, mediastinal	M	+	M	M	+	+	M	+	+	+	+	+	+	M	M	M	M	+	+	M	M	+	+	M	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	M	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	M	+	+	+	+	M	+	+	M	M	M	+	M	M	M	+	+	+	+	M	+	+	+
Integumentary System																									
Mammary gland	M	M	M	M	M	+	M	+	+	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibroma																								X	
Subcutaneous tissue, fibroma, multiple																									
Subcutaneous tissue, fibrosarcoma			X		X	X			X		X							X	X						
Subcutaneous tissue, fibrous histiocytoma																						X			
Subcutaneous tissue, neurofibrosarcoma				X											X										
Subcutaneous tissue, sarcoma							X	X					X	X											
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	
Carcass ID Number	0 0 5 1	0 0 5 2	0 0 5 5	0 0 6 4	0 0 7 1	0 0 7 5	0 0 8 2	0 0 8 5	0 0 9 1	0 0 9 2	0 0 9 3	0 0 9 4	0 0 9 5	0 1 0 3	0 2 2 3	0 2 3 3	0 2 4 5	0 2 5 1	0 2 5 3	0 2 5 5		**Total Tissues/ Tumors**
Genital System																						
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		69
Penis																						2
Preputial gland																						4
Prostate	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		65
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		66
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		69
Hematopoietic System																						
Blood																						3
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		70
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Lymph node, bronchial	+	+	+	+	+	+	+	M	M	+	+	M	+	+	+	+	+	+	+	M		38
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M		61
Lymph node, mediastinal	+	+	+	M	M	M	+	M	+	M	+	+	+	+	+	M	+	+	+	+		37
Lymph node, mesenteric	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+		57
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		69
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+		47
Integumentary System																						
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	+		5
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		69
Subcutaneous tissue, fibroma	X		X																			3
Subcutaneous tissue, fibroma, multiple																			X			1
Subcutaneous tissue, fibrosarcoma				X					X							X				X		11
Subcutaneous tissue, fibrous histiocytoma																						1
Subcutaneous tissue, neurofibrosarcoma																						2
Subcutaneous tissue, sarcoma		X													X							6
Musculoskeletal System																						
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		70
Nervous System																						
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		70

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

Number of Days on Study	0	0	0	0	0	0	0	0	0	1	1	1	1	1	2	2	2	3	3	3	3	3	3	3	3
	1	4	4	8	8	8	8	8	8	1	3	5	8	9	3	5	8	2	2	2	6	8	8	8	9
	5	8	8	3	3	3	3	4	8	2	4	8	3	6	5	5	2	0	6	7	1	2	3	9	6
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2	0	2	0	1	1	1	2	1	0	0	0	0	2	0	2	0	0	2	0	0	0	0	0	0
	4	6	3	8	0	0	0	2	0	7	4	7	5	3	6	5	2	7	5	6	6	4	2	3	1
	2	2	1	3	2	4	5	2	1	2	5	3	4	4	1	4	1	4	2	3	5	2	3	2	2
Respiratory System																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Hepatocellular carcinoma, metastatic, liver																									
Sarcoma, metastatic, skin																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear								+																	
Eye							+				+		+												
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Urethra																									
Urinary bladder	+	A	A	+	+	+	M	+	A	A	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																	X								

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

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

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	
Carcass ID Number	0 0 5 1	0 0 5 2	0 0 5 5	0 0 6 4	0 0 7 1	0 0 7 5	0 0 8 2	0 0 8 5	0 0 9 1	0 0 9 2	0 0 9 3	0 0 9 4	0 0 9 5	0 1 0 3	0 2 2 3	0 2 3 3	0 2 4 5	0 2 5 1	0 2 5 3	0 2 5 5	**Total Tissues/ Tumors**	
Respiratory System																						
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69	
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	70	
Alveolar/bronchiolar adenoma				X					X	X		X									7	
Hepatocellular carcinoma, metastatic, liver															X						3	
Sarcoma, metastatic, skin																					1	
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	70	
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	70	
Special Senses System																						
Ear			+																		2	
Eye																					3	
Harderian gland													+								1	
Adenoma													X								1	
Urinary System																						
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	70	
Adenoma	X																				1	
Urethra																					1	
Urinary bladder	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	60	
Systemic Lesions																						
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	70	
Lymphoma malignant histiocytic																					1	
Lymphoma malignant lymphocytic							X														3	

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm

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

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

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

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

Number of Days on Study	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	
Carcass ID Number	1 2 6 2	1 2 6 3	1 2 7 1	1 2 8 1	1 2 8 2	1 2 8 3	1 2 8 4	1 2 8 5	1 2 9 1	1 2 9 2	1 2 9 3	1 3 0 1	1 3 0 2	1 3 0 3	1 3 1 1	1 3 1 2	1 3 1 3	1 3 1 4	1 3 1 7	1 3 1 9	**Total Tissues/ Tumors**
Alimentary System																					
Esophagus																					7
Gallbladder																					7
Intestine large																					7
Intestine large, cecum																					5
Intestine large, colon																					7
Intestine large, rectum																					5
Intestine small																					8
Intestine small, duodenum																					5
Intestine small, ileum																					6
Intestine small, jejunum																					5
Liver	+	+				+		+		+				+		+				+	33
Hepatocellular carcinoma	X																				4
Hepatocellular adenoma		X												X						X	8
Hepatocellular adenoma, multiple						X															2
Pancreas																	+				10
Salivary glands																					11
Stomach							+														10
Stomach, forestomach							+														10
Stomach, glandular							+														10
Cardiovascular System																					
Heart																					10
Endocrine System																					
Adrenal gland																					11
Adrenal gland, cortex																					9
Adrenal gland, medulla																					11
Pheochromocytoma benign																					1
Islets, pancreatic																					9
Parathyroid gland																					6
Pituitary gland																					5
Thyroid gland																					8
General Body System																					
None																					

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

Number of Days on Study	0 1 4	0 3 0	0 3 1	1 1 9	1 4 7	2 6 5	2 8 7	3 0 3	3 3 0	3 7 2	5 3 6	6 2 9	6 4 0	6 5 9	6 8 0	6 9 0	6 9 2	7 3 3	7 3 7	7 4 8	7 4 4	7 4 4	7 4 4	7 4 4
Carcass ID Number	0 9 1 1	0 9 4 1	0 9 7 1	0 9 3 1	1 0 9 1	0 9 3 2	0 9 2 1	0 9 3 3	0 9 3 4	0 9 5 1	0 9 4 2	1 0 8 5	0 9 2 2	1 1 0 5	1 3 1 1	1 1 9 5	0 9 1 1	0 9 3 2	1 1 9 1	0 9 0 2	0 9 6 1	0 9 6 2	0 9 6 3	0 9 6 4	1 0 8 1
Genital System																								
Ductus deferens																+								
Epididymis	+	+	+	+		+	+	+	+	+	+					+								
Penis						+	+																	
Preputial gland																								
Prostate	+	+	+	+		+	+	+	+	M	+					+								
Seminal vesicle	+	+	+	+		+	+	M	+	+	+			+	+	+								
Testes	+	+	+	+		+	+	+	+	+	+			+			+							
Fibrosarcoma, metastatic, skin														X										
Hematopoietic System																								
Bone marrow	+	+	+	+		+	+	+	+	+	+													
Lymph node	+	+	+	+		+	+	+	+	+	+													
Lymph node, bronchial	M	M	M	M		+	+	+	M	M	M													
Lymph node, mandibular	+	+	M	+		+	M	+	+	+	+													
Lymph node, mediastinal	+	M	+	M		M	M	M	M	+	M													
Lymph node, mesenteric	A	M	M	+		+	M	M	M	M	+													
Spleen	+	+	+	+		+	+	+	+	A	+				+	+								
Thymus	M	M	M	M		+	M	M	M	M	M													
Integumentary System																								
Mammary gland	M	M	M	M		M	M	M	M	M	M													
Skin	+	+	+	+		+	+	+	+	+	+		+	+			+	+		+				
Subcutaneous tissue, fibroma																								
Subcutaneous tissue, fibrosarcoma											X		X	X				X		X				
Subcutaneous tissue, sarcoma																X								
Musculoskeletal System																								
Bone	+	+	+	+		+	+	+	+	+	+							+						
Skeletal muscle		+	+																					
Sarcoma, metastatic, skin																								
Nervous System																								
Brain	+	+	+	+		+	+	+	+	+	+													

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

Number of Days on Study	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 5
Carcass ID Number	1 0 8 2	1 0 8 3	1 0 8 4	1 1 0 2	1 1 0 3	1 1 0 4	1 1 1 1	1 1 1 2	1 1 1 3	1 1 1 4	1 1 8 1	1 1 8 2	1 1 8 3	1 1 8 4	1 1 9 1	1 1 9 2	1 2 0 1	1 2 0 2	1 2 0 3	1 2 3 1	1 2 3 2	1 2 4 1	1 2 4 2	1 2 4 3	1 2 6 1
Genital System																									
Ductus deferens																									
Epididymis																									
Penis																									
Preputial gland																									
Prostate																									
Seminal vesicle						+												+							
Testes																									
Fibrosarcoma, metastatic, skin																									
Hematopoietic System																									
Bone marrow																									
Lymph node			+															+							
Lymph node, bronchial																									
Lymph node, mandibular																									
Lymph node, mediastinal																		+							
Lymph node, mesenteric			+																						
Spleen					+					+								+			+				
Thymus																									
Integumentary System																									
Mammary gland																									
Skin			+															+							
Subcutaneous tissue, fibroma																									
Subcutaneous tissue, fibrosarcoma																									
Subcutaneous tissue, sarcoma																		X							
Musculoskeletal System																									
Bone																									
Skeletal muscle			+															+							
Sarcoma, metastatic, skin																		X							
Nervous System																									
Brain																									

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

Number of Days on Study	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	
Carcass ID Number	1 2 6 2	1 2 6 3	1 2 7 1	1 2 8 1	1 2 8 2	1 2 8 3	1 2 8 4	1 2 8 5	1 2 9 1	1 2 9 2	1 2 9 3	1 3 0 1	1 3 0 2	1 3 0 3	1 3 1 1	1 3 1 2	1 3 1 3	1 4 1 1	1 7 1 1	1 9 1 3	**Total Tissues/ Tumors**
Genital System																					
Ductus deferens																					1
Epididymis																					11
Penis																					2
Preputial gland					+																1
Prostate										+											11
Seminal vesicle													+				+				16
Testes																					12
Fibrosarcoma, metastatic, skin																					1
Hematopoietic System																					
Bone marrow																					10
Lymph node		+					+														14
Lymph node, bronchial		+					+														5
Lymph node, mandibular																					8
Lymph node, mediastinal																					4
Lymph node, mesenteric																					4
Spleen		+									+					+					18
Thymus																					1
Integumentary System																					
Mammary gland																					
Skin						+			+	+		+									21
Subcutaneous tissue, fibroma									X	X		X									3
Subcutaneous tissue, fibrosarcoma						X															6
Subcutaneous tissue, sarcoma																					2
Musculoskeletal System																					
Bone																					11
Skeletal muscle																					4
Sarcoma, metastatic, skin																					1
Nervous System																					
Brain																					10

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

Number of Days on Study	0 1 4	0 3 0	0 3 1	1 1 9	1 4 7	2 6 5	2 8 7	3 0 3	3 3 0	3 7 2	5 3 6	6 2 9	6 4 0	6 5 9	6 8 0	6 9 0	6 9 2	6 9 3	7 3 7	7 3 8	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4
Carcass ID Number	0 9 1 1	0 9 4 1	0 9 7 1	0 9 3 1	1 0 9 1	0 9 3 2	0 9 2 1	0 9 3 3	0 9 3 4	0 9 5 1	0 9 4 2	1 0 8 5	0 9 2 2	1 1 0 5	1 3 9 1	1 1 1 5	1 9 6 1	0 9 8 1	0 3 9 2	1 1 0 1	1 9 6 2	0 9 6 3	0 9 6 4	0 9 6 5	1 0 8 1
Respiratory System																									
Larynx	+	+	+	+		+	+	+	+	A	+														
Lung	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar adenoma, multiple																									
Alveolar/bronchiolar carcinoma												X									X				
Fibrosarcoma, metastatic											X														
Fibrosarcoma, metastatic, skin														X											
Sarcoma, metastatic, skin																									
Nose	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+		+	+	M	+	+	+														
Special Senses System																									
Eye		+	+			+																			
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney	+	+	+	+		+	+	+	+	+	+			+	+			+							
Urinary bladder	+	+	+	+		+	+	A	+	M	+				+	+									
Systemic Lesions																									
Multiple organs	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																									

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

Number of Days on Study	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 5
Carcass ID Number	1 0 8 2	1 0 8 3	1 0 8 4	1 1 0 2	1 1 0 3	1 1 0 4	1 1 1 1	1 1 1 2	1 1 1 3	1 1 1 4	1 1 8 1	1 1 8 2	1 1 8 3	1 1 8 4	1 1 9 1	1 1 9 2	1 2 0 1	1 2 0 2	1 2 0 3	1 2 3 1	1 2 3 2	1 2 4 1	1 2 4 2	1 2 4 3	1 2 6 1
Respiratory System																									
Larynx																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma		X		X			X				X			X								X	X	X	X
Alveolar/bronchiolar adenoma, multiple												X													
Alveolar/bronchiolar carcinoma							X																		
Fibrosarcoma, metastatic																									
Fibrosarcoma, metastatic, skin																									
Sarcoma, metastatic, skin																		X							
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea																									
Special Senses System																									
Eye									+																
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney						+																+			
Urinary bladder																				+			+		
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic			X																						
Lymphoma malignant lymphocytic										X															

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

Number of Days on Study	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	
Carcass ID Number	1 2 6 2	1 2 6 3	1 2 7 1	1 2 8 1	1 2 8 2	1 2 8 3	1 2 8 4	1 2 8 5	1 2 9 1	1 2 9 2	1 2 9 3	1 3 0 1	1 3 0 2	1 3 0 3	1 3 1 1	1 3 1 2	1 3 1 3	1 3 4 1	1 3 7 1	1 3 9 3		**Total Tissues/ Tumors**
Respiratory System																						
Larynx																						9
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		69
Alveolar/bronchiolar adenoma			X							X									X	X		13
Alveolar/bronchiolar adenoma, multiple									X													2
Alveolar/bronchiolar carcinoma																						3
Fibrosarcoma, metastatic																						1
Fibrosarcoma, metastatic, skin																						1
Sarcoma, metastatic, skin																						1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		69
Trachea																						9
Special Senses System																						
Eye																						4
Harderian gland																			+			1
Adenoma																			X			1
Urinary System																						
Kidney										+												16
Urinary bladder				+	+					+						+						16
Systemic Lesions																						
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		69
Lymphoma malignant histiocytic																						1
Lymphoma malignant lymphocytic			X																			2

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm

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

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

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

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 3 8	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	
Carcass ID Number	0 4 0 5	0 5 2 1	0 5 2 2	0 5 2 3	0 5 2 4	0 5 3 1	0 5 3 2	0 5 3 3	0 5 3 4	0 5 4 1	0 5 4 2	0 5 4 3	0 5 4 4	0 5 4 5	0 5 5 1	0 5 5 2	0 5 5 3	0 5 5 4	0 5 5 5	0 5 5 5	**Total Tissues/ Tumors**
Alimentary System																					
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	64
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	61
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	64
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Intestine small, duodenum	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	64
Adenocarcinoma																					1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	64
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	64
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Hepatocellular carcinoma																					4
Hepatocellular adenoma											X					X					3
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Cardiovascular System																					
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Endocrine System																					
Adrenal gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	65
Adrenal gland, cortex	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	65
Adenoma				X																	2
Adrenal gland, medulla	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	64
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	62
Pituitary gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	M	58
Pars distalis, adenoma																					1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
General Body System																					
None																					

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	1 8 2	1 8 2	1 9 6	2 8 0	3 0 2	5 0 4	5 4 7	5 7 8	6 4 4	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8
Carcass ID Number	0 3 1 5	0 5 3 5	0 3 5 4	0 3 2 1	0 3 2 5	0 3 4 5	0 3 5 5	0 3 7 3	0 3 3 1	0 3 1 1	0 3 1 2	0 3 1 3	0 3 1 4	0 3 2 2	0 3 2 3	0 3 2 4	0 3 3 2	0 3 3 3	0 3 3 4	0 3 3 5	0 3 4 1	0 3 4 2	0 3 4 3	0 3 4 4	0 3 4 1	0 3 5 1
Genital System																										
Epididymis	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																										
Bone marrow	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, bronchial	+		+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Lymph node, mandibular	+		+	+	+	+	+	+	+	M	+	+	+	+	M	M	M	+	+	+	+	+	+	+	+	M
Lymph node, mediastinal	+		M	+	M	+	+	+	M	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	M
Lymph node, mesenteric	+		+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+		M	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																										
Mammary gland	M		M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																										
Bone	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																										
Brain	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																										
Larynx	+		+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Lung	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																X	X									
Alveolar/bronchiolar adenoma, multiple									X																	
Alveolar/bronchiolar carcinoma											X															X
Sarcoma, metastatic, uncertain primary site	X																									
Nose	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8
Carcass ID Number	0 3 5 2	0 3 5 3	0 3 6 1	0 3 6 2	0 3 6 3	0 3 6 4	0 3 6 5	0 3 7 1	0 3 7 2	0 3 7 4	0 3 7 5	0 3 8 1	0 3 8 2	0 3 8 3	0 3 8 4	0 3 8 5	0 3 9 1	0 3 9 2	0 3 9 3	0 3 9 4	0 3 9 5	0 4 0 1	0 4 0 2	0 4 0 3	0 4 0 4
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, bronchial	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mediastinal	+	M	+	+	M	M	M	+	+	+	+	+	M	M	+	M	M	+	+	M	+	+	+	+	M
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma	X			X													X			X				X
Alveolar/bronchiolar adenoma, multiple														X									X		
Alveolar/bronchiolar carcinoma									X																
Sarcoma, metastatic, uncertain primary site																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 3 8	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	
Carcass ID Number	0 4 0 5	0 5 2 1	0 5 2 2	0 5 2 3	0 5 2 4	0 5 3 1	0 5 3 2	0 5 3 3	0 5 3 4	0 5 4 1	0 5 4 2	0 5 4 3	0 5 4 4	0 5 4 5	0 5 5 1	0 5 5 2	0 5 5 3	0 5 5 4	0 5 5 5	**Total Tissues/ Tumors**
Genital System																				
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Hematopoietic System																				
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Lymph node, bronchial	+	+	M	M	M	M	+	+	+	M	+	+	+	+	+	+	+	+	M	57
Lymph node, mandibular	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	59
Lymph node, mediastinal	+	+	+	+	+	+	+	M	M	M	M	+	+	M	M	M	M	+	+	43
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Thymus	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	63
Integumentary System																				
Mammary gland	M	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M	M	M	1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Musculoskeletal System																				
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Nervous System																				
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Respiratory System																				
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	64
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Alveolar/bronchiolar adenoma									X			X				X	X	X		12
Alveolar/bronchiolar adenoma, multiple																				3
Alveolar/bronchiolar carcinoma												X								4
Sarcoma, metastatic, uncertain primary site																				1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

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

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

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

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 3 8	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	
Carcass ID Number	0 4 0 5	0 5 2 1	0 5 2 2	0 5 2 3	0 5 2 4	0 5 3 1	0 5 3 2	0 5 3 3	0 5 3 4	0 5 4 1	0 5 4 2	0 5 4 3	0 5 4 4	0 5 4 5	0 5 5 1	0 5 5 2	0 5 5 3	0 5 5 4	0 5 5 5	0 5 5 5	**Total Tissues/ Tumors**
Special Senses System																					
Ear																					1
Eye						+															4
Harderian gland																					1
Adenoma																					1
Urinary System																					
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Systemic Lesions																					
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Lymphoma malignant lymphocytic																					3

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm

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

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

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

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	
Carcass ID Number	0 7 0 5	0 8 2 1	0 8 2 3	0 8 2 5	0 8 3 1	0 8 3 2	0 8 3 3	0 8 3 4	0 8 3 5	0 8 4 1	0 8 4 2	0 8 4 3	0 8 4 4	0 8 4 5	0 8 5 1	0 8 5 2	0 8 5 3	0 8 5 4	**Total Tissues/ Tumors**
Alimentary System																			
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Adenocarcinoma																			1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Hemangiosarcoma		X																	1
Hepatocellular carcinoma				X								X							3
Hepatocellular adenoma	X						X		X	X							X		12
Hepatocellular adenoma, multiple																		X	1
Mesentery																			1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Cardiovascular System																			
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Endocrine System																			
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	66
Pheochromocytoma benign																			1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Pituitary gland	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	55
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
General Body System																			
None																			

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	0 1 4	4 9 3	6 1 1	6 1 6	6 3 1	6 5 6	6 7 2	6 9 6	7 0 0	7 0 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2
Carcass ID Number	0 6 9 1	0 6 1 4	0 6 8 2	0 6 7 1	0 7 0 1	0 6 3 5	0 6 2 2	0 6 7 2	0 6 2 3	0 8 5 5	0 6 1 1	0 6 1 2	0 6 1 3	0 6 1 5	0 6 2 1	0 6 2 4	0 6 2 5	0 6 3 1	0 6 3 2	0 6 3 3	0 6 3 4	0 6 4 1	0 6 4 2	0 6 4 3	0 6 4 4
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Penis					+																				
Preputial gland							+																		
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Blood								+																	
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, bronchial	M	+	M	+	+	+	M	+	M	+	M	+	+	M	+	M	+	+	+	+	M	+	M	M	M
Lymph node, mandibular	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mediastinal	M	M	+	M	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	M	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	M	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibroma																									
Subcutaneous tissue, fibrosarcoma			X	X																					
Subcutaneous tissue, fibrous histiocytoma									X																
Subcutaneous tissue, neurofibrosarcoma		X																							
Subcutaneous tissue, sarcoma								X							X										
Subcutaneous tissue, sarcoma, multiple																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3
Carcass ID Number	0 6 4 5	0 6 5 1	0 6 5 2	0 6 5 3	0 6 5 4	0 6 5 5	0 6 6 1	0 6 6 2	0 6 6 3	0 6 6 4	0 6 6 5	0 6 7 4	0 6 7 3	0 6 7 5	0 6 8 1	0 6 8 3	0 6 8 4	0 6 8 5	0 6 9 2	0 6 9 3	0 6 9 4	0 6 9 5	0 7 0 2	0 7 0 3	0 7 0 4
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Penis																									
Preputial gland	+		+																						
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Blood																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, bronchial	+	+	M	+	+	+	M	+	+	+	M	+	+	+	+	+	+	M	+	M	M	+	+	+	M
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Lymph node, mediastinal	+	+	+	M	M	M	+	M	M	M	+	+	+	+	+	+	+	M	+	+	M	M	+	M	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibroma																		X							
Subcutaneous tissue, fibrosarcoma														X				X							
Subcutaneous tissue, fibrous histiocytoma																									
Subcutaneous tissue, neurofibrosarcoma																									
Subcutaneous tissue, sarcoma																									
Subcutaneous tissue, sarcoma, multiple												X													
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	
Carcass ID Number	0 7 0 5	0 8 2 1	0 8 2 3	0 8 2 5	0 8 3 1	0 8 3 2	0 8 3 3	0 8 3 4	0 8 3 5	0 8 4 1	0 8 4 2	0 8 4 3	0 8 4 4	0 8 4 5	0 8 5 1	0 8 5 2	0 8 5 3	0 8 5 4	**Total Tissues/ Tumors**
Genital System																			
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Penis																			1
Preputial gland																			3
Prostate	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Hematopoietic System																			
Blood																			1
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Lymph node, bronchial	M	+	+	M	+	+	+	+	+	+	M	M	M	+	+	M	M	+	43
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Lymph node, mediastinal	+	+	+	M	M	M	+	+	M	+	+	M	+	+	+	+	+	M	47
Lymph node, mesenteric	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	63
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Thymus	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	63
Integumentary System																			
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Subcutaneous tissue, fibroma																			1
Subcutaneous tissue, fibrosarcoma																			4
Subcutaneous tissue, fibrous histiocytoma																			1
Subcutaneous tissue, neurofibrosarcoma																			1
Subcutaneous tissue, sarcoma																			2
Subcutaneous tissue, sarcoma, multiple																			1
Musculoskeletal System																			
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Nervous System																			
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	0 1 4	4 9 3	6 1 1	6 1 6	6 3 1	6 5 6	6 7 2	6 9 6	7 0 0	7 0 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2
Carcass ID Number	0 6 9 1	0 6 1 4	0 6 8 2	0 6 7 1	0 7 0 1	0 6 3 5	0 6 2 2	0 6 7 2	0 6 2 3	0 8 5 5	0 6 1 1	0 6 1 2	0 6 1 3	0 6 1 5	0 6 2 1	0 6 2 4	0 6 2 5	0 6 3 1	0 6 3 2	0 6 3 3	0 6 3 4	0 6 4 1	0 6 4 2	0 6 4 3	0 6 4 4
Respiratory System																									
Larynx	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma														X					X						
Alveolar/bronchiolar adenoma, multiple						X																			
Alveolar/bronchiolar carcinoma														X				X							
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear					+																				
Eye	+																								
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma												X													
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia granulocytic					X																				
Lymphoma malignant lymphocytic										X															

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3
Carcass ID Number	0 6 4 5	0 6 5 1	0 6 5 2	0 6 5 3	0 6 5 4	0 6 5 5	0 6 6 1	0 6 6 2	0 6 6 3	0 6 6 4	0 6 6 5	0 6 7 4	0 6 7 3	0 6 7 5	0 6 8 1	0 6 8 3	0 6 8 4	0 6 8 5	0 6 9 2	0 6 9 3	0 6 9 4	0 6 9 5	0 7 0 2	0 7 0 3	0 7 0 4
Respiratory System																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma								X						X					X						
Alveolar/bronchiolar adenoma, multiple										X			X												
Alveolar/bronchiolar carcinoma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																									
Eye																									
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia granulocytic																									
Lymphoma malignant lymphocytic																									

TABLE A2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	
Carcass ID Number	0 7 0 5	0 8 2 1	0 8 2 3	0 8 2 5	0 8 3 1	0 8 3 2	0 8 3 3	0 8 3 4	0 8 3 5	0 8 4 1	0 8 4 2	0 8 4 3	0 8 4 4	0 8 4 5	0 8 5 1	0 8 5 2	0 8 5 3	0 8 5 4	**Total Tissues/ Tumors**	
Respiratory System																				
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67	
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68	
Alveolar/bronchiolar adenoma		X	X																7	
Alveolar/bronchiolar adenoma, multiple															X		X		5	
Alveolar/bronchiolar carcinoma		X																	3	
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68	
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67	
Special Senses System																				
Ear																			1	
Eye						+	+												3	
Harderian gland	+																		1	
Adenoma	X																		1	
Urinary System																				
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68	
Carcinoma																			1	
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68	
Systemic Lesions																				
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68	
Leukemia granulocytic																			1	
Lymphoma malignant lymphocytic																			1	

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Inhalation Study of Naphthalene

	0 ppm	10 ppm	30 ppm
Adrenal Medulla: Benign Pheochromocytoma			
Overall rates[a]	2/66 (3%)	1/11 (9%)[e]	1/130 (1%)
Adjusted rates[b]	6.0%		0.9%
Terminal rates[c]	1/25 (4%)		1/115 (1%)
First incidence (days)	389		736 (T)
Life table tests[d]			P=0.104N
Logistic regression tests[d]			P=0.291N
Fisher exact test[d]			P=0.263N
Liver: Hepatocellular Adenoma			
Overall rates	3/70 (4%)	10/33 (30%)[e]	16/135 (12%)
Adjusted rates	9.3%		13.6%
Terminal rates	1/26 (4%)		16/118 (14%)
First incidence (days)	382		736 (T)
Life table tests			P=0.493
Logistic regression tests			P=0.232
Fisher exact test			P=0.059
Liver: Hepatocellular Carcinoma			
Overall rates	6/70 (9%)	4/33 (12%)[e]	7/135 (5%)
Adjusted rates	19.2%		5.9%
Terminal rates	3/26 (12%)		7/118 (6%)
First incidence (days)	655		736 (T)
Life table tests			P=0.014N
Logistic regression tests			P=0.048N
Fisher exact test			P=0.256N
Liver: Hepatocellular Adenoma or Carcinoma			
Overall rates	8/70 (11%)	14/33 (42%)[e]	23/135 (17%)
Adjusted rates	23.7%		19.5%
Terminal rates	3/26 (12%)		23/118 (19%)
First incidence (days)	382		736 (T)
Life table tests			P=0.201N
Logistic regression tests			P=0.530N
Fisher exact test			P=0.197
Lung: Alveolar/bronchiolar Adenoma			
Overall rates	7/70 (10%)	15/69 (22%)	27/135 (20%)
Adjusted rates	25.7%	28.8%	22.7%
Terminal rates	6/26 (23%)	15/52 (29%)	26/118 (22%)
First incidence (days)	714	736 (T)	656
Life table tests	P=0.274N	P=0.529	P=0.441N
Logistic regression tests	P=0.411N	P=0.450	P=0.541
Cochran-Armitage test[d]	P=0.108		
Fisher exact test		P=0.047	P=0.049

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Inhalation Study of Naphthalene
(continued)

	0 ppm	10 ppm	30 ppm
Lung: Alveolar/bronchiolar Carcinoma			
Overall rates	0/70 (0%)	3/69 (4%)	7/135 (5%)
Adjusted rates	0.0%	5.5%	5.9%
Terminal rates	0/26 (0%)	2/52 (4%)	7/118 (6%)
First incidence (days)	-[f]	629	736 (T)
Life table tests	P=0.256	P=0.246	P=0.222
Logistic regression tests	P=0.180	P=0.176	P=0.222
Cochran-Armitage test	P=0.079		
Fisher exact test		P=0.120	P=0.051
Lung: Alveolar/bronchiolar Adenoma or Carcinoma			
Overall rates	7/70 (10%)	17/69 (25%)	31/135 (23%)
Adjusted rates	25.7%	31.9%	26.0%
Terminal rates	6/26 (23%)	16/52 (31%)	30/118 (25%)
First incidence (days)	714	629	656
Life table tests	P=0.363N	P=0.384	P=0.580N
Logistic regression tests	P=0.530	P=0.212	P=0.394
Cochran-Armitage test	P=0.054		
Fisher exact test		P=0.019	P=0.016
Skin (Subcutaneous Tissue): Fibroma			
Overall rates	4/70 (6%)	3/69 (4%)	1/135 (1%)
Adjusted rates	15.4%	5.8%	0.8%
Terminal rates	4/26 (15%)	3/52 (6%)	1/118 (1%)
First incidence (days)	736 (T)	736 (T)	736 (T)
Life table tests	P=0.002N	P=0.165N	P=0.001N
Logistic regression tests	P=0.002N	P=0.165N	P=0.001N
Cochran-Armitage test	P=0.030N		
Fisher exact test		P=0.508N	P=0.047N
Skin (Subcutaneous Tissue): Fibrosarcoma			
Overall rates	11/70 (16%)	6/69 (9%)	4/135 (3%)
Adjusted rates	31.0%	10.4%	3.2%
Terminal rates	4/26 (15%)	2/52 (4%)	2/118 (2%)
First incidence (days)	558	536	611
Life table tests	P≤0.001N	P=0.016N	P≤0.001N
Logistic regression tests	P≤0.001N	P=0.055N	P≤0.001N
Cochran-Armitage test	P=0.001N		
Fisher exact test		P=0.158N	P=0.002N
Skin (Subcutaneous Tissue): Neurofibrosarcoma, Fibrosarcoma, or Sarcoma			
Overall rates	19/70 (27%)	8/69 (12%)	8/135 (6%)
Adjusted rates	47.2%	13.8%	6.4%
Terminal rates	6/26 (23%)	3/52 (6%)	4/118 (3%)
First incidence (days)	558	536	493
Life table tests	P≤0.001N	P≤0.001N	P≤0.001N
Logistic regression tests	P≤0.001N	P=0.001N	P≤0.001N
Cochran-Armitage test	P≤0.001N		
Fisher exact test		P=0.017N	P≤0.001N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Inhalation Study of Naphthalene
(continued)

	0 ppm	10 ppm	30 ppm
Skin (Subcutaneous Tissue): Fibroma, Fibrosarcoma, Neurofibrosarcoma, or Sarcoma			
Overall rates	23/70 (33%)	11/69 (16%)	8/135 (6%)
Adjusted rates	57.8%	19.1%	6.4%
Terminal rates	10/26 (38%)	6/52 (12%)	4/118 (3%)
First incidence (days)	558	536	493
Life table tests	P≤0.001N	P≤0.001N	P≤0.001N
Logistic regression tests	P≤0.001N	P≤0.001N	P≤0.001N
Cochran-Armitage test	P≤0.001N		
Fisher exact test		P=0.016N	P≤0.001N
Skin (Subcutaneous Tissue): Sarcoma			
Overall rates	6/70 (9%)	2/69 (3%)	3/135 (2%)
Adjusted rates	17.7%	3.7%	2.5%
Terminal rates	2/26 (8%)	1/52 (2%)	2/118 (2%)
First incidence (days)	652	692	696
Life table tests	P=0.005N	P=0.031N	P=0.001N
Logistic regression tests	P=0.013N	P=0.054N	P=0.006N
Cochran-Armitage test	P=0.048N		
Fisher exact test		P=0.142N	P=0.044N
All Organs: Malignant Lymphoma (Histiocytic or Lymphocytic)			
Overall rates	4/70 (6%)	3/69 (4%)	4/135 (3%)
Adjusted rates	12.5%	5.8%	3.3%
Terminal rates	2/26 (8%)	3/52 (6%)	2/118 (2%)
First incidence (days)	282	736 (T)	280
Life table tests	P=0.057N	P=0.205N	P=0.059N
Logistic regression tests	P=0.218N	P=0.389N	P=0.332N
Cochran-Armitage test	P=0.237N		
Fisher exact test		P=0.508N	P=0.272N
All Organs: Benign Tumors			
Overall rates	15/70 (21%)	24/69 (35%)	44/135 (33%)
Adjusted rates	48.6%	45.2%	36.6%
Terminal rates	11/26 (42%)	23/52 (44%)	42/118 (36%)
First incidence (days)	382	536	504
Life table tests	P=0.052N	P=0.310N	P=0.075N
Logistic regression tests	P=0.346N	P=0.393	P=0.534N
Cochran-Armitage test	P=0.124		
Fisher exact test		P=0.059	P=0.064
All Organs: Malignant Tumors			
Overall rates	26/70 (37%)	16/69 (23%)	32/135 (24%)
Adjusted rates	60.1%	27.4%	25.1%
Terminal rates	9/26 (35%)	10/52 (19%)	23/118 (19%)
First incidence (days)	282	536	182
Life table tests	P≤0.001N	P≤0.001N	P≤0.001N
Logistic regression tests	P=0.006N	P=0.002N	P=0.001N
Cochran-Armitage test	P=0.058N		
Fisher exact test		P=0.054N	P=0.032N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Inhalation Study of Naphthalene
(continued)

	0 ppm	10 ppm	30 ppm
All Organs: Benign and Malignant Tumors			
Overall rates	36/70 (51%)	36/69 (52%)	67/135 (50%)
Adjusted rates	79.7%	62.0%	51.9%
Terminal rates	17/26 (65%)	30/52 (58%)	56/118 (47%)
First incidence (days)	282	536	182
Life table tests	P≤0.001N	P≤0.001N	P≤0.001N
Logistic regression tests	P=0.011N	P=0.036N	P=0.014N
Cochran-Armitage test	P=0.410N		
Fisher exact test		P=0.533	P=0.461N

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

TABLE A4a
Historical Incidence of Lung Alveolar/bronchiolar Tumors in Male B6C3F$_1$ Mice in Inhalation Studies[a]

	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Overall Historical Incidence			
Total	69/478 (14.4%)	30/478 (6.3%)	94/478 (19.7%)
Standard deviation	5.5	5.5	8.1
Range	6%-24%	0%-14%	10%-30%

[a] Data as of 15 September 1990

TABLE A4b
Historical Incidence of Subcutaneous Mesenchymal Tumors in Male B6C3F$_1$ Mice in Inhalation Studies[a]

	Incidence in Controls		
	Neurofibrosarcoma	Fibroma, Fibrosarcoma or Sarcoma	Fibroma, Fibrosarcoma, Neurofibrosarcoma or Sarcoma
Overall Historical Incidence			
Total	2/479 (0.4%)	23/479 (4.8%)	25/479 (5.2%)
Standard deviation	1.0%	9.9%	7.0%
Range	0%-3%	0%-30%	0%-33%

[a] Data as of 15 September 1990

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Naphthalene[a]

	0 ppm	10 ppm	30 ppm	30 ppm
Disposition Summary				
Animals initially in study	75	75	75	75
Special study animals[b]	5	5	6	7
Early deaths				
Natural death	31	10	2	5
Moribund	13	7	3	5
Accidental deaths			2	
Survivors				
Died last week of study		2	1	
Terminal sacrifice	26	50	59	58
Missing		1	2	
Animals examined microscopically	70	69	67	68
Alimentary System				
Gallbladder	(57)	(7)	(61)	(65)
Dilatation		1 (14%)		
Hemorrhage, focal				1 (2%)
Epithelium, hyperplasia, papillary, focal			1 (2%)	
Intestine large, cecum	(56)	(5)	(65)	(65)
Hyperplasia, lymphoid, focal			1 (2%)	1 (2%)
Inflammation, diffuse	1 (2%)			
Intestine large, colon	(56)	(7)	(65)	(68)
Parasite metazoan			4 (6%)	3 (4%)
Intestine large, rectum	(58)	(5)	(64)	(66)
Diverticulum	1 (2%)			
Hemorrhage, focal				1 (2%)
Inflammation, diffuse	1 (2%)			
Parasite metazoan			1 (2%)	
Prolapse				1 (2%)
Intestine small	(57)	(8)	(65)	(66)
Serosa, fibrosis		1 (13%)		
Intestine small, duodenum	(49)	(5)	(64)	(66)
Submucosa, dilatation, focal			1 (2%)	
Intestine small, ileum	(51)	(6)	(64)	(66)
Inflammation, multifocal	1 (2%)			
Intestine small, jejunum	(51)	(5)	(64)	(66)
Hyperplasia, lymphoid, focal				2 (3%)
Liver	(70)	(33)	(67)	(68)
Basophilic focus	2 (3%)		5 (7%)	
Basophilic focus, multifocal			1 (1%)	
Clear cell focus			1 (1%)	2 (3%)
Clear cell focus, multifocal				1 (1%)
Cyst, focal				1 (1%)
Cytoplasmic alteration, focal				1 (1%)
Degeneration, focal		1 (3%)		1 (1%)
Eosinophilic focus				1 (1%)
Fatty change, focal	2 (3%)			
Fibrosis, focal			1 (1%)	
Hematopoietic cell proliferation, focal	1 (1%)		2 (3%)	2 (3%)
Hematopoietic cell proliferation, multifocal	1 (1%)		1 (1%)	1 (1%)
Hematopoietic cell proliferation granulocytic	1 (1%)			
Hemorrhage, focal				1 (1%)

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Naphthalene (continued)

	0 ppm	10 ppm	30 ppm	30 ppm
Alimentary System (continued)				
Liver (continued)				
Infarct, focal				1 (1%)
Infiltration cellular, lymphocyte, focal			1 (1%)	2 (3%)
Infiltration cellular, lymphocyte, multifocal			3 (4%)	1 (1%)
Mineralization, focal			1 (1%)	
Mixed cell focus			2 (3%)	1 (1%)
Necrosis, focal		2 (6%)		
Necrosis, multifocal	4 (6%)	2 (6%)		1 (1%)
Thrombus, multifocal				1 (1%)
Hepatocyte, cytomegaly, focal				1 (1%)
Serosa, fibrosis		1 (3%)		
Sinusoid, ectasia, focal	1 (1%)			1 (1%)
Mesentery	(1)			(1)
Fat, necrosis, focal	1 (100%)			
Pancreas	(67)	(10)	(66)	(68)
Atrophy	3 (4%)		1 (2%)	4 (6%)
Infiltration cellular, lymphocyte, focal	3 (4%)		1 (2%)	1 (1%)
Infiltration cellular, lymphocyte, multifocal	3 (4%)		3 (5%)	3 (4%)
Infiltration cellular, polymorphonuclear	1 (1%)			
Inflammation, chronic active, diffuse		1 (10%)		
Inflammation, focal			1 (2%)	1 (1%)
Salivary glands	(69)	(11)	(67)	(68)
Atrophy, multifocal				1 (1%)
Infiltration cellular, lymphocyte, focal	1 (1%)		8 (12%)	4 (6%)
Infiltration cellular, lymphocyte, multifocal	13 (19%)	1 (9%)	14 (21%)	16 (24%)
Infiltration cellular, polymorphonuclear	1 (1%)			
Stomach, forestomach	(63)	(10)	(65)	(68)
Hyperplasia, focal			1 (2%)	1 (1%)
Inflammation, focal	1 (2%)			
Stomach, glandular	(62)	(10)	(65)	(68)
Cyst, focal				1 (1%)
Infiltration cellular, polymorphonuclear	1 (2%)			
Inflammation, acute, focal	1 (2%)		1 (2%)	
Mineralization, focal			1 (2%)	
Cardiovascular System				
Heart	(70)	(10)	(67)	(68)
Infiltration cellular, polymorphonuclear	1 (1%)			
Myocardium, inflammation, multifocal	1 (1%)			1 (1%)
Valve, pigmentation, focal	5 (7%)		7 (10%)	5 (7%)
Valve, pigmentation, multifocal	4 (6%)		3 (4%)	3 (4%)
Ventricle, thrombus, focal				1 (1%)

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Naphthalene (continued)

	0 ppm	10 ppm	30 ppm	30 ppm
Endocrine System				
Adrenal gland	(66)	(11)	(65)	(68)
Capsule, hyperplasia, focal			3 (5%)	2 (3%)
Capsule, hyperplasia, multifocal	45 (68%)	2 (18%)	49 (75%)	49 (72%)
Adrenal gland, cortex	(66)	(9)	(65)	(68)
Atrophy, focal	1 (2%)			
Atypical cells, focal				1 (1%)
Clear cell focus	1 (2%)			
Cyst			1 (2%)	
Focal cellular change	1 (2%)		3 (5%)	
Giant cell, multifocal				1 (1%)
Hyperplasia, focal				1 (1%)
Hypertrophy, focal	2 (3%)		4 (6%)	1 (1%)
Adrenal gland, medulla	(66)	(11)	(64)	(66)
Hyperplasia	1 (2%)	1 (9%)		
Islets, pancreatic	(67)	(9)	(66)	(68)
Infiltration cellular, polymorphonuclear	1 (1%)			
Infiltration cellular, polymorphonuclear, focal			1 (2%)	
Parathyroid gland	(64)	(6)	(62)	(66)
Cyst, focal	1 (2%)		4 (6%)	2 (3%)
Ectopic tissue				1 (2%)
Pituitary gland	(52)	(5)	(58)	(55)
Cyst			1 (2%)	
Pars distalis, congestion	1 (2%)			
Thyroid gland	(67)	(8)	(66)	(68)
Cyst			1 (2%)	
Infiltration cellular, lymphocyte, focal				1 (1%)
C-cell, hyperplasia	1 (1%)			
Follicle, dilatation, focal				3 (4%)
Follicular cell, hyperplasia, focal	1 (1%)		1 (2%)	2 (3%)
General Body System				
None				
Genital System				
Ductus deferens		(1)		
Serosa, inflammation, chronic		1 (100%)		
Epididymis	(69)	(11)	(67)	(68)
Granuloma sperm			2 (3%)	1 (1%)
Infiltration cellular, lymphocyte, focal			1 (1%)	
Infiltration cellular, polymorphonuclear	1 (1%)			
Inflammation, focal				1 (1%)
Spermatocele, focal	1 (1%)			1 (1%)
Duct, dilatation, focal			2 (3%)	
Serosa, inflammation, chronic		1 (9%)		
Penis	(2)	(2)		(1)
Inflammation, multifocal	1 (50%)			
Preputial gland	(4)	(1)		(3)
Hyperplasia				1 (33%)
Inflammation	1 (25%)			1 (33%)
Duct, dilatation	3 (75%)	1 (100%)		1 (33%)
Prostate	(65)	(11)	(67)	(66)
Infiltration cellular, lymphocyte	1 (2%)	1 (9%)		1 (2%)
Infiltration cellular, polymorphonuclear	1 (2%)			
Inflammation, acute	8 (12%)	2 (18%)		1 (2%)
Serosa, inflammation, chronic		1 (9%)		

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Naphthalene (continued)

	0 ppm	10 ppm	30 ppm	30 ppm
Genital System (continued)				
Seminal vesicle	(66)	(16)	(67)	(68)
Dilatation	3 (5%)	2 (13%)		1 (1%)
Inflammation, focal	2 (3%)			1 (1%)
Serosa, inflammation, chronic		2 (13%)		
Testes	(69)	(12)	(67)	(68)
Angiectasis, focal			1 (1%)	
Atrophy		1 (8%)	1 (1%)	2 (3%)
Mineralization, focal	4 (6%)		2 (3%)	4 (6%)
Thrombus, focal			1 (1%)	
Bilateral, atrophy	1 (1%)			1 (1%)
Interstitial cell, hyperplasia, multifocal			1 (1%)	
Hematopoietic System				
Blood	(3)			(1)
Leukocytosis	3 (100%)			1 (100%)
Bone marrow	(70)	(10)	(67)	(68)
Angiectasis, focal			1 (1%)	
Congestion				1 (1%)
Hemorrhage, focal			1 (1%)	1 (1%)
Hyperplasia	9 (13%)		1 (1%)	5 (7%)
Myelofibrosis, focal			1 (1%)	
Thrombus	1 (1%)			
Myeloid cell, hyperplasia	1 (1%)			
Lymph node, bronchial	(38)	(5)	(57)	(43)
Giant cell, multifocal			2 (4%)	1 (2%)
Hyperplasia, lymphoid	1 (3%)	1 (20%)	2 (4%)	
Infiltration cellular, polymorphonuclear	1 (3%)			
Pigmentation	3 (8%)		2 (4%)	3 (7%)
Lymphocyte, necrosis		1 (20%)		
Lymph node, mandibular	(61)	(8)	(59)	(66)
Angiectasis	1 (2%)			
Hemorrhage	1 (2%)			
Hyperplasia, lymphoid			2 (3%)	
Infiltration cellular, polymorphonuclear	1 (2%)			
Pigmentation	12 (20%)	1 (13%)	5 (8%)	11 (17%)
Lymphocyte, necrosis, multifocal	1 (2%)			
Lymph node, mediastinal	(37)	(4)	(43)	(47)
Hyperplasia, lymphoid		1 (25%)	1 (2%)	1 (2%)
Infiltration cellular, polymorphonuclear	1 (3%)			
Inflammation, acute		1 (25%)		
Pigmentation	2 (5%)		1 (2%)	3 (6%)
Lymph node, mesenteric	(57)	(4)	(66)	(63)
Angiectasis	1 (2%)			
Erythrophagocytosis	7 (12%)		13 (20%)	13 (21%)
Giant cell, multifocal	11 (19%)		24 (36%)	16 (25%)
Hematopoietic cell proliferation granulocytic	3 (5%)			
Hemorrhage	12 (21%)		16 (24%)	13 (21%)
Hyperplasia, lymphoid	1 (2%)		4 (6%)	4 (6%)
Hyperplasia, plasma cell	1 (2%)			
Infiltration cellular, polymorphonuclear	1 (2%)			
Inflammation, acute	3 (5%)			
Lymphocyte, necrosis, multifocal	1 (2%)		1 (2%)	

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Naphthalene (continued)

	0 ppm	10 ppm	30 ppm	30 ppm
Hematopoietic System (continued)				
Spleen	(69)	(18)	(67)	(68)
Congestion	1 (1%)			1 (1%)
Depletion lymphoid		1 (6%)		
Hematopoietic cell proliferation	20 (29%)	5 (28%)		13 (19%)
Hematopoietic cell proliferation granulocytic	1 (1%)			
Hyperplasia, lymphoid	1 (1%)	1 (6%)	2 (3%)	5 (7%)
Capsule, fibrosis		1 (6%)		
Lymphocyte, necrosis	2 (3%)		1 (1%)	
Thymus	(47)	(1)	(63)	(63)
Cyst	2 (4%)		4 (6%)	2 (3%)
Cyst, multifocal			2 (3%)	2 (3%)
Depletion lymphoid, diffuse	1 (2%)			
Ectopic parathyroid gland, focal				1 (2%)
Hyperplasia, lymphoid, multifocal	1 (2%)			
Epithelial cell, cytoplasmic alteration, focal				1 (2%)
Thymocyte, necrosis	8 (17%)	1 (100%)	1 (2%)	
Integumentary System				
Skin	(69)	(21)	(67)	(68)
Acanthosis, focal	2 (3%)		1 (1%)	
Cyst epithelial inclusion	1 (1%)			
Infiltration cellular, polymorphonuclear	1 (1%)			
Inflammation, focal	5 (7%)	2 (10%)	1 (1%)	2 (3%)
Ulcer	4 (6%)	2 (10%)		
Lymphatic, dilatation				2 (3%)
Prepuce, inflammation, chronic active	1 (1%)			
Prepuce, ulcer	3 (4%)			
Subcutaneous tissue, angiectasis				1 (1%)
Subcutaneous tissue, edema, diffuse	1 (1%)			
Subcutaneous tissue, fibrosis, multifocal	1 (1%)			1 (1%)
Subcutaneous tissue, hemorrhage	1 (1%)			
Sweat gland, ectasia, multifocal			1 (1%)	
Tail, inflammation, necrotizing, multifocal	1 (1%)			
Musculoskeletal System				
Bone	(70)	(11)	(67)	(68)
Vertebra, developmental malformation	1 (1%)			
Vertebra, fracture healed		1 (9%)		
Skeletal muscle		(4)		
Inflammation, chronic		3 (75%)		
Nervous System				
Brain	(70)	(10)	(67)	(68)
Mineralization, focal	1 (1%)		7 (10%)	4 (6%)
Mineralization, multifocal	18 (26%)	1 (10%)	25 (37%)	25 (37%)
Olfactory lobe, hemorrhage, focal			1 (1%)	

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Naphthalene (continued)

	0 ppm	10 ppm	30 ppm	30 ppm
Respiratory System				
Larynx	(69)	(9)	(64)	(67)
Infiltration cellular, lymphocyte, focal			1 (2%)	
Inflammation, focal	1 (1%)			2 (3%)
Epithelium, hyperplasia, focal	2 (3%)			
Lung	(70)	(69)	(67)	(68)
Congestion	9 (13%)	1 (1%)		
Hemorrhage	4 (6%)	3 (4%)	5 (7%)	
Infiltration cellular, lymphocyte	3 (4%)		4 (6%)	4 (6%)
Infiltration cellular, polymorphonuclear	1 (1%)			
Infiltration cellular, histiocyte	1 (1%)	12 (17%)	11 (16%)	5 (7%)
Inflammation		21 (30%)	28 (42%)	28 (41%)
Inflammation, granulomatous		19 (28%)	3 (4%)	12 (18%)
Alveolar epithelium, hyperplasia	2 (3%)	7 (10%)	8 (12%)	4 (6%)
Glands, dilatation	2 (3%)			
Glands, inflammation	7 (10%)	14 (20%)	14 (21%)	8 (12%)
Peribronchiolar, cyst, multifocal	1 (1%)			
Nose	(70)	(69)	(67)	(68)
Congestion, multifocal	3 (4%)			
Hemorrhage			1 (1%)	
Inflammation		67 (97%)	66 (99%)	67 (99%)
Olfactory epithelium, metaplasia		66 (96%)	67 (100%)	67 (99%)
Respiratory epithelium, hyperplasia		66 (96%)	67 (100%)	67 (99%)
Trachea	(70)	(9)	(67)	(67)
Glands, dilatation	2 (3%)		1 (1%)	
Glands, infiltration cellular, lymphocyte, focal			1 (1%)	
Glands, inflammation, suppurative, focal			3 (4%)	
Special Senses System				
Ear	(2)		(1)	(1)
Pinna, inflammation, focal	1 (50%)			
Eye	(3)	(4)	(4)	(3)
Degeneration		1 (25%)		
Dysplasia, multifocal			1 (25%)	
Cornea, inflammation, focal				1 (33%)
Iris, hyperplasia, melanocyte, multifocal				1 (33%)
Lens, cataract	1 (33%)			1 (33%)
Harderian gland	(1)	(1)	(1)	(1)
Cyst, multiple		1 (100%)		
Inflammation, chronic		1 (100%)		
Urinary System				
Kidney	(70)	(16)	(67)	(68)
Congestion, multifocal	1 (1%)			
Degeneration		1 (6%)		
Hydronephrosis	1 (1%)	1 (6%)		
Hypoplasia				1 (1%)
Infarct, focal	1 (1%)		1 (1%)	2 (3%)
Infiltration cellular, lymphocyte, focal			3 (4%)	3 (4%)
Infiltration cellular, lymphocyte, multifocal	17 (24%)	2 (13%)	30 (45%)	18 (26%)
Infiltration cellular, polymorphonuclear	1 (1%)			

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Naphthalene (continued)

	0 ppm	10 ppm	30 ppm	30 ppm
Urinary System (continued)				
Kidney (continued)				
Inflammation, acute, multifocal	2 (3%)	1 (6%)		1 (1%)
Nephropathy	6 (9%)	2 (13%)	8 (12%)	6 (9%)
Pelvis, inflammation, acute	3 (4%)			
Renal tubule, dilatation, focal	1 (1%)	1 (6%)	3 (4%)	
Renal tubule, giant cell, focal				1 (1%)
Renal tubule, hyperplasia, focal	1 (1%)		3 (4%)	
Renal tubule, mineralization, focal	4 (6%)	1 (6%)	1 (1%)	3 (4%)
Urethra	(1)			
Distal, dilatation	1 (100%)			
Epithelium, necrosis, multifocal	1 (100%)			
Urinary bladder	(60)	(16)	(66)	(68)
Dilatation	7 (12%)	6 (38%)	3 (5%)	2 (3%)
Hemorrhage	2 (3%)			
Infiltration cellular, lymphocyte, focal				2 (3%)
Infiltration cellular, lymphocyte, multifocal			6 (9%)	7 (10%)
Infiltration cellular, polymorphonuclear	1 (2%)			
Inflammation, acute	3 (5%)			
Inflammation, chronic active	3 (5%)	2 (13%)		1 (1%)
Serosa, inflammation, chronic		1 (6%)		
Transitional epithelium, hyperplasia, multifocal	1 (2%)			

[a] Incidences are expressed as the ratio of animals with lesions to the number of animals examined microscopically at the site.
[b] Animals from the hematology group that were sacrificed or died prior to becoming part of the 2-year studies; these animals were not examined microscopically.

APPENDIX B
SUMMARY OF LESIONS IN FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF NAPHTHALENE

TABLE B1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Inhalation Study of Naphthalene[a]

	0 ppm	10 ppm	30 ppm	30 ppm
Disposition Summary				
Animals initially in study	75	75	75	75
Special study animals[b]	5	7	6	6
Early deaths				
Natural death	8	6	10	7
Moribund	2	2	6	10
Accidental deaths	1	0		
Survivors				
Died last week of study		1	1	
Terminal sacrifice	59	56	51	50
Missing		3	1	2
Animals examined microscopically	69	65	68	67
Alimentary System				
Gallbladder	(65)	(2)	(60)	(64)
Intestine large, cecum	(66)	(1)	(60)	(64)
Intestine large, colon	(67)	(2)	(62)	(66)
Intestine large, rectum	(67)	(3)	(63)	(63)
Intestine small, duodenum	(66)	(4)	(61)	(63)
Adenocarcinoma		1 (25%)		
Intestine small, ileum	(66)	(1)	(61)	(63)
Sarcoma, metastatic, uncertain primary site				1 (2%)
Intestine small, jejunum	(65)	(1)	(61)	(63)
Liver	(68)	(12)	(67)	(67)
Hepatocellular carcinoma			1 (1%)	
Hepatocellular adenoma	2 (3%)	2 (17%)		2 (3%)
Osteosarcoma, metastatic, bone				1 (1%)
Plasma cell tumor malignant			1 (1%)	
Sarcoma, metastatic, uncertain primary site				1 (1%)
Sarcoma stromal, metastatic		1 (8%)		
Mesentery	(6)		(3)	(3)
Fat, sarcoma, metastatic, uncertain primary site				1 (33%)
Pancreas	(69)	(5)	(65)	(67)
Sarcoma, metastatic, uncertain primary site				1 (1%)
Salivary glands	(68)	(5)	(64)	(67)
Fibrosarcoma				1 (1%)
Stomach, forestomach	(67)	(5)	(67)	(67)
Papilloma squamous	2 (3%)			
Squamous cell carcinoma				1 (1%)
Stomach, glandular	(67)	(5)	(65)	(67)
Cardiovascular System				
Heart	(69)	(4)	(68)	(67)
Fibrous histiocytoma				1 (1%)
Osteosarcoma, metastatic, bone			1 (1%)	
Sarcoma, metastatic, uncertain primary site				1 (1%)

TABLE B1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Inhalation Study of Naphthalene
(continued)

	0 ppm	10 ppm	30 ppm	30 ppm
Endocrine System				
Adrenal gland	(66)	(4)	(67)	(67)
Capsule, adenoma	1 (2%)			
Capsule, sarcoma, metastatic, uncertain primary site				1 (1%)
Adrenal gland, cortex	(66)	(4)	(67)	(67)
Osteosarcoma, metastatic, bone			1 (1%)	
Adrenal gland, medulla	(64)	(4)	(66)	(66)
Osteosarcoma, metastatic, bone			1 (2%)	
Pheochromocytoma benign	1 (2%)			
Islets, pancreatic	(69)	(4)	(66)	(67)
Sarcoma, metastatic, uncertain primary site				1 (1%)
Pituitary gland	(61)	(4)	(50)	(54)
Pars distalis, adenoma	1 (2%)			
Thyroid gland	(69)	(4)	(67)	(66)
General Body System				
Tissue NOS	(1)	(1)	(2)	
Osteosarcoma, metastatic, bone			1 (50%)	
Genital System				
Clitoral gland				(1)
Squamous cell carcinoma				1 (100%)
Ovary	(69)	(14)	(66)	(65)
Cystadenocarcinoma, papillary	1 (1%)	1 (7%)		
Cystadenoma, papillary	2 (3%)		4 (6%)	
Granulosa cell tumor benign	1 (1%)		1 (2%)	
Granulosa-theca tumor benign				1 (2%)
Osteosarcoma, metastatic, bone			1 (2%)	
Sarcoma stromal, metastatic		1 (7%)		
Teratoma benign				1 (2%)
Endothelium, sarcoma stromal, metastatic	1 (1%)			
Oviduct	(2)	(1)	(4)	(4)
Uterus	(69)	(41)	(67)	(66)
Sarcoma stromal	1 (1%)	2 (5%)		
Endometrium, polyp stromal		1 (2%)		1 (2%)
Hematopoietic System				
Bone marrow	(69)	(4)	(68)	(67)
Hemangioma				1 (1%)
Hemangiosarcoma				1 (1%)
Osteosarcoma, metastatic, bone			1 (1%)	
Lymph node	(69)	(9)	(67)	(67)
Iliac, sarcoma stromal, metastatic, uterus	1 (1%)			
Inguinal, osteosarcoma, metastatic, bone				1 (1%)
Renal, sarcoma stromal, metastatic, uterus	1 (1%)			
Lymph node, bronchial	(46)	(1)	(46)	(40)
Sarcoma, metastatic, uncertain primary site				1 (3%)
Lymph node, mandibular	(66)	(6)	(62)	(65)
Fibrosarcoma				1 (2%)

TABLE B1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Inhalation Study of Naphthalene
(continued)

	0 ppm	10 ppm	30 ppm	30 ppm
Hematopoietic System (continued)				
Lymph node, mediastinal	(60)	(6)	(52)	(57)
Sarcoma, metastatic, uncertain primary site				1 (2%)
Lymph node, mesenteric	(67)	(4)	(60)	(62)
Spleen	(67)	(13)	(67)	(67)
Hemangiosarcoma				3 (4%)
Plasma cell tumor malignant			1 (1%)	
Capsule, sarcoma, metastatic, uncertain primary site				1 (1%)
Thymus	(64)	(3)	(60)	(59)
Integumentary System				
Mammary gland	(69)	(5)	(66)	(66)
Adenocarcinoma	2 (3%)	1 (20%)	1 (2%)	2 (3%)
Skin	(69)	(6)	(67)	(67)
Papilloma squamous			1 (1%)	
Subcutaneous tissue, fibroma				1 (1%)
Subcutaneous tissue, fibrosarcoma	1 (1%)	1 (17%)		2 (3%)
Subcutaneous tissue, sarcoma		1 (17%)		1 (1%)
Musculoskeletal System				
Bone	(69)	(4)	(68)	(67)
Femur, osteosarcoma			1 (1%)	
Humerus, osteosarcoma				1 (1%)
Skeletal muscle			(3)	(3)
Back, osteosarcoma, metastatic, bone				1 (33%)
Hindlimb, fibrosarcoma			1 (33%)	
Hindlimb, hemangiosarcoma				1 (33%)
Sternal, osteosarcoma, metastatic, bone			1 (33%)	
Nervous System				
Brain	(69)	(4)	(68)	(67)
Respiratory System				
Larynx	(68)	(4)	(64)	(64)
Lung	(69)	(65)	(68)	(67)
Adenocarcinoma, metastatic, mammary gland			1 (1%)	1 (1%)
Alveolar/bronchiolar adenoma	5 (7%)	1 (2%)	9 (13%)	12 (18%)
Alveolar/bronchiolar adenoma, multiple		1 (2%)	4 (6%)	3 (4%)
Alveolar/bronchiolar carcinoma				1 (1%)
Fibrosarcoma, metastatic, skin		1 (2%)		
Osteosarcoma, metastatic, bone			1 (1%)	1 (1%)
Sarcoma, metastatic, skin				1 (1%)
Sarcoma, metastatic, uncertain primary site				1 (1%)
Mediastinum, sarcoma, metastatic, uncertain primary site				1 (1%)
Nose	(69)	(65)	(68)	(67)
Adenoma		2 (3%)		
Trachea	(69)	(4)	(68)	(66)

TABLE B1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Inhalation Study of Naphthalene
(continued)

	0 ppm	10 ppm	30 ppm	30 ppm
Special Senses System				
Ear		(1)		
Pinna, fibrosarcoma		1 (100%)		
Eye	(2)	(6)	(2)	(4)
Lids, papilloma squamous				1 (25%)
Harderian gland	(1)	(2)	(1)	(1)
Adenocarcinoma		2 (100%)		
Adenoma				1 (100%)
Urinary System				
Kidney	(69)	(7)	(67)	(67)
Plasma cell tumor malignant			1 (1%)	
Urinary bladder	(67)	(1)	(62)	(63)
Sarcoma, metastatic, uncertain primary site				1 (2%)
Systemic Lesions				
Multiple organs[c]	(69)	(65)	(68)	(67)
Lymphoma malignant histiocytic	1 (1%)	2 (3%)	1 (1%)	3 (4%)
Lymphoma malignant lymphocytic	6 (9%)	5 (8%)	2 (3%)	2 (3%)
Lymphoma malignant mixed	1 (1%)	1 (2%)	4 (6%)	2 (3%)
Tumor Summary				
Total animals with primary neoplasms[d]	23	22	28	35
Total primary neoplasms	28	25	33	48
Total animals with benign neoplasms	15	7	19	22
Total benign neoplasms	15	7	19	24
Total animals with malignant neoplasms	12	18	12	19
Total malignant neoplasms	13	18	14	24
Total animals with secondary neoplasms[e]	1	2	3	4
Total secondary neoplasms	3	3	10	19
Total animals with malignant neoplasms uncertain primary site				1

[a] Incidences are expressed as the ratio of animals with lesions to the number of animals examined microscopically at the site.
[b] Animals from the hematology group that were sacrificed or died prior to becoming part of the 2-year studies; these animals were not examined microscopically.
[c] Number of animals with any tissue examined microscopically
[d] Primary tumors: all tumors except metastatic tumors
[e] Secondary tumors: metastatic tumors or tumors invasive to an adjacent organ

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm

Number of Days on Study	1 1 1 5 5 5 6 6 6 6 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7
	4 4 8 6 7 9 4 5 6 7 2 3 3 3 3 3 3 3 3 3 3 3 3 3 3
	0 0 3 1 4 0 4 5 2 8 9 6 6 6 6 6 6 6 6 6 6 6 6 6 6
Carcass ID Number	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	1 1 2 3 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
	6 6 7 0 9 5 4 2 7 2 2 1 1 1 1 1 2 2 3 3 3 3 3 4 4
	3 5 2 2 2 5 3 1 1 3 4 1 2 3 4 5 2 5 1 2 3 4 5 1 2
Alimentary System	
Esophagus	+ + + + + + + + M + + + + + + + + + + + + + +
Gallbladder	A + + + A A + + A + + + + + + + + + + + + + +
Intestine large	A +
Intestine large, cecum	A + + + A A + + + + + + + + + + + + + + + + +
Intestine large, colon	A + + + + + + + A + + + + + + + + + + + + + +
Intestine large, rectum	A + + + + A + + + + + + + + + + + + + + + + +
Intestine small	A +
Intestine small, duodenum	A + + + A A + + + + + + + + + + + + + + + + +
Intestine small, ileum	A + + + + A + + + + + + + + + + + + + + + + +
Intestine small, jejunum	A + A + A + + + A + + + + + + + + + + + + + +
Liver	A +
Hepatocellular adenoma	X
Mesentery	+ + + + + +
Pancreas	+ +
Salivary glands	+ +
Stomach	+ + + + M A + + + + + + + + + + + + + + + +
Stomach, forestomach	+ + + + M A + + + + + + + + + + + + + + + +
Papilloma squamous	X
Stomach, glandular	+ + + + M A + + + + + + + + + + + + + + + +
Cardiovascular System	
Heart	+ +
Endocrine System	
Adrenal gland	+ + + + + + + + M + + + + + + + + + + + + + +
Capsule, adenoma	
Adrenal gland, cortex	+ + + + + + + + M + + + + + + + + + + + + + +
Adrenal gland, medulla	+ + + + + + + + M + + + + + + + + + + + + + +
Pheochromocytoma benign	
Islets, pancreatic	+ +
Parathyroid gland	+ +
Pituitary gland	+ + + M M + + M + + M + + M + + + + + + + + +
Pars distalis, adenoma	
Thyroid gland	+ +

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

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

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

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 2 0 5	0 2 7 1	0 2 7 3	0 2 7 4	0 2 7 5	0 2 8 1	0 2 8 2	0 2 8 3	0 2 8 4	0 2 8 5	0 2 9 1	0 2 9 3	0 2 9 5	0 1 7 5	0 2 9 2	0 2 9 4	0 2 9 5	0 3 0 1	0 3 0 3	0 3 0 4	0 3 0 5	**Total Tissues/ Tumors**
Alimentary System																						
Esophagus	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	66
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Intestine small, ileum	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Hepatocellular adenoma										X												2
Mesentery																						6
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Salivary glands	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Papilloma squamous												X										2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Cardiovascular System																						
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Endocrine System																						
Adrenal gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Capsule, adenoma																						1
Adrenal gland, cortex	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Adrenal gland, medulla	+	+	+	M	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	64
Pheochromocytoma benign								X														1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Parathyroid gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	68
Pituitary gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	61
Pars distalis, adenoma																						1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

Number of Days on Study	1	1	1	5	5	5	6	6	6	6	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	4	4	8	6	7	9	4	5	6	7	2	3	3	3	3	3	3	3	3	3	3	3	3	3	3
	0	0	3	1	4	0	4	5	2	8	9	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1	1	2	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	6	6	7	0	9	5	4	2	7	2	2	1	1	1	1	1	2	2	3	3	3	3	3	4	4
	3	5	2	2	2	5	3	1	1	3	4	1	2	3	4	5	2	5	1	2	3	4	5	1	2
General Body System																									
Tissue NOS								+																	
Genital System																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenocarcinoma, papillary																									
Cystadenoma, papillary																									
Granulosa cell tumor benign																									
Endothelium, sarcoma stromal, metastatic																	X								
Oviduct	+								+																
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma stromal																	X								
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Iliac, sarcoma stromal, metastatic, uterus																	X								
Renal, sarcoma stromal, metastatic, uterus																	X								
Lymph node, bronchial	M	M	+	M	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	M	M	
Lymph node, mandibular	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymph node, mediastinal	M	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	M	+	
Lymph node, mesenteric	A	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Spleen	M	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Thymus	M	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6
Carcass ID Number	0 1 4 4	0 1 4 5	0 1 5 1	0 1 5 2	0 1 5 3	0 1 5 4	0 1 6 1	0 1 6 2	0 1 6 4	0 1 7 2	0 1 7 3	0 1 7 4	0 1 8 1	0 1 8 2	0 1 8 3	0 1 8 4	0 1 8 5	0 1 9 1	0 1 9 3	0 1 9 4	0 1 9 5	0 2 0 1	0 2 0 2	0 2 0 3	0 2 0 4
General Body System																									
Tissue NOS																									
Genital System																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenocarcinoma, papillary																		X							
Cystadenoma, papillary																		X							
Granulosa cell tumor benign				X																					
Endothelium, sarcoma stromal, metastatic																									
Oviduct																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma stromal																									
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Iliac, sarcoma stromal, metastatic, uterus																									
Renal, sarcoma stromal, metastatic, uterus																									
Lymph node, bronchial	+	M	+	+	M	+	+	+	+	M	+	+	M	+	M	M	+	+	M	+	+	+	M	+	M
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mediastinal	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma							X																		
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 2 0 5	0 2 7 1	0 2 7 3	0 2 7 4	0 2 7 5	0 2 8 1	0 2 8 2	0 2 8 3	0 2 8 4	0 2 8 5	0 2 9 1	0 2 9 3	0 2 7 5	0 1 9 2	0 2 9 4	0 2 9 5	0 2 3 1	0 3 0 3	0 3 0 4	0 3 0 5	**Total Tissues/ Tumors**
General Body System																					
Tissue NOS																					1
Genital System																					
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Cystadenocarcinoma, papillary																					1
Cystadenoma, papillary				X																	2
Granulosa cell tumor benign																					1
Endothelium, sarcoma stromal, metastatic																					1
Oviduct																					2
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Sarcoma stromal																					1
Hematopoietic System																					
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Iliac, sarcoma stromal, metastatic, uterus																					1
Renal, sarcoma stromal, metastatic, uterus																					1
Lymph node, bronchial	M	+	M	+	M	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	46
Lymph node, mandibular	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Lymph node, mediastinal	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	60
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	64
Integumentary System																					
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Adenocarcinoma										X								X			2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Subcutaneous tissue, fibrosarcoma																					1
Musculoskeletal System																					
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Nervous System																					
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

Number of Days on Study	1 4 0	1 4 0	1 8 3	5 6 1	5 7 4	5 9 0	6 4 4	6 5 5	6 6 2	6 7 8	7 2 9	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6
Carcass ID Number	0 1 6 3	0 1 6 5	0 2 7 2	0 3 0 2	0 1 9 2	0 1 5 5	0 1 4 3	0 1 2 1	0 1 7 1	0 1 2 3	0 1 2 4	0 1 1 1	0 1 1 2	0 1 1 3	0 1 1 4	0 1 1 5	0 1 2 2	0 1 2 5	0 1 3 1	0 1 3 2	0 1 3 3	0 1 3 4	0 1 3 5	0 1 4 1	0 1 4 2
Respiratory System																									
Larynx	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma											X										X				
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye	+																								
Harderian gland															+										
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic				X																					
Lymphoma malignant lymphocytic							X	X		X	X						X								
Lymphoma malignant mixed															X										

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6
Carcass ID Number	0 1 4 4	0 1 4 5	0 1 5 1	0 1 5 2	0 1 5 3	0 1 5 4	0 1 6 1	0 1 6 2	0 1 6 4	0 1 7 2	0 1 7 3	0 1 7 4	0 1 8 1	0 1 8 2	0 1 8 3	0 1 8 4	0 1 8 5	0 1 9 1	0 1 9 3	0 1 9 4	0 1 9 5	0 2 0 1	0 2 0 2	0 2 0 3	0 2 0 4
Respiratory System																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																									
Harderian gland																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																									X
Lymphoma malignant mixed																									

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 0 ppm
(continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 2 0 5	0 2 7 1	0 2 7 3	0 2 7 4	0 2 7 5	0 2 8 1	0 2 8 2	0 2 8 3	0 2 8 4	0 2 8 5	0 2 9 1	0 2 9 3	0 2 9 5	0 1 7 5	0 2 9 2	0 2 9 4	0 2 9 5	0 3 0 1	0 3 0 3	0 3 0 4	0 3 0 5	**Total Tissues/ Tumors**
Respiratory System																						
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Alveolar/bronchiolar adenoma														X					X	X		5
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Special Senses System																						
Eye															+							2
Harderian gland																						1
Urinary System																						
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	67
Systemic Lesions																						
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	69
Lymphoma malignant histiocytic																						1
Lymphoma malignant lymphocytic																						6
Lymphoma malignant mixed																						1

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm

Number of Days on Study	1 2 7	1 2 7	1 8 3	1 9 7	2 8 7	4 6 3	5 4 8	5 8 6	6 6 9	7 1 6	7 1 8	7 3 7	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4
Carcass ID Number	1 0 1 1	1 0 3 1	1 1 3 3	1 1 6 2	1 1 5 2	1 0 5 2	1 1 4 4	1 0 1 2	1 0 0 1	1 0 3 2	0 9 9 1	1 3 8 1	0 9 9 2	0 9 9 3	1 0 1 3	1 0 1 4	1 0 2 1	1 0 2 2	1 0 2 3	1 0 2 4	1 0 2 5	1 0 4 1	1 0 4 2	1 0 4 3	1 0 4 4
Alimentary System																									
Esophagus			+	+	+		+																		
Gallbladder			+	A	+		A																		
Intestine large			+	A	+		+																		
Intestine large, cecum			+	A	A		M																		
Intestine large, colon			+	A	+		M																		
Intestine large, rectum			+	A	+		+																		
Intestine small			+	A	A		A																		
Intestine small, duodenum			+	A	A		A																		
Adenocarcinoma																									
Intestine small, ileum			+	A	A		M																		
Intestine small, jejunum			+	A	A		M																		
Liver			+	+	+	+	+			+		+						+							
Hepatocellular adenoma																		X							
Sarcoma stromal, metastatic												X													
Pancreas			+	+	+		+								+										
Salivary glands			+	+	+		+																		
Stomach			+	+	+		+		+																
Stomach, forestomach			+	+	+		+		+																
Stomach, glandular			+	+	+		+		+																
Cardiovascular System																									
Heart			+	+	+		+																		
Endocrine System																									
Adrenal gland			+	+	+		+																		
Adrenal gland, cortex			+	+	+		+																		
Adrenal gland, medulla			+	+	+		+																		
Islets, pancreatic			+	+	+		+																		
Parathyroid gland			M	M	M		M																		
Pituitary gland			+	M	+	+	M																		
Thyroid gland			+	+	+		+																		
General Body System																									
Tissue NOS																									

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

Number of Days on Study	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4
Carcass ID Number	1 0 4 5	1 0 5 1	1 0 5 3	1 0 5 4	1 0 5 5	1 0 6 1	1 0 6 2	1 0 6 3	1 0 6 4	1 0 6 5	1 0 6 6	1 1 3 1	1 1 3 5	1 1 4 1	1 1 4 2	1 1 4 3	1 1 4 5	1 1 5 1	1 1 5 3	1 1 5 4	1 1 5 5	1 1 6 1	1 1 6 3	1 1 6 4	1 1 6 5	1 1 7 1
Alimentary System																									
Esophagus																									
Gallbladder																									
Intestine large																									
Intestine large, cecum																									
Intestine large, colon																									
Intestine large, rectum																									
Intestine small			+								+					+									
Intestine small, duodenum			+								+					+									
Adenocarcinoma																X									
Intestine small, ileum																									
Intestine small, jejunum																									
Liver														+										+	+
Hepatocellular adenoma														X											
Sarcoma stromal, metastatic																									
Pancreas																									
Salivary glands																			+						
Stomach																									
Stomach, forestomach																									
Stomach, glandular																									
Cardiovascular System																									
Heart																									
Endocrine System																									
Adrenal gland																									
Adrenal gland, cortex																									
Adrenal gland, medulla																									
Islets, pancreatic																									
Parathyroid gland																									
Pituitary gland																					+				
Thyroid gland																									
General Body System																									
Tissue NOS																									

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

Number of Days on Study	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	
Carcass ID Number	1 2 1 1	1 2 1 2	1 2 1 3	1 2 1 4	1 2 2 1	1 2 5 1	1 2 5 1	1 2 5 2	1 2 8 3	1 3 5 2	1 2 2 4	1 3 2 1	1 3 2 2	1 3 3 1	1 3 3 2	1 3 3 3	1 3 5 1	1 3 6 1	1 3 6 2	**Total Tissues/ Tumors**
Alimentary System																				
Esophagus																				4
Gallbladder																				2
Intestine large																				3
Intestine large, cecum																				1
Intestine large, colon																				2
Intestine large, rectum																				3
Intestine small																				4
Intestine small, duodenum																				4
Adenocarcinoma																				1
Intestine small, ileum																				1
Intestine small, jejunum																				1
Liver	+	+																		12
Hepatocellular adenoma																				2
Sarcoma stromal, metastatic																				1
Pancreas																				5
Salivary glands																				5
Stomach																				5
Stomach, forestomach																				5
Stomach, glandular																				5
Cardiovascular System																				
Heart																				4
Endocrine System																				
Adrenal gland																				4
Adrenal gland, cortex																				4
Adrenal gland, medulla																				4
Islets, pancreatic																				4
Parathyroid gland																				
Pituitary gland																				4
Thyroid gland																				4
General Body System																				
Tissue NOS									+											1

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

Number of Days on Study	1 2 7	1 2 7	1 8 3	1 9 7	2 8 7	4 6 3	5 4 8	5 8 6	6 1 9	7 1 6	7 1 8	7 3 7	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4
Carcass ID Number	1 0 1 1	1 0 3 1	1 1 3 3	1 1 6 2	1 1 5 2	1 0 5 2	1 1 4 4	1 0 1 2	1 0 0 1	1 0 3 2	1 0 9 1	1 3 9 1	0 9 8 1	0 9 9 2	0 9 9 3	1 0 1 3	1 0 1 4	1 0 2 1	1 0 2 2	1 0 2 3	1 0 2 4	1 0 2 5	1 0 4 1	1 0 4 2	1 0 4 3	1 0 4 4
Genital System																									
Ovary			+	M	+		M					+				+	+					+			
Cystadenocarcinoma, papillary																									
Sarcoma stromal, metastatic												X													
Oviduct										+															
Uterus			+	M	+		M					+	+			+		+	+		+	+	+		+	+
Sarcoma stromal												X													
Endometrium, polyp stromal																									
Hematopoietic System																									
Bone marrow			+	+	+		+																		
Lymph node			+	+	+		+									+		+							
Lymph node, bronchial			M	M	M		+																		
Lymph node, mandibular			+	+	+		+											+							
Lymph node, mediastinal			+	+	+		+																		
Lymph node, mesenteric			+	M	+		M									+									
Spleen			+	A	+		+		+											+					
Thymus			+	M	+		M																		
Integumentary System																									
Mammary gland			+	+	+		+																		
Adenocarcinoma																									
Skin			+	+	+		+		+		+														
Subcutaneous tissue, fibrosarcoma											X														
Subcutaneous tissue, sarcoma									X																
Musculoskeletal System																									
Bone			+	+	+		+																		
Nervous System																									
Brain			+	+	+		+																		
Respiratory System																									
Larynx			+	+	+		+																		
Lung			+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar adenoma, multiple																									
Fibrosarcoma, metastatic, skin											X														

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

Number of Days on Study	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4
Carcass ID Number	1 0 4 5	1 0 5 1	1 0 5 3	1 0 5 4	1 0 5 5	1 0 6 1	1 0 6 2	1 0 6 3	1 0 6 4	1 0 6 5	1 1 3 1	1 1 3 5	1 1 4 1	1 1 4 2	1 1 4 3	1 1 4 5	1 1 5 1	1 1 5 3	1 1 5 4	1 1 5 5	1 1 6 1	1 1 6 3	1 1 6 4	1 1 6 5	1 1 6 7	1 1 7 1
Genital System																									
Ovary					+											+			+	+	+			+	
Cystadenocarcinoma, papillary																									
Sarcoma stromal, metastatic																									
Oviduct																									
Uterus	+	+	+	+			+		+	+	+	+				+	+		+	+			+	+	+	+
Sarcoma stromal																									
Endometrium, polyp stromal			X																						
Hematopoietic System																									
Bone marrow																									
Lymph node						+																			
Lymph node, bronchial																									
Lymph node, mandibular																									
Lymph node, mediastinal						+																			
Lymph node, mesenteric																									
Spleen															+									+	
Thymus																									
Integumentary System																									
Mammary gland														+											
Adenocarcinoma														X											
Skin																									
Subcutaneous tissue, fibrosarcoma																									
Subcutaneous tissue, sarcoma																									
Musculoskeletal System																									
Bone																									
Nervous System																									
Brain																									
Respiratory System																									
Larynx																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																X									
Alveolar/bronchiolar adenoma, multiple																					X				
Fibrosarcoma, metastatic, skin																									

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

Number of Days on Study	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	
Carcass ID Number	1 2 1 1	1 2 1 2	1 2 1 3	1 2 1 4	1 2 2 1	1 2 5 1	1 2 5 1	1 2 5 2	1 2 8 3	1 2 5 2	1 3 2 4	1 3 2 1	1 3 3 2	1 3 3 1	1 3 3 2	1 3 3 3	1 3 5 1	1 3 6 1	1 3 6 2	**Total Tissues/ Tumors**
Genital System																			
Ovary		+											+						14
Cystadenocarcinoma, papillary		X																	1
Sarcoma stromal, metastatic																			1
Oviduct																			1
Uterus		+	+	+	+		+		+	+	+		+	+	+			+	41
Sarcoma stromal																		X	2
Endometrium, polyp stromal																			1
Hematopoietic System																			
Bone marrow																			4
Lymph node								+										+	9
Lymph node, bronchial																			1
Lymph node, mandibular																		+	6
Lymph node, mediastinal								+											6
Lymph node, mesenteric																		+	4
Spleen		+	+								+				+	+		+	13
Thymus								+											3
Integumentary System																			
Mammary gland																			5
Adenocarcinoma																			1
Skin																			6
Subcutaneous tissue, fibrosarcoma																			1
Subcutaneous tissue, sarcoma																			1
Musculoskeletal System																			
Bone																			4
Nervous System																			
Brain																			4
Respiratory System																			
Larynx																			4
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Alveolar/bronchiolar adenoma																			1
Alveolar/bronchiolar adenoma, multiple																			1
Fibrosarcoma, metastatic, skin																			1

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

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

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

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

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 10 ppm
(continued)

Number of Days on Study	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	
Carcass ID Number	1 2 1 1	1 2 1 2	1 2 1 3	1 2 1 4	1 2 2 1	1 2 5 1	1 2 5 2	1 2 5 3	1 3 8 2	1 2 5 4	1 3 2 1	1 3 2 2	1 3 3 1	1 3 3 2	1 3 3 3	1 3 5 1	1 3 6 1	1 3 6 2	**Total Tissues/ Tumors**
Respiratory System (continued)																			
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Adenoma																			2
Trachea																			4
Special Senses System																			
Ear																			1
Pinna, fibrosarcoma																			1
Eye															+				6
Harderian gland															+				2
Adenocarcinoma															X				2
Urinary System																			
Kidney																			7
Urinary bladder																			1
Systemic Lesions																			
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65
Lymphoma malignant histiocytic																			2
Lymphoma malignant lymphocytic			X					X								X			5
Lymphoma malignant mixed																		X	1

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm

Number of Days on Study	0 6 7	2 3 4	3 5 1	3 6 6	4 2 7	4 6 6	6 1 4	6 2 6	6 4 8	6 6 3	6 6 7	6 7 8	6 8 8	6 9 6	7 1 1	7 1 3	7 1 4	7 2 2	7 3 6	7 3 8	7 3 8	7 3 8	7 3 9	7 3 9	7 3 9
Carcass ID Number	0 5 0 5	0 4 8 4	0 4 8 5	0 4 7 2	0 5 7 4	0 4 9 5	0 5 9 1	0 4 5 5	0 4 5 1	0 4 1 1	0 5 8 4	0 5 8 1	0 4 4 1	0 4 7 1	0 4 5 4	0 4 5 4	0 4 9 2	0 4 4 5	0 4 5 2	0 4 1 3	0 4 1 4	0 4 1 5	0 4 1 2	0 4 2 1	0 4 2 2	0 4 2 3
Alimentary System																									
Esophagus	+		+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Gallbladder	+		+	+	M	+	+	+	A	M	+	A	+	+	A	+	A	A	+	+	+	+	+	+	+	+
Intestine large	+		+	+	M	+	+	+	A	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Intestine large, cecum	+		+	+	M	M	+	A	A	M	+	A	+	+	M	+	+	M	+	+	+	+	+	+	+	+
Intestine large, colon	+		+	A	M	+	+	+	A	M	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+
Intestine large, rectum	+		+	+	M	+	+	+	M	A	+	+	+	+	+	+	+	A	+	+	+	+	M	+	+	+
Intestine small	+		+	A	M	+	+	A	A	M	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+
Intestine small, duodenum	+		+	M	M	+	+	A	A	M	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+
Intestine small, ileum	+		+	A	M	+	+	A	A	M	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+
Intestine small, jejunum	+		+	A	M	+	+	A	A	M	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+
Liver	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																	X								
Plasma cell tumor malignant												X													
Mesentery																				+					
Pancreas	+		+	+	+	+	+	+	+	A	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+
Salivary glands	M		+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Stomach	+		+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+		+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+		+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel																									
Heart	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone					X																				
Endocrine System																									
Adrenal gland	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+		+		+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone					X																				
Adrenal gland, medulla	+		+		+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone					X																				
Islets, pancreatic	+		+		+	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Parathyroid gland	+		+		+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Pituitary gland	+		+		M	+	+	M	+	M	+	+	+	+	M	M	+	+	M	+	+	+	M	+	+	+
Thyroid gland	+		+		+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 4 2	7 4 2
Carcass ID Number	0 4 2 4	0 4 2 5	0 4 3 1	0 4 3 2	0 4 3 3	0 4 3 4	0 4 3 5	0 4 4 2	0 4 4 3	0 4 4 4	0 4 4 5	0 4 5 3	0 4 6 1	0 4 6 2	0 4 6 3	0 4 6 4	0 4 6 5	0 4 7 1	0 4 7 3	0 4 7 5	0 4 8 1	0 4 8 2	0 4 8 3	0 4 9 1	0 4 9 3	0 4 9 4
Alimentary System																									
Esophagus	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																									
Plasma cell tumor malignant																									
Mesentery								+																	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel														+											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone																									
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone																									
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	M	+	+	M	+	+	+	+	+	M	+	+	M	+	+	+	+	M	M	+	+	M	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	
Carcass ID Number	0 5 0 1	0 5 0 2	0 5 0 3	0 5 0 4	0 5 7 1	0 5 7 3	0 5 7 5	0 5 8 2	0 5 8 3	0 5 8 5	0 5 9 2	0 5 9 3	0 5 9 4	0 5 9 5	0 6 0 1	0 6 0 2	0 6 0 3	0 6 0 4	0 6 0 5		**Total Tissues/ Tumors**
Alimentary System																					
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		65
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		60
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		64
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		60
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		62
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		63
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		61
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		61
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		61
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		61
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Hepatocellular carcinoma																					1
Plasma cell tumor malignant																					1
Mesentery													+								3
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		65
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		64
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		65
Cardiovascular System																					
Blood vessel																					1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		68
Osteosarcoma, metastatic, bone																					1
Endocrine System																					
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Osteosarcoma, metastatic, bone																					1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		66
Osteosarcoma, metastatic, bone																					1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		66
Parathyroid gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+		66
Pituitary gland	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	M	M	+		50
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	0 6 7	2 3 4	3 5 1	3 6 6	4 2 7	4 6 6	6 1 4	6 2 6	6 4 8	6 6 3	6 7 7	6 8 8	6 9 6	7 1 1	7 1 3	7 1 4	7 2 2	7 3 6	7 3 8	7 3 8	7 3 9	7 3 9	7 3 9	7 3 9
Carcass ID Number	0 5 0 5	0 4 8 4	0 4 8 5	0 4 7 2	0 5 7 4	0 4 9 5	0 5 9 1	0 4 5 5	0 4 5 1	0 4 1 1	0 5 8 4	0 5 8 1	0 4 4 1	0 4 7 4	0 4 5 4	0 4 9 2	0 4 4 5	0 4 5 2	0 4 1 3	0 4 1 4	0 4 1 5	0 4 2 2	0 4 2 1	0 4 2 3
General Body System																								
Tissue NOS					+			+																
Osteosarcoma, metastatic, bone					X																			
Genital System																								
Ovary	+		+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Cystadenoma, papillary																								
Granulosa cell tumor benign																								
Osteosarcoma, metastatic, bone					X																			
Oviduct						+		+	+								+							
Uterus	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Hematopoietic System																								
Blood													+											
Bone marrow	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone					X																			
Lymph node	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Lymph node, bronchial	M		M	+	M	+	+	+	+	+	+	M	M	M	+	+	M	M	+	M	+	+	+	+
Lymph node, mandibular	M		+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+
Lymph node, mediastinal	M		+	M	M	+	+	+	+	M	+	M	+	+	M	M	+	M	+	+	+	+	+	+
Lymph node, mesenteric	+		+	+	+	M	M	M	+	+	M	+	+	+	M	+	+	M	+	+	+	+	+	+
Spleen	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Plasma cell tumor malignant												X												
Thymus	+		+	+	M	+	M	+	+	M	+	M	+	+	+	+	+	M	+	+	+	+	+	+
Integumentary System																								
Mammary gland	+		+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma													X											
Skin	+		+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																								
Musculoskeletal System																								
Bone	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Femur, osteosarcoma					X																			
Skeletal muscle	+				+		+																	
Hindlimb, fibrosarcoma							X																	
Sternal, osteosarcoma, metastatic, bone					X																			

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 4 2	7 4 2
Carcass ID Number	0 4 2 4	0 4 2 5	0 4 3 1	0 4 3 2	0 4 3 3	0 4 3 4	0 4 3 5	0 4 4 2	0 4 4 3	0 4 4 4	0 4 4 3	0 4 5 1	0 4 6 2	0 4 6 3	0 4 6 4	0 4 6 5	0 4 7 1	0 4 7 3	0 4 7 5	0 4 8 1	0 4 8 2	0 4 8 3	0 4 9 1	0 4 9 3	0 4 9 4
General Body System																									
Tissue NOS																									
Osteosarcoma, metastatic, bone																									
Genital System																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma, papillary	X	X													X									X	
Granulosa cell tumor benign													X												
Osteosarcoma, metastatic, bone																									
Oviduct																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Blood																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone																									
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, bronchial	+	+	+	+	M	+	+	+	M	+	M	+	M	M	M	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mediastinal	+	+	+	+	M	+	M	+	+	M	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Plasma cell tumor malignant																									
Thymus	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																X									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Femur, osteosarcoma																									
Skeletal muscle																									
Hindlimb, fibrosarcoma																									
Sternal, osteosarcoma, metastatic, bone																									

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	
Carcass ID Number	0 5 0 1	0 5 0 2	0 5 0 3	0 5 0 4	0 5 7 1	0 5 7 3	0 5 7 5	0 5 8 2	0 5 8 3	0 5 8 5	0 5 9 2	0 5 9 3	0 5 9 4	0 5 9 5	0 6 0 1	0 6 0 2	0 6 0 3	0 6 0 4	0 6 0 5	**Total Tissues/ Tumors**
General Body System																				
Tissue NOS																				2
Osteosarcoma, metastatic, bone																				1
Genital System																				
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Cystadenoma, papillary																				4
Granulosa cell tumor benign																				1
Osteosarcoma, metastatic, bone																				1
Oviduct																				4
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Hematopoietic System																				
Blood																				1
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Osteosarcoma, metastatic, bone	/																			1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Lymph node, bronchial	+	+	+	+	M	+	+	+	+	+	+	M	M	M	M	+	M	+	M	46
Lymph node, mandibular	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	62
Lymph node, mediastinal	+	M	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	52
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	60
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Plasma cell tumor malignant																				1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	60
Integumentary System																				
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Adenocarcinoma																				1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Papilloma squamous																				1
Musculoskeletal System																				
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Femur, osteosarcoma																				1
Skeletal muscle																				3
Hindlimb, fibrosarcoma																				1
Sternal, osteosarcoma, metastatic, bone																				1

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	0 6 7	2 3 4	3 5 1	3 6 6	4 2 7	4 6 6	6 1 4	6 2 6	6 4 8	6 6 3	6 7 7	6 8 8	6 9 6	7 1 1	7 1 3	7 1 4	7 2 2	7 3 6	7 3 8	7 3 8	7 3 8	7 3 9	7 3 9	7 3 9	7 3 9
Carcass ID Number	0 5 0 5	0 4 8 4	0 4 8 5	0 4 7 2	0 5 7 4	0 4 9 5	0 5 9 1	0 4 5 5	0 4 5 1	0 4 5 1	0 5 1 4	0 5 8 1	0 4 8 1	0 4 7 4	0 4 5 4	0 4 9 2	0 4 4 2	0 4 5 5	0 4 1 2	0 4 1 3	0 4 1 4	0 4 1 5	0 4 2 2	0 4 2 1	0 4 2 3
Nervous System																									
Brain	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Larynx	+		+	M	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Lung	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, mammary gland													X												
Alveolar/bronchiolar adenoma												X		X	X							X			X
Alveolar/bronchiolar adenoma, multiple																									
Lymphoma malignant histiocytic, metastatic, liver																				X					
Osteosarcoma, metastatic, bone					X																				
Nose	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																									
Harderian gland																									
Urinary System																									
Kidney	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Plasma cell tumor malignant												X													
Urinary bladder	+		+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																				X					
Lymphoma malignant lymphocytic																	X		X						
Lymphoma malignant mixed										X															

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 3 9	7 4 2	7 4 2
Carcass ID Number	0 4 2 4	0 4 2 5	0 4 3 1	0 4 3 2	0 4 3 3	0 4 3 4	0 4 3 5	0 4 4 2	0 4 4 3	0 4 4 4	0 4 4 5	0 4 5 3	0 4 6 1	0 4 6 2	0 4 6 3	0 4 6 4	0 4 6 5	0 4 7 1	0 4 7 3	0 4 7 5	0 4 8 1	0 4 8 2	0 4 8 3	0 4 9 1	0 4 9 3	0 4 9 4
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma, metastatic, mammary gland																										
Alveolar/bronchiolar adenoma								X		X																
Alveolar/bronchiolar adenoma, multiple						X									X											
Lymphoma malignant histiocytic, metastatic, liver																										
Osteosarcoma, metastatic, bone																										
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Special Senses System																										
Eye																+										
Harderian gland							+																			
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Plasma cell tumor malignant																										
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymphoma malignant histiocytic																										
Lymphoma malignant lymphocytic																										
Lymphoma malignant mixed						X				X																

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	
Carcass ID Number	0 5 0 1	0 5 0 2	0 5 0 3	0 5 0 4	0 5 7 1	0 5 7 3	0 5 7 5	0 5 8 2	0 5 8 3	0 5 8 5	0 5 9 2	0 5 9 3	0 5 9 4	0 5 9 5	0 6 0 1	0 6 0 2	0 6 0 3	0 6 0 4	0 6 0 5	0 6 0 6	**Total Tissues/ Tumors**
Nervous System																					
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Respiratory System																					
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	64
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Adenocarcinoma, metastatic, mammary gland																					1
Alveolar/bronchiolar adenoma			X						X												9
Alveolar/bronchiolar adenoma, multiple															X					X	4
Lymphoma malignant histiocytic, metastatic, liver																					1
Osteosarcoma, metastatic, bone																					1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Special Senses System																					
Eye							+														2
Harderian gland																					1
Urinary System																					
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Plasma cell tumor malignant																					1
Urinary bladder	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	62
Systemic Lesions																					
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	68
Lymphoma malignant histiocytic																					1
Lymphoma malignant lymphocytic																					2
Lymphoma malignant mixed		X																			4

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm

Number of Days on Study	1 5 6	2 1 5	4 2 3	4 7 1	6 1 1	6 2 3	6 2 5	6 2 7	6 4 8	6 5 8	6 5 9	6 6 0	6 6 8	6 8 9	6 9 6	7 0 2	7 0 8	7 2 1	7 3 1	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3
Carcass ID Number	0 7 2 4	0 7 7 2	0 7 1 5	0 7 2 1	0 9 0 4	0 7 3 5	0 9 0 5	0 7 7 1	0 8 7 1	0 7 1 4	0 7 8 4	0 7 8 2	0 7 4 3	0 7 9 4	0 8 0 5	0 8 9 4	0 7 1 2	0 7 3 1	0 7 5 3	0 7 1 1	0 7 1 3	0 7 2 2	0 7 2 3	0 7 2 5	0 7 3 2
Alimentary System																									
Esophagus			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder			+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Intestine large			+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum			A	+	+	+	+	+	+	+	+	+	+	M	+	+	+	A	+	+	+	+	+	+	+
Intestine large, colon			+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum			A	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+
Intestine small			A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum			A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Intestine small, ileum			A	+	+	+	+	+	A	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uncertain primary site																			X						
Intestine small, jejunum			A	+	+	+	+	+	+	+	+	+	+	M	+	+	+	A	+	+	+	+	+	+	+
Liver			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma													X												
Osteosarcoma, metastatic, bone																	X								
Sarcoma, metastatic, uncertain primary site																			X						
Mesentery					+														+						
Fat, sarcoma, metastatic, uncertain primary site																			X						
Pancreas			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uncertain primary site																			X						
Salivary glands			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																								X	
Stomach			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Stomach, glandular			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma														X											
Sarcoma, metastatic, uncertain primary site																			X						

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3
Carcass ID Number	0 7 3 3	0 7 3 4	0 7 4 1	0 7 4 2	0 7 4 4	0 7 4 5	0 7 5 1	0 7 5 2	0 7 5 4	0 7 5 5	0 7 6 1	0 7 6 2	0 7 6 3	0 7 6 4	0 7 6 5	0 7 7 3	0 7 7 4	0 7 7 5	0 7 8 1	0 7 8 3	0 7 8 5	0 7 9 1	0 7 9 2	0 7 9 3	0 7 9 5
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uncertain primary site																									
Intestine small, jejunum	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Osteosarcoma, metastatic, bone																									
Sarcoma, metastatic, uncertain primary site																									
Mesentery																							+		
Fat, sarcoma, metastatic, uncertain primary site																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uncertain primary site																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																							X		
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Sarcoma, metastatic, uncertain primary site																									

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	
Carcass ID Number	0 8 0 1	0 8 0 2	0 8 0 3	0 8 0 4	0 8 7 2	0 8 7 4	0 8 7 5	0 8 8 1	0 8 8 2	0 8 8 3	0 8 8 4	0 8 8 5	0 8 9 1	0 8 9 2	0 8 9 3	0 8 9 5	0 9 0 1	0 9 0 2	0 9 0 3		**Total Tissues/ Tumors**
Alimentary System																					
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		64
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		66
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		64
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		66
Intestine large, rectum	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+		63
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		65
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		63
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		63
Sarcoma, metastatic, uncertain primary site																					1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		63
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Hepatocellular adenoma					X																2
Osteosarcoma, metastatic, bone																					1
Sarcoma, metastatic, uncertain primary site																					1
Mesentery																					3
Fat, sarcoma, metastatic, uncertain primary site																					1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Sarcoma, metastatic, uncertain primary site																					1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Fibrosarcoma																					1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Squamous cell carcinoma																					1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Cardiovascular System																					
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Fibrous histiocytoma																					1
Sarcoma, metastatic, uncertain primary site																					1

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	1 5 6	2 1 5	4 2 3	4 7 1	6 1 1	6 2 3	6 2 5	6 2 7	6 4 8	6 5 8	6 5 9	6 6 0	6 6 8	6 8 9	6 9 6	7 0 2	7 0 8	7 2 1	7 3 1	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3
Carcass ID Number	0 7 2 4	0 7 7 2	0 7 1 5	0 7 2 1	0 9 0 4	0 7 3 5	0 9 0 5	0 7 7 1	0 8 7 1	0 7 1 4	0 7 8 4	0 7 8 2	0 7 4 3	0 7 9 4	0 8 0 5	0 8 9 4	0 7 1 2	0 7 3 1	0 7 5 3	0 7 1 1	0 7 1 3	0 7 2 2	0 7 2 3	0 7 3 5	0 7 3 2
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, sarcoma, metastatic, uncertain primary site																			X						
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uncertain primary site																			X						
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	M	+	+	M	M	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																									
None																									
Genital System																									
Clitoral gland																									
Squamous cell carcinoma																									
Ovary	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa-theca tumor benign																						X			
Teratoma benign														X											
Oviduct	+			+							+							+							
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Endometrium, polyp stromal																									
Hematopoietic System																									
Blood						+				+					+	+									+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma									X																
Hemangiosarcoma																								X	
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Inguinal, osteosarcoma, metastatic, bone																	X	X							
Lymph node, bronchial	M	M	+	M	M	M	+	+	M	+	M	+	+	M	+	M	+	+	+	+	M	M	+	+	
Sarcoma, metastatic, uncertain primary site																			X						
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																								X	
Lymph node, mediastinal	M	+	+	+	+	+	+	M	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uncertain primary site																			X						

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3
Carcass ID Number	0 7 3 3	0 7 3 4	0 7 4 1	0 7 4 2	0 7 4 4	0 7 4 5	0 7 5 1	0 7 5 2	0 7 5 4	0 7 5 5	0 7 6 1	0 7 6 2	0 7 6 3	0 7 6 4	0 7 6 5	0 7 7 3	0 7 7 4	0 7 7 5	0 7 8 1	0 7 8 3	0 7 8 5	0 7 9 1	0 7 9 2	0 7 9 3	0 7 9 5
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, sarcoma, metastatic, uncertain primary site																									
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uncertain primary site																									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																									
None																									
Genital System																									
Clitoral gland		+																							
Squamous cell carcinoma		X																							
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa-theca tumor benign																									
Teratoma benign																									
Oviduct																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrium, polyp stromal																									
Hematopoietic System																									
Blood																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Hemangiosarcoma																									
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Inguinal, osteosarcoma, metastatic, bone																									
Lymph node, bronchial	+	M	+	+	M	M	+	M	+	+	M	M	+	M	+	+	+	+	M	M	+	M	M	M	M
Sarcoma, metastatic, uncertain primary site																									
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Lymph node, mediastinal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	M	+
Sarcoma, metastatic, uncertain primary site																									

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	
Carcass ID Number	0 8 0 1	0 8 0 2	0 8 0 3	0 8 0 4	0 8 7 2	0 8 7 4	0 8 7 5	0 8 8 1	0 8 8 2	0 8 8 3	0 8 8 4	0 8 8 5	0 8 9 1	0 8 9 2	0 8 9 3	0 8 9 5	0 9 0 1	0 9 0 2	0 9 0 3	**Total Tissues/ Tumors**	
Endocrine System																					
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67	
Capsule, sarcoma, metastatic, uncertain primary site																				1	
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67	
Adrenal gland, medulla	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	66	
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67	
Sarcoma, metastatic, uncertain primary site																				1	
Parathyroid gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	64	
Pituitary gland	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	M	+	+	54	
Thyroid gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	66	
General Body System																					
None																					
Genital System																					
Clitoral gland																				1	
Squamous cell carcinoma																				1	
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	65	
Granulosa-theca tumor benign																				1	
Teratoma benign																				1	
Oviduct																				4	
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66	
Endometrium, polyp stromal					X															1	
Hematopoietic System																					
Blood																				5	
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67	
Hemangioma																				1	
Hemangiosarcoma																				1	
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67	
Inguinal, osteosarcoma, metastatic, bone																				1	
Lymph node, bronchial	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	40	
Sarcoma, metastatic, uncertain primary site																				1	
Lymph node, mandibular	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	65	
Fibrosarcoma																				1	
Lymph node, mediastinal	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	M	+	+	57	
Sarcoma, metastatic, uncertain primary site																				1	

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	1 5 6	2 1 5	4 2 3	4 7 1	6 1 1	6 2 3	6 2 5	6 2 7	6 4 8	6 5 8	6 5 9	6 6 0	6 6 8	6 8 9	6 9 6	7 0 2	7 0 8	7 2 1	7 3 1	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3
Carcass ID Number	0 7 2 4	0 7 7 2	0 7 1 5	0 7 2 1	0 9 0 4	0 7 3 5	0 9 0 5	0 7 7 1	0 8 7 1	0 7 1 4	0 7 8 4	0 7 8 2	0 7 4 3	0 7 9 4	0 8 0 5	0 8 9 4	0 7 1 2	0 7 3 1	0 7 5 3	0 7 1 1	0 7 1 3	0 7 2 2	0 7 2 3	0 7 3 5	0 7 7 2
Hematopoietic System (continued)																									
Lymph node, mesenteric	+	+	+	+	M	M	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Hemangiosarcoma								X						X											
Capsule, sarcoma, metastatic, uncertain primary site																		X							
Thymus	+	+	M	+	M	M	+	+	+	M	M	+	+	M	+	M	+	+	+	+	+	+	+	+	
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma									X							X									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Subcutaneous tissue, fibroma																									
Subcutaneous tissue, fibrosarcoma				X																				X	
Subcutaneous tissue, sarcoma						X																			
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Humerus, osteosarcoma																	X								
Skeletal muscle									+								+								
Back, osteosarcoma, metastatic, bone																	X								
Hindlimb, hemangiosarcoma									X																
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Respiratory System																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma, metastatic, mammary gland											X														
Alveolar/bronchiolar adenoma			X								X					X								X	
Alveolar/bronchiolar adenoma, multiple																									
Alveolar/bronchiolar carcinoma																									
Osteosarcoma, metastatic, bone																	X								
Sarcoma, metastatic, skin						X																			
Sarcoma, metastatic, uncertain primary site																		X							
Mediastinum, sarcoma, metastatic, uncertain primary site																		X							

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3
Carcass ID Number	0 7 3 3	0 7 3 4	0 7 4 1	0 7 4 2	0 7 4 4	0 7 4 5	0 7 5 1	0 7 5 2	0 7 5 4	0 7 5 5	0 7 6 1	0 7 6 2	0 7 6 3	0 7 6 4	0 7 6 5	0 7 7 3	0 7 7 4	0 7 7 5	0 7 8 1	0 7 8 3	0 7 8 5	0 7 9 1	0 7 9 2	0 7 9 3	0 7 9 5
Hematopoietic System (continued)																									
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma										X															
Capsule, sarcoma, metastatic, uncertain primary site																									
Thymus	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Adenocarcinoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibroma																							X		
Subcutaneous tissue, fibrosarcoma																									
Subcutaneous tissue, sarcoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Humerus, osteosarcoma																									
Skeletal muscle														+											
Back, osteosarcoma, metastatic, bone																									
Hindlimb, hemangiosarcoma																									
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, mammary gland																									
Alveolar/bronchiolar adenoma														X											X
Alveolar/bronchiolar adenoma, multiple			X				X		X																
Alveolar/bronchiolar carcinoma										X															
Osteosarcoma, metastatic, bone																									
Sarcoma, metastatic, skin																									
Sarcoma, metastatic, uncertain primary site																									
Mediastinum, sarcoma, metastatic, uncertain primary site																									

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	
Carcass ID Number	0 8 0 1	0 8 0 2	0 8 0 3	0 8 0 4	0 8 7 2	0 8 7 4	0 8 7 5	0 8 8 1	0 8 8 2	0 8 8 3	0 8 8 4	0 8 8 5	0 8 9 1	0 8 9 2	0 8 9 3	0 8 9 5	0 9 0 1	0 9 0 2	0 9 0 3	**Total Tissues/ Tumors**
Hematopoietic System (continued)																				
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	62
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Hemangiosarcoma																				3
Capsule, sarcoma, metastatic, uncertain primary site																				1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	59
Integumentary System																				
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	66
Adenocarcinoma																				2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Subcutaneous tissue, fibroma																				1
Subcutaneous tissue, fibrosarcoma																				2
Subcutaneous tissue, sarcoma																				1
Musculoskeletal System																				
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Humerus, osteosarcoma																				1
Skeletal muscle																				3
Back, osteosarcoma, metastatic, bone																				1
Hindlimb, hemangiosarcoma																				1
Nervous System																				
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Respiratory System																				
Larynx	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	64
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	67
Adenocarcinoma, metastatic, mammary gland																				1
Alveolar/bronchiolar adenoma		X		X		X			X						X				X	12
Alveolar/bronchiolar adenoma, multiple																				3
Alveolar/bronchiolar carcinoma																				1
Osteosarcoma, metastatic, bone																				1
Sarcoma, metastatic, skin																				1
Sarcoma, metastatic, uncertain primary site																				1
Mediastinum, sarcoma, metastatic, uncertain primary site																				1

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	1 5 6	2 1 5	4 2 3	4 7 1	6 1 1	6 2 3	6 2 5	6 2 7	6 4 8	6 5 8	6 5 9	6 6 0	6 6 8	6 8 9	6 9 6	7 0 2	7 0 8	7 2 1	7 3 1	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3
Carcass ID Number	0 7 2 4	0 7 7 2	0 7 1 5	0 7 2 1	0 9 0 4	0 7 3 5	0 9 0 5	0 7 7 1	0 8 7 1	0 7 7 4	0 7 1 4	0 7 8 4	0 7 8 2	0 7 4 3	0 7 9 4	0 8 0 5	0 8 9 4	0 7 1 2	0 7 3 1	0 7 5 3	0 7 1 1	0 7 1 3	0 7 2 2	0 7 2 3	0 7 3 2
Respiratory System (continued)																									
Nose			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye				+												+									
Lids, papilloma squamous																									
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder			+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+
Sarcoma, metastatic, uncertain primary site																			X						
Systemic Lesions																									
Multiple organs			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic			X				X							X											
Lymphoma malignant lymphocytic					X																				
Lymphoma malignant mixed													X												

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	3	3	4	4	4	4	5	5	5	5	6	6	6	6	6	7	7	7	8	8	8	9	9	9	9
	3	4	1	2	4	5	1	2	4	5	1	2	3	4	5	3	4	5	1	3	5	1	2	3	5
Respiratory System (continued)																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																									
Lids, papilloma squamous																									
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uncertain primary site																									
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed															X										

TABLE B2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Naphthalene: 30 ppm
(continued)

Number of Days on Study	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	
Carcass ID Number	0 8 0 1	0 8 0 2	0 8 0 3	0 8 0 4	0 8 7 2	0 8 7 4	0 8 7 5	0 8 8 1	0 8 8 2	0 8 8 3	0 8 8 4	0 8 8 5	0 8 9 1	0 8 9 2	0 8 9 3	0 8 9 5	0 9 0 1	0 9 0 2	0 9 0 3		**Total Tissues/ Tumors**
Respiratory System (continued)																					
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Trachea	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+		66
Special Senses System																					
Eye				+	+																4
Lids, papilloma squamous				X																	1
Harderian gland			+																		1
Adenoma			X																		1
Urinary System																					
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Urinary bladder	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+		63
Sarcoma, metastatic, uncertain primary site																					1
Systemic Lesions																					
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		67
Lymphoma malignant histiocytic																					3
Lymphoma malignant lymphocytic																			X		2
Lymphoma malignant mixed																					2

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Inhalation Study of Naphthalene

	0 ppm	10 ppm	30 ppm
Liver: Hepatocellular Adenoma			
Overall rates[a]	2/68 (3%)	2/12 (17%)[e]	2/134 (1%)
Adjusted rates[b]	3.4%		1.8%
Terminal rates[c]	2/59 (3%)		1/101 (1%)
First incidence (days)	736 (T)		668
Life table tests[d]			P=0.480N
Logistic regression tests[d]			P=0.443N
Fisher exact test[d]			P=0.413N
Liver: Hepatocellular Adenoma or Carcinoma			
Overall rates	2/68 (3%)	2/12 (17%)[e]	3/134 (2%)
Adjusted rates	3.4%		2.8%
Terminal rates	2/59 (3%)		1/101 (1%)
First incidence (days)	736 (T)		668
Life table tests	P=0.424N		P=0.615N
Logistic regression tests	P=0.342N		P=0.577N
Fisher exact test			P=0.547N
Lung: Alveolar/bronchiolar Adenoma			
Overall rates	5/69 (7%)	2/65 (3%)	28/135 (21%)
Adjusted rates	8.3%	3.5%	25.6%
Terminal rates	4/59 (7%)	2/57 (4%)	22/102 (22%)
First incidence (days)	729	736 (T)	471
Life table tests	P≤0.001	P=0.236N	P=0.006
Logistic regression tests	P≤0.001	P=0.233N	P=0.010
Cochran-Armitage test[d]	P≤0.001		
Fisher exact test		P=0.246N	P=0.009
Lung: Alveolar/bronchiolar Adenoma or Carcinoma			
Overall rates	5/69 (7%)	2/65 (3%)	29/135 (21%)
Adjusted rates	8.3%	3.5%	26.5%
Terminal rates	4/59 (7%)	2/57 (4%)	23/102 (23%)
First incidence (days)	729	736 (T)	471
Life table tests	P≤0.001	P=0.236N	P=0.004
Logistic regression tests	P≤0.001	P=0.233N	P=0.007
Cochran-Armitage test	P≤0.001		
Fisher exact test		P=0.246N	P=0.006
Uterus: Stromal Polyp or Stromal Sarcoma			
Overall rates	1/69 (1%)	3/65 (5%)	1/135 (1%)
Adjusted rates	1.7%	5.3%	1.0%
Terminal rates	1/59 (2%)	3/57 (5%)	1/102 (1%)
First incidence (days)	736 (T)	736 (T)	736 (T)
Life table tests	P=0.323N	P=0.294	P=0.634N
Logistic regression tests	P=0.323N	P=0.294	P=0.634N
Cochran-Armitage test	P=0.274N		
Fisher exact test		P=0.287	P=0.563N

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Inhalation Study of Naphthalene (continued)

	0 ppm	10 ppm	30 ppm
All Organs: Hemangiosarcoma			
Overall rates	0/69 (0%)	0/65 (0%)	5/135 (4%)
Adjusted rates	0.0%	0.0%	4.4%
Terminal rates	0/59 (0%)	0/57 (0%)	2/102 (2%)
First incidence (days)			648
Life table tests	P=0.030	–[f]	P=0.118
Logistic regression tests	P=0.034	–[f]	P=0.127
Cochran-Armitage test	P=0.034		
Fisher exact test		–[f]	P=0.124
All Organs: Malignant Lymphoma and Histiocytic Sarcoma			
Overall rates	8/69 (12%)	8/65 (12%)	14/135 (10%)
Adjusted rates	12.4%	14.0%	12.2%
Terminal rates	3/59 (5%)	8/57 (14%)	7/102 (7%)
First incidence (days)	574	736 (T)	423
Life table tests	P=0.520N	P=0.568	P=0.557N
Logistic regression tests	P=0.416N	P=0.554	P=0.487N
Cochran-Armitage test	P=0.417N		
Fisher exact test		P=0.554	P=0.481N
All Organs: Malignant Lymphoma (Histiocytic, Lymphocytic, or Mixed)			
Overall rates	8/69 (12%)	8/65 (12%)	14/135 (10%)
Adjusted rates	12.4%	14.0%	12.2%
Terminal rates	3/59 (5%)	8/57 (14%)	7/102 (7%)
First incidence (days)	574	736 (T)	423
Life table tests	P=0.520N	P=0.568	P=0.557N
Logistic regression tests	P=0.416N	P=0.554	P=0.487N
Cochran-Armitage test	P=0.417N		
Fisher exact test		P=0.554	P=0.481N
All Organs: Benign Tumors			
Overall rates	15/69 (22%)	7/65 (11%)	41/135 (30%)
Adjusted rates	24.6%	12.3%	36.6%
Terminal rates	13/59 (22%)	7/57 (12%)	32/102 (31%)
First incidence (days)	662	736 (T)	471
Life table tests	P=0.006	P=0.063N	P=0.064
Logistic regression tests	P=0.015	P=0.066N	P=0.112
Cochran-Armitage test	P=0.018		
Fisher exact test		P=0.069N	P=0.126
All Organs: Malignant Tumors			
Overall rates	12/69 (17%)	18/65 (28%)	32/135 (24%)
Adjusted rates	18.7%	30.5%	25.5%
Terminal rates	7/59 (12%)	16/57 (28%)	11/102 (11%)
First incidence (days)	574	669	423
Life table tests	P=0.201	P=0.135	P=0.158
Logistic regression tests	P=0.303	P=0.108	P=0.197
Cochran-Armitage test	P=0.302		
Fisher exact test		P=0.111	P=0.203

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Inhalation Study of Naphthalene (continued)

	0 ppm	10 ppm	30 ppm
All Organs: Benign and Malignant Tumors			
Overall rates	23/69 (33%)	22/65 (34%)	64/135 (47%)
Adjusted rates	35.4%	37.3%	49.9%
Terminal rates	17/59 (29%)	20/57 (35%)	38/102 (37%)
First incidence (days)	574	669	423
Life table tests	P=0.006	P=0.557N	P=0.025
Logistic regression tests	P=0.016	P=0.540	P=0.038
Cochran-Armitage test	P=0.018		
Fisher exact test		P=0.548	P=0.037

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

TABLE B4a
Historical Incidence of Lung Alveolar/bronchiolar Tumors in Female B6C3F$_1$ Mice in Inhalation Studies[a]

	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Overall Historical Incidence			
Total	27/466 (5.8%)	13/466 (2.8%)	39/466 (8.4%)
Standard deviation	3.2	2.7	3.5
Range	0%–10%	0%–6%	0%–12%

[a] Data as of 15 September 1990

TABLE B4b
Historical Incidence of Hemangiomas and Hemangiosarcomas in Female B6C3F$_1$ Mice in Inhalation Studies[a]

	Incidence in Controls		
	Hemangiomas	Hemangiosarcomas	Hemangiomas or Hemangiosarcomas
Overall Historical Incidence			
Total	5/467 (1.1%)	12/467 (2.6%)	17/467 (3.6%)
Standard deviation	1.8	2.2	3.4
Range	0%-4%	0%-6%	0%-8%

[a] Data as of 15 September 1990

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Inhalation Study of Naphthalene[a]

	0ppm	10 ppm	30 ppm	30 ppm
Disposition Summary				
Animals initially in study	75	75	75	75
Special study animals[b]	5	7	6	6
Early deaths				
Natural death	8	6	10	7
Moribund	2	2	6	10
Accidental deaths	1	0		
Survivors				
Died last week of study		1	1	
Terminal sacrifice	59	56	51	50
Missing		3	1	2
Animals examined microscopically	69	65	68	67
Alimentary System				
Gallbladder	(65)	(2)	(60)	(64)
Dilatation				1 (2%)
Infiltration cellular, lymphocyte, focal			2 (3%)	
Infiltration cellular, lymphocyte, multifocal			1 (2%)	1 (2%)
Serosa, inflammation, chronic, multifocal	1 (2%)			
Intestine large, cecum	(66)	(1)	(60)	(64)
Hyperplasia, lymphoid, focal			1 (2%)	1 (2%)
Serosa, inflammation, chronic, multifocal	1 (2%)			
Intestine large, colon	(67)	(2)	(62)	(66)
Parasite metazoan			4 (6%)	3 (5%)
Intestine small, duodenum	(66)	(4)	(61)	(63)
Hyperplasia, lymphoid, focal		1 (25%)	1 (2%)	
Intestine small, ileum	(66)	(1)	(61)	(63)
Amyloid deposition, multifocal				1 (2%)
Serosa, inflammation, chronic, multifocal	1 (2%)			
Intestine small, jejunum	(65)	(1)	(61)	(63)
Serosa, inflammation, chronic, multifocal	1 (2%)			
Liver	(68)	(12)	(67)	(67)
Angiectasis, focal			1 (1%)	1 (1%)
Basophilic focus	1 (1%)			
Clear cell focus			1 (1%)	
Cyst	1 (1%)			
Focal cellular change, focal			1 (1%)	
Hematopoietic cell proliferation, focal			2 (3%)	
Hematopoietic cell proliferation, multifocal	5 (7%)		7 (10%)	5 (7%)
Infiltration cellular, lymphocyte, focal	1 (1%)		5 (7%)	7 (10%)
Infiltration cellular, lymphocyte, multifocal	16 (24%)	1 (8%)	16 (24%)	17 (25%)
Inflammation, chronic, multifocal	2 (3%)			
Mineralization, focal			1 (1%)	1 (1%)
Necrosis, focal			1 (1%)	2 (3%)
Necrosis, multifocal		1 (8%)	2 (3%)	1 (1%)
Pigmentation, focal	1 (1%)			1 (1%)
Bile duct, cytoplasmic alteration, multifocal			1 (1%)	
Hepatocyte, atrophy, diffuse				1 (1%)
Mesentery	(6)		(3)	(3)
Infiltration cellular, lymphocyte, multifocal	1 (17%)			1 (33%)
Infiltration cellular, mixed cell, multifocal			1 (33%)	
Inflammation, chronic, multifocal	1 (17%)			
Inflammation, granulomatous, focal	1 (17%)			
Fat, necrosis	2 (33%)		1 (33%)	

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Inhalation Study of Naphthalene (continued)

	0ppm	10 ppm	30 ppm	30 ppm
Alimentary System (continued)				
Pancreas	(69)	(5)	(65)	(67)
Atrophy, diffuse	2 (3%)			
Atrophy, focal				1 (1%)
Atrophy, multifocal	1 (1%)		1 (2%)	1 (1%)
Infiltration cellular, lymphocyte, focal	3 (4%)		3 (5%)	1 (1%)
Infiltration cellular, lymphocyte, multifocal	18 (26%)		17 (26%)	17 (25%)
Inflammation, multifocal	3 (4%)		1 (2%)	1 (1%)
Vacuolization cytoplasmic, multifocal			1 (2%)	
Acinus, hyperplasia, focal				1 (1%)
Duct, dilatation	1 (1%)		2 (3%)	1 (1%)
Salivary glands	(68)	(5)	(64)	(67)
Infiltration cellular, lymphocyte, focal	3 (4%)	1 (20%)	3 (5%)	10 (15%)
Infiltration cellular, lymphocyte, multifocal	40 (59%)		34 (53%)	30 (45%)
Stomach, forestomach	(67)	(5)	(67)	(67)
Hyperkeratosis, focal				1 (1%)
Hyperplasia, focal			1 (1%)	1 (1%)
Stomach, glandular	(67)	(5)	(65)	(67)
Hemorrhage, focal				1 (1%)
Infiltration cellular, lymphocyte, multifocal	1 (1%)			
Mucosa, cyst				1 (1%)
Cardiovascular System				
Blood vessel			(1)	
Adventitia, inflammation, multifocal			1 (100%)	
Media, hypertrophy, multifocal			1 (100%)	
Heart	(69)	(4)	(68)	(67)
Infiltration cellular, lymphocyte, focal	1 (1%)			
Mineralization, multifocal		1 (25%)		
Myocardium, inflammation, chronic, focal			1 (1%)	
Myocardium, inflammation, suppurative, focal			1 (1%)	
Valve, pigmentation, focal	3 (4%)		6 (9%)	6 (9%)
Valve, pigmentation, multifocal	7 (10%)		7 (10%)	7 (10%)
Endocrine System				
Adrenal gland	(66)	(4)	(67)	(67)
Capsule, hyperplasia, multifocal	66 (100%)	2 (50%)	67 (100%)	66 (99%)
Capsule, inflammation, chronic, multifocal	1 (2%)			
Adrenal gland, cortex	(66)	(4)	(67)	(67)
Accessory adrenal cortical nodule	1 (2%)			
Congestion, multifocal	1 (2%)		3 (4%)	
Cyst	1 (2%)			
Degeneration, focal	1 (2%)		1 (1%)	
Focal cellular change	2 (3%)			1 (1%)
Hypertrophy, focal			1 (1%)	
Pigmentation, focal	2 (3%)			
Adrenal gland, medulla	(64)	(4)	(66)	(66)
Congestion, multifocal			1 (2%)	
Degeneration				1 (2%)
Hyperplasia	1 (2%)			1 (2%)
Islets, pancreatic	(69)	(4)	(66)	(67)
Hyperplasia, focal	1 (1%)			

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Inhalation Study of Naphthalene (continued)

	0ppm	10 ppm	30 ppm	30 ppm
Endocrine System (continued)				
Parathyroid gland	(68)		(66)	(64)
Cyst, focal	1 (1%)			1 (2%)
Degeneration, focal				1 (2%)
Infiltration cellular, lymphocyte, focal				1 (2%)
Infiltration cellular, lymphocyte, multifocal				1 (2%)
Bilateral, hyperplasia				1 (2%)
Pituitary gland	(61)	(4)	(50)	(54)
Cyst, multifocal				1 (2%)
Pars distalis, angiectasis	1 (2%)		2 (4%)	
Pars distalis, hyperplasia	4 (7%)	1 (25%)		1 (2%)
Thyroid gland	(69)	(4)	(67)	(66)
Infiltration cellular, lymphocyte, focal			1 (1%)	2 (3%)
Inflammation, acute, focal	1 (1%)		2 (3%)	2 (3%)
Follicle, dilatation, focal	2 (3%)		2 (3%)	5 (8%)
Follicular cell, hyperplasia, focal	3 (4%)		2 (3%)	4 (6%)
Follicular cell, hyperplasia, multifocal	1 (1%)		1 (1%)	1 (2%)
Follicular cell, hypertrophy, multifocal	1 (1%)			1 (2%)
General Body System				
None				
Genital System				
Ovary	(69)	(14)	(66)	(65)
Cyst	11 (16%)	9 (64%)	16 (24%)	11 (17%)
Cyst, multifocal	1 (1%)	1 (7%)	1 (2%)	2 (3%)
Giant cell, multiple				1 (2%)
Hematocyst, focal		2 (14%)	2 (3%)	2 (3%)
Infiltration cellular, histiocyte				1 (2%)
Inflammation, suppurative, multifocal			1 (2%)	
Metaplasia, osseous, focal			1 (2%)	
Mineralization, multifocal				1 (2%)
Pigmentation	1 (1%)			
Follicle, hemorrhage, focal	3 (4%)			1 (2%)
Interstitium, hyperplasia	1 (1%)			
Oviduct	(2)	(1)	(4)	(4)
Mucosa, hyperplasia, cystic		1 (100%)		
Mucosa, vacuolization cytoplasmic, multifocal	1 (50%)			
Uterus	(69)	(41)	(67)	(66)
Angiectasis, multifocal	1 (1%)	1 (2%)	1 (1%)	
Dilatation		2 (5%)	7 (10%)	6 (9%)
Inflammation, suppurative			1 (1%)	1 (2%)
Endometrium, hyperplasia, cystic	61 (88%)	36 (88%)	49 (73%)	56 (85%)

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Inhalation Study of Naphthalene (continued)

	0ppm	10 ppm	30 ppm	30 ppm
Hematopoietic System				
Blood			(1)	(5)
Leukocytosis			1 (100%)	3 (60%)
Bone marrow	(69)	(4)	(68)	(67)
Angiectasis	1 (1%)		1 (1%)	
Atrophy			4 (6%)	
Congestion			1 (1%)	
Fibrous osteodystrophy, focal				1 (1%)
Fibrous osteodystrophy, multifocal	1 (1%)			
Hyperplasia	2 (3%)		1 (1%)	1 (1%)
Hyperplasia, lymphoid	4 (6%)			
Hyperplasia, neutrophil				1 (1%)
Myelofibrosis	2 (3%)		3 (4%)	
Pigmentation, focal			1 (1%)	
Pigmentation, multifocal			1 (1%)	
Lymph node	(69)	(9)	(67)	(67)
Hyperplasia				1 (1%)
Lymph node, bronchial	(46)	(1)	(46)	(40)
Congestion			1 (2%)	
Hyperplasia, lymphoid			1 (2%)	2 (5%)
Pigmentation	1 (2%)			
Lymph node, mandibular	(66)	(6)	(62)	(65)
Edema	1 (2%)			
Erythrophagocytosis			1 (2%)	
Hemorrhage			1 (2%)	1 (2%)
Hyperplasia, lymphoid	2 (3%)	1 (17%)		4 (6%)
Infiltration cellular, histiocyte				1 (2%)
Pigmentation	15 (23%)		12 (19%)	13 (20%)
Lymph node, mediastinal	(60)	(6)	(52)	(57)
Angiectasis	1 (2%)			
Erythrophagocytosis			1 (2%)	
Hyperplasia, lymphoid	1 (2%)		1 (2%)	2 (4%)
Infiltration cellular, histiocyte		1 (17%)		
Pigmentation	8 (13%)		3 (6%)	1 (2%)
Lymph node, mesenteric	(67)	(4)	(60)	(62)
Erythrophagocytosis	2 (3%)		1 (2%)	1 (2%)
Giant cell, multifocal	17 (25%)		16 (27%)	8 (13%)
Hemorrhage	4 (6%)		2 (3%)	2 (3%)
Hyperplasia, lymphoid	1 (1%)		1 (2%)	1 (2%)
Hyperplasia, plasma cell, multifocal	1 (1%)			
Infiltration cellular, polymorphonuclear	1 (1%)			
Spleen	(67)	(13)	(67)	(67)
Angiectasis, multifocal			1 (1%)	
Congestion			1 (1%)	
Hematopoietic cell proliferation	4 (6%)	3 (23%)	7 (10%)	10 (15%)
Hyperplasia, lymphoid	9 (13%)	3 (23%)	6 (9%)	12 (18%)
Hyperplasia, neutrophil				1 (1%)
Hyperplasia, plasma cell	1 (1%)			1 (1%)
Infiltration cellular, histiocyte		1 (8%)		
Capsule, inflammation, chronic, multifocal	1 (1%)			
Thymus	(64)	(3)	(60)	(59)
Angiectasis	1 (2%)			
Cyst, multiple	1 (2%)			
Depletion lymphoid			1 (2%)	
Hyperplasia, lymphoid	1 (2%)			

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Inhalation Study of Naphthalene (continued)

	0ppm	10 ppm	30 ppm	30 ppm
Integumentary System				
Mammary gland	(69)	(5)	(66)	(66)
Hyperplasia, focal	2 (3%)			
Infiltration cellular, lymphocyte, focal			1 (2%)	1 (2%)
Infiltration cellular, lymphocyte, multifocal	1 (1%)		1 (2%)	2 (3%)
Duct, galactocele, multifocal			1 (2%)	
Skin	(69)	(6)	(67)	(67)
Acanthosis, multifocal				1 (1%)
Inflammation, focal				1 (1%)
Subcutaneous tissue, infiltration cellular, lymphocyte, multifocal	1 (1%)			
Subcutaneous tissue, infiltration cellular, polymorphonuclear, multifocal				1 (1%)
Musculoskeletal System				
Bone	(69)	(4)	(68)	(67)
Fibrous osteodystrophy, focal	3 (4%)		4 (6%)	6 (9%)
Fibrous osteodystrophy, multifocal	7 (10%)		12 (18%)	11 (16%)
Hyperplasia, multifocal			1 (1%)	
Metaplasia, cartilagenous, focal			1 (1%)	
Skeletal muscle			(3)	(3)
Head, hemorrhage, multifocal			1 (33%)	
Hindlimb, infiltration cellular, lymphocyte, focal				1 (33%)
Nervous System				
Brain	(69)	(4)	(68)	(67)
Fibrosis, multifocal			1 (1%)	
Hemorrhage, multifocal			1 (1%)	2 (3%)
Metaplasia, osseous, focal	1 (1%)			
Mineralization, focal	3 (4%)	1 (25%)	11 (16%)	3 (4%)
Mineralization, multifocal	34 (49%)		8 (12%)	21 (31%)
Cerebrum, necrosis, focal			1 (1%)	
Respiratory System				
Lung	(69)	(65)	(68)	(67)
Congestion	2 (3%)	1 (2%)	1 (1%)	
Hemorrhage	1 (1%)	1 (2%)	1 (1%)	
Infiltration cellular, lymphocyte	11 (16%)	21 (32%)	20 (29%)	26 (39%)
Infiltration cellular, histiocyte	1 (1%)	5 (8%)	2 (3%)	2 (3%)
Inflammation	3 (4%)	13 (20%)	34 (50%)	18 (27%)
Inflammation, granulomatous		38 (58%)	14 (21%)	28 (42%)
Metaplasia, osseous, focal			1 (1%)	
Alveolar epithelium, hyperplasia	3 (4%)	6 (9%)	5 (7%)	7 (10%)
Glands, inflammation	1 (1%)	3 (5%)	7 (10%)	8 (12%)
Nose	(69)	(65)	(68)	(67)
Hemorrhage	1 (1%)		2 (3%)	1 (1%)
Infiltration cellular, lymphocyte, multifocal	1 (1%)			
Inflammation	1 (1%)	65 (100%)	68 (100%)	67 (100%)
Olfactory epithelium, metaplasia		65 (100%)	68 (100%)	67 (100%)
Respiratory epithelium, hyperplasia		65 (100%)	68 (100%)	67 (100%)
Trachea	(69)	(4)	(68)	(66)
Glands, dilatation, multifocal				1 (2%)
Glands, inflammation, suppurative, multifocal	1 (1%)			

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Inhalation Study of Naphthalene (continued)

	0ppm	10 ppm	30 ppm	30 ppm
Special Senses System				
Eye	(2)	(6)	(2)	(4)
Degeneration		3 (50%)	1 (50%)	
Inflammation				1 (25%)
Mineralization			1 (50%)	
Pigmentation	1 (50%)			1 (25%)
Bilateral, lens, cataract	1 (50%)			
Cornea, degeneration	1 (50%)			
Lens, cataract		2 (33%)	1 (50%)	2 (50%)
Optic nerve, degeneration	1 (50%)			
Retina, atrophy	1 (50%)			1 (25%)
Harderian gland	(1)	(2)	(1)	(1)
Infiltration cellular, lymphocyte, multifocal	1 (100%)			
Urinary System				
Kidney	(69)	(7)	(67)	(67)
Congestion, multifocal	1 (1%)			
Fibrosis, focal			1 (1%)	
Hemorrhage, multifocal			1 (1%)	
Infarct, focal	1 (1%)		1 (1%)	
Infiltration cellular, lymphocyte, focal	2 (3%)		7 (10%)	1 (1%)
Infiltration cellular, lymphocyte, multifocal	45 (65%)	1 (14%)	40 (60%)	42 (63%)
Inflammation, acute, focal		1 (14%)		
Metaplasia, osseous, focal	1 (1%)			
Nephropathy	3 (4%)	1 (14%)	4 (6%)	4 (6%)
Capsule, inflammation, chronic, multifocal	1 (1%)			
Glomerulus, amyloid deposition, multifocal				1 (1%)
Renal tubule, hyperplasia, focal				1 (1%)
Renal tubule, mineralization, multifocal		1 (14%)		
Urinary bladder	(67)	(1)	(62)	(63)
Dilatation			1 (2%)	1 (2%)
Infiltration cellular, lymphocyte, focal	4 (6%)		6 (10%)	5 (8%)
Infiltration cellular, lymphocyte, multifocal	47 (70%)		42 (68%)	37 (59%)

[a] Incidences are expressed as the ratio of animals with lesions to the number of animals examined microscopically at the site.
[b] Animals from the hematology group that were sacrificed or died prior to becoming part of the 2-year studies; these animals were not examined microscopically.

APPENDIX C
GENETIC TOXICOLOGY

SALMONELLA PROTOCOL

Testing was performed as reported in Haworth *et al.* (1983) and Mortelmans *et al.* (1986). Naphthalene was sent to the laboratory as a coded aliquot from Radian Corporation (Austin, TX). It was incubated with the *Salmonella typhimurium* tester strains (TA98, TA100, TA1535, TA1537) either in buffer or S9 mix (metabolic activation enzymes and cofactors from Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver) for 20 minutes at 37° C prior to the addition of soft agar supplemented with *l*-histidine and *d*-biotin, and subsequent plating on minimal glucose agar plates. Incubation continued for 48 hours.

Each trial consisted of triplicate plates of concurrent positive and negative controls and of at least five doses of naphthalene. High dose was limited by toxicity. All assays were repeated.

A positive response in this assay is defined as a reproducible, dose-related increase in histidine-independent (revertant) colonies in any one strain/activation combination. An equivocal response is defined as an increase in revertants which was not dose-related, not reproducible, or of insufficient magnitude to support a determination of mutagenicity. A negative response is obtained when no increase in revertant colonies occurs following chemical treatment.

CHINESE HAMSTER OVARY CELL CYTOGENETICS ASSAYS

Testing was performed as reported by Galloway *et al.* (1985, 1987) and presented briefly below. Naphthalene was sent to the laboratory as a coded aliquot from Radian Corporation (Austin, TX). It was tested in cultured Chinese hamster ovary (CHO) cells for induction of sister chromatid exchanges (SCE) and chromosomal aberrations (Abs) both in the presence and in the absence of Aroclor 1254-induced male Sprague-Dawley rat liver S9 and cofactor mix. Cultures were handled under gold lights to prevent photolysis of bromodeoxyuridine-substituted DNA. Each test consisted of concurrent solvent and positive controls and of at least three doses of test chemical; the high dose was limited by toxicity.

In the SCE test without S9, CHO cells were incubated for 26 hours with the study chemical in McCoy's 5A medium supplemented with 10% fetal bovine serum, *l*-glutamine (2mM), and antibiotics. Bromodeoxyuridine (BrdU) was added 2 hours after culture initiation. After 26 hours, the medium containing the test chemical was removed and replaced with fresh medium plus BrdU and Colcemid, and incubation was continued for 2 to 3 hours. Cells were then harvested by mitotic shake-off, fixed, and stained with Hoechst 33258 and Giemsa. In the SCE test with S9, cells were incubated with the chemical, serum-free medium, and S9 for 2 hours. The medium was then removed and replaced with medium containing BrdU and no test chemical and incubation proceeded for an additional 26 hours, with Colcemid present for the final 2 to 3 hours. Harvesting and staining was the same as for cells treated without S9.

In the Abs test without S9, cells were incubated in McCoy's 5A medium with the study chemical for 8 to 10 hours; Colcemid was added and incubation continued for 2 to 3 hours. The cells were then harvested by mitotic shake-off, fixed, and stained with Giemsa. For the Abs test with S9, cells were treated with the study chemical and S9 for 2 hours, after which the treatment medium was removed and the cells were incubated for 8 to 10 hours in fresh medium, with Colcemid present for the final 2 to 3 hours. Cells were harvested in the same manner as for the treatment without S9.

For the SCE test, if significant chemical-induced cell cycle delay was seen, incubation time was lengthened to ensure a sufficient number of scorable cells. The harvest time for the Abs test was based on the cell cycle information obtained in the SCE test; if cell cycle delay was anticipated, the incubation period was extended.

Cells were selected for scoring on the basis of good morphology and completeness of karyotype (21 ± 2 chromosomes). All slides were scored blind and those from a single test were read by the same person. For the SCE test, usually 25 or 50 second-division metaphase cells were scored for frequency of SCE per cell from each dose level; 200 first-division metaphase cells were scored at each dose level for the Abs test. Classes of aberrations included simple (breaks and terminal deletions), complex (rearrangements and translocations), and other (pulverized cells, despiralized chromosomes, and cells containing 10 or more aberrations).

Statistical analyses were conducted on both the slopes of the dose-response curves and the individual dose points. An SCE frequency 20% above the concurrent solvent control value was chosen as a statistically conservative positive response. The probability of this level of difference occurring by chance at one dose point is less than 0.01; the probability for such a chance occurrence at two dose points is less than 0.001. Chromosomal aberration data are presented as percentage of cells with aberrations. As with SCE, both the dose-response curve and individual dose points were statistically analyzed. A statistically significant ($P \leq 0.05$) difference for one dose point was considered weak evidence for a positive response (+w); significant differences for two or more doses indicated the trial was positive (+) (Galloway *et al.*, 1987).

RESULTS

Naphthalene (0.3-100.0 μg/plate) was negative for the induction of gene mutations in *Salmonella typhimurium* strains TA100, TA1535, TA1537, and TA98 when tested in a preincubation protocol in the presence and the absence of Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver S9 (Mortelmans *et al.*, 1986) (Table C1). In cytogenetic tests with Chinese hamster ovary cells, naphthalene induced both sister chromatid exchanges and chromosomal aberrations. Sister chromatid exchanges were induced, generally within a dose range of 27 to 90 μg/mL naphthalene, both in the presence and the absence of Aroclor 1254-induced male Sprague-Dawley rat liver S9 (Table C2). The positive responses in the chromosomal aberration test were obtained only in the presence of S9, over a dose range of 30 to 67.5 μg/mL naphthalene (Table C3); a delayed harvest protocol was employed to offset naphthalene-induced cell cycle delay and allow accumulation of sufficient metaphases for scoring.

TABLE C1
Mutagenicity of Naphthalene in *Salmonella typhimurium*[a]

Strain	Dose (μg/plate)	Revertants/plate[b] -S9 Trial 1	-S9 Trial 2	+10% hamster S9 Trial 1	+10% hamster S9 Trial 2	+10% rat S9 Trial 1	+10% rat S9 Trial 2
TA100	0	143 ± 4.5	141 ± 4.2	143 ± 11.9	128 ± 6.2	144 ± 2.4	137 ± 8.2
	0.3		121 ± 3.5				
	1	146 ± 5.8	124 ± 3.6	143 ± 13.2	115 ± 7.9	130 ± 2.7	143 ± 16.0
	3.3	124 ± 12.0	117 ± 8.5	155 ± 4.9	135 ± 2.4	133 ± 13.2	133 ± 5.9
	10	145 ± 5.8	113 ± 6.2	140 ± 3.5	118 ± 9.8	135 ± 8.7	121 ± 6.6
	33	141 ± 9.4[c]	113 ± 5.1	147 ± 5.7	133 ± 6.8	142 ± 6.6	121 ± 7.3
	100	Toxic		141 ± 2.0[c]	145 ± 9.0[c]	104 ± 0.6[c]	127 ± 5.4[c]
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control[d]		1,636 ± 45.5	801 ± 28.7	2,534 ± 77.9	754 ± 19.2	1,074 ± 13.2	792 ± 26.4
TA1535	0	22 ± 1.5	19 ± 2.6	11 ± 2.3	8 ± 0.6	9 ± 0.6	12 ± 2.4
	0.3		24 ± 3.1				
	1	21 ± 3.0	26 ± 2.7	10 ± 3.3	11 ± 2.9	13 ± 1.2	16 ± 1.5
	3.3	22 ± 5.2	23 ± 2.3	10 ± 0.9	11 ± 3.8	9 ± 0.7	10 ± 1.7
	10	30 ± 2.6	20 ± 1.2	12 ± 0.6	11 ± 0.3	8 ± 0.7	10 ± 2.6
	33	20 ± 1.2[c]	15 ± 2.3	13 ± 1.0	11 ± 1.7	11 ± 1.5	13 ± 1.2
	100	15 ± 3.5[c]		6 ± 1.9[c]	10 ± 3.2[c]	13 ± 3.4[c]	11 ± 2.9[c]
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		1,258 ± 18.8	687 ± 6.4	126 ± 1.7	75 ± 8.9	63 ± 8.0	48 ± 1.9
TA1537	0	8 ± 1.8	8 ± 1.9	10 ± 1.2	6 ± 2.4	11 ± 3.8	10 ± 2.3
	0.3		7 ± 1.2				
	1	8 ± 0.6	5 ± 0.6	11 ± 1.2	8 ± 0.3	10 ± 0.9	8 ± 0.7
	3.3	7 ± 1.5	9 ± 0.6	9 ± 3.2	7 ± 0.9	9 ± 0.9	9 ± 0.9
	10	8 ± 0.7	9 ± 1.5	12 ± 2.0	10 ± 1.5	8 ± 1.7	5 ± 2.2
	33	6 ± 2.0[c]	4 ± 0.9	12 ± 1.5	10 ± 1.5	10 ± 1.9	7 ± 1.5
	100	Toxic		10 ± 1.0[c]	5 ± 0.6[c]	5 ± 1.9[c]	4 ± 0.6[c]
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		1,010 ± 39.4	185 ± 12.0	205 ± 22.1	77 ± 5.3	87 ± 5.2	86 ± 2.9
TA98	0	14 ± 3.8	17 ± 1.0	35 ± 4.8	20 ± 3.1	29 ± 4.1	23 ± 0.3
	0.3		12 ± 2.2				
	1	15 ± 2.2	17 ± 1.5	30 ± 2.6	29 ± 2.1	27 ± 1.8	23 ± 2.2
	3.3	22 ± 2.3	12 ± 2.6	42 ± 5.5	21 ± 1.9	32 ± 1.7	24 ± 0.7
	10	16 ± 3.3	12 ± 2.6	32 ± 4.2	26 ± 1.2	25 ± 2.6	21 ± 0.9
	33	19 ± 2.5[c]	12 ± 3.2	32 ± 3.1	21 ± 1.2	29 ± 1.9	24 ± 2.8
	100	14 ± 0.3[c]		34 ± 1.5[c]	23 ± 2.4	22 ± 1.2[c]	24 ± 1.2
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		1,772 ± 9.6	1,072 ± 40.3	2,064 ± 71.4	183 ± 10.1	982 ± 43.1	176 ± 16.6

[a] Study performed at EG&G Mason Research Institute. The detailed protocol and these data are presented in Mortelmans *et al.* (1986). Cells and study compound or solvent (acetone) were incubated in the absence of exogenous metabolic activation (-S9) or with Aroclor 1254-induced S9 from male Syrian hamster liver or male Sprague-Dawley rat liver. High dose was limited by toxicity; 0 μg/plate dose is the solvent control.

[b] Revertants are presented as mean ± the standard error from three plates.

[c] Slight toxicity

[d] 2-aminoanthracene was used on all strains in the presence of S9. In the absence of metabolic activation, 4-nitro-*o*-phenylenediamine was tested on TA98, sodium azide was tested on TA100 and TA1535, and 9-aminoacridine was tested on TA1537.

TABLE C2
Induction of Sister Chromatid Exchanges in Chinese Hamster Ovary Cells by Naphthalene[a]

Compound	Dose (μg/mL)	Total Cells	No. of Chromosomes	No. of SCEs	SCEs/ Chromosome	SCEs/ Cell	Hrs in BrdU	Relative SCEs/Chromosome (%)[b]
-S9								
Trial 1								
Summary: Weak Positive								
Dimethylsulfoxide		50	1,046	388	0.37	7.8	25.8	
Mitomycin-C	0.0010	50	1,049	597	0.56	11.9	25.8	53.43
	0.0100	5	105	217	2.06	43.4	25.8	457.16
Naphthalene	9	50	1,048	406	0.38	8.1	25.8	4.44
	27	50	1,041	442	0.42	8.8	25.8	14.47
	90	50	1,042	578	0.558	11.6	30.9[c]	49.54*
								P≤0.001[d]
Trial 2								
Summary: Positive								
Dimethylsulfoxide		25	525	178	0.33	7.1	25.8	
Mitomycin-C	0.0010	25	525	376	0.71	15.0	25.8	111.24
	0.0100	5	105	263	2.50	52.6	25.8	638.78
Naphthalene	27	25	525	222	0.42	8.9	25.8	24.72*
	45	25	525	268	0.51	10.7	25.8	50.56*
	90	25	525	268	0.51	10.7	25.8	50.56*
								P≤0.001
+S9								
Trial 1								
Summary: Questionable								
Dimethylsulfoxide		50	1,050	423	0.40	8.5	25.8	
Cyclophosphamide	0.4	50	1,050	792	0.75	15.8	25.8	87.24
	2	5	105	197	1.87	39.4	25.8	365.73
Naphthalene	2.7	50	1,050	411	0.39	8.2	25.8	-2.84
	9	50	1,050	493	0.46	9.9	25.8	16.55
	27	50	1,045	505	0.48	10.1	30.9[c]	19.96
								P≤0.001

TABLE C2
Induction of Sister Chromatid Exchanges in Chinese Hamster Ovary Cells by Naphthalene (continued)

Compound	Dose (μg/mL)	Total Cells	No. of Chromosomes	No. of SCEs	SCEs/ Chromosome	SCEs/ Cell	Hrs in BrdU	Relative SCEs/Chromosome (%)
+S9								
Trial 2								
Summary: Positive								
Dimethylsulfoxide		25	525	189	0.36	7.6	25.8	
Cyclophosphamide	0.4	25	525	334	0.63	13.4	25.8	76.72
	2	5	105	174	1.65	34.8	25.8	360.32
Naphthalene	9	25	525	199	0.37	8.0	25.8	5.29
	15	25	525	239	0.45	9.6	25.8	26.45*
	27	25	525	266	0.50	10.6	25.8	40.74*
								P≤0.001

* Positive (≥20% increase over solvent control)
[a] Study performed at Litton Bionetics, Inc. SCE = sister chromatid exchange; BrdU = bromodeoxyuridine. A detailed description of the SCE protocol is presented by Galloway *et al.* (1985, 1987).
[b] Percent increase in SCEs/chromosome of culture exposed to study chemical relative to those of culture exposed to solvent.
[c] Because some chemicals induce a delay in the cell division cycle, harvest times are occasionally extended to maximize the proportion of second division cells available for analysis.
[d] Significance of relative SCEs/chromosome tested by the linear regression trend test vs. log of the dose

TABLE C3
Induction of Chromosomal Aberrations in Chinese Hamster Ovary Cells by Naphthalene[a]

-S9[b]					+S9[c]				
Dose (μg/mL)	Total Cells	No. of Abs	Abs/ Cell	Percent Cells with Abs	Dose (μg/mL)	Total Cells	No. of Abs	Abs/ Cell	Percent Cells with Abs
Trial 1 – Harvest time: 20.5 hours[d] Summary: Negative					**Trial 1** – Harvest time: 20.5 hours[d] Summary: Positive				
Dimethylsulfoxide					Dimethylsulfoxide				
	200	1	0.01	0.5		200	3	0.02	1.5
Mitomycin-C					Cyclophosphamide				
0.05	200	31	0.16	11.0	6.25	200	31	0.16	13.5
0.08	25	25	1.00	48.0	12.50	25	17	0.68	44.0
Naphthalene					Naphthalene				
37.5	200	2	0.01	1.0	30	200	29	0.15	11.0*
75	200	3	0.02	1.5	45	100	27	0.27	20.0*
					67.5	100	50	0.50	32.0*
				P=0.157[e]					P≤0.001
Trial 2 – Harvest time: 10.1 hours Summary: Negative					**Trial 2** – Harvest time: 20.2 hours[d] Summary: Positive				
Dimethylsulfoxide					Dimethylsulfoxide				
	200	1	0.01	0.5		200	0	0.00	0.0
Mitomycin-C					Cyclophosphamide				
0.25	200	19	0.10	8.5	6.25	200	23	0.12	11.5
0.75	25	6	0.24	24.0	12.50	25	19	0.76	52.0
Naphthalene					Naphthalene				
15	200	2	0.01	0.5	45	200	29	0.15	8.5*
37.5	200	0	0.00	0.0	56.25	200	39	0.20	13.5*
					67.5	200	37	0.19	16.0*
				P=0.807					P≤0.001

* Positive (P≤0.05)

[a] Study performed at Litton Bionetics, Inc. Abs = aberrations. A detailed presentation of the technique for detecting chromosomal aberrations is found in Galloway *et al.* (1985, 1987). Briefly, Chinese hamster ovary cells were incubated with study compound or solvent (dimethylsulfoxide) as described in [b] and [c]. Cells were arrested in first metaphase by addition of Colcemid and harvested by mitotic shake off, fixed, and stained in 6% Giemsa.

[b] In the absence of S9, cells were incubated with naphthalene or solvent for 8 to 10 hours at 37° C. Cells were then washed and fresh medium containing Colcemid was added for an additional 2 to 3 hours followed by harvest.

[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 to 10 hours. Colcemid was added for the last 2 to 3 hours of incubation before harvest. S9 was from the livers of Aroclor 1254-induced male Sprague-Dawley rats.

[d] Delayed harvest

[e] Significance of the percentage of cells with aberrations tested by the linear regression trend test vs. log of the dose

APPENDIX D
HEMATOLOGY RESULTS

TABLE D1
Hematology Data at the 14-Day Interim Evaluation in the 2-Year Inhalation Studies of Naphthalene

Analysis	0 ppm	10 ppm	30 ppm
Male			
n	5	4	10
Hematocrit (%)	38.2 ± 0.4	40.1 ± 0.9	39.8 ± 0.6
Hemoglobin (g/dL)	16.8 ± 0.3	17.2 ± 0.2	17.1 ± 0.2
Erythrocytes ($10^6/\mu L$)	7.04 ± 0.15	7.48 ± 0.12	7.49 ± 0.09
Mean cell volume (μ^3)	55.0 ± 0.8	54.5 ± 1.2	53.7 ± 0.3
Reticulocytes ($10^6/\mu L$)	0.17 ± 0.02	0.18 ± 0.02	0.20 ± 0.02
Leukocytes ($10^3/\mu L$)	6.69 ± 0.73	10.65 ± 1.43	5.35 ± 0.28
Female			
n	4	5	10
Hematocrit (%)	39.2 ± 0.4	38.2 ± 0.4	37.6 ± 0.4*
Hemoglobin (g/dL)	17.2 ± 0.2	16.6 ± 0.3	17.6 ± 0.1
Erythrocytes ($10^6/\mu L$)	7.35 ± 0.08	7.22 ± 0.06	7.21 ± 0.05
Mean cell volume (μ^3)	54.0 ± 0.4	53.4 ± 0.2	52.6 ± 0.3*
Reticulocytes ($10^6/\mu L$)	0.20 ± 0.01	0.16 ± 0.01	0.17 ± 0.02
Leukocytes ($10^3/\mu L$)	2.79 ± 0.25	5.18 ± 0.52*	6.93 ± 0.61**

* Statistically significant ($P \leq 0.05$) from the control group by Dunn's or Shirley's test
** $P \leq 0.01$

APPENDIX E
CHEMICAL CHARACTERIZATION, ANALYSIS, AND GENERATION OF CHAMBER CONCENTRATIONS

CHEMICAL CHARACTERIZATION, ANALYSIS, AND GENERATION OF CHAMBER CONCENTRATIONS

PROCUREMENT AND CHARACTERIZATION OF NAPHTHALENE

Naphthalene (scintillation grade) was obtained from Fisher Scientific Company (Fair Lawn, NJ) in two lots (lot numbers 775379 and 735773). Identity, purity, and stability analyses were performed by the analytical chemistry laboratory, Midwest Research Institute (MRI; Kansas City, MO). MRI reports on the analyses performed in support of the naphthalene studies are on file at the National Institute of Environmental Health Sciences.

The study chemical, a white, crystalline solid, was identified as naphthalene by infrared, ultraviolet/visible, and nuclear magnetic resonance spectroscopy. The spectra were consistent with those expected for the structure and with the literature spectra of naphthalene (Figures E1 and E2) (Sadtler Standard Spectra).

The purity of lot number 775379 was found to be greater than 99% by elemental analysis, Karl Fischer water analysis, thin-layer chromatography, and gas chromatography. Thin-layer chromatography was performed on silica gel plates with two solvent systems: hexanes (100%), and pentane:carbon tetrachloride (50:50). Visualization was accomplished at 254 nm and with iodine vapor. Gas chromatography was performed with flame ionization detection using two columns, 3% SP2100 on 100/120 Supelcoport and 10% Carbowax 20M-TPA on 80/100 Chromasorb W (AW), with nitrogen as the carrier gas at 70 mL/min.

Results of elemental analysis for carbon and hydrogen showed a slightly low level of carbon and a slightly high level of hydrogen. Karl Fischer water analysis indicated the presence of 0.23% water. No impurities were detected by thin-layer chromatography. Gas chromatography showed one impurity with an area of 0.1% relative to the area of the major peak using the first solvent system. The second solvent system detected two impurities that had a combined area of 0.15% relative to that of the major peak.

Heat stability studies performed with gas chromatography (column, 3% SP2100 on 100/120 Supelcoport, nitrogen carrier at 70 mL/min) found that the bulk chemical was stable for 2 weeks at temperatures up to 60° C.

GENERATION AND MONITORING OF CHAMBER CONCENTRATIONS

Vapor Generation System: In each of three Hinners-type inhalation chambers, naphthalene vapor was generated by direct sublimation from a 500 mL flask and was delivered through metering valves using nitrogen (Table E1).

Vapor Concentration Monitoring: Naphthalene chamber concentrations were determined with a Miran Model 80 infrared analyzer at a wavelength of 12.8 μm and computer-adjusted to the desired concentration by a software feedback arrangement. Individual monitors were used for each of the exposure chambers. Calibration was performed daily using 1.0 mL injections of freshly prepared naphthalene standard into a closed loop system. Air from each chamber was sampled every 40 seconds and averaged over 5-minute intervals. A summary of the exposure concentrations for the 2-year studies is presented in Table E1 and weekly mean exposure concentrations are presented in Figures E3, E4, and E5.

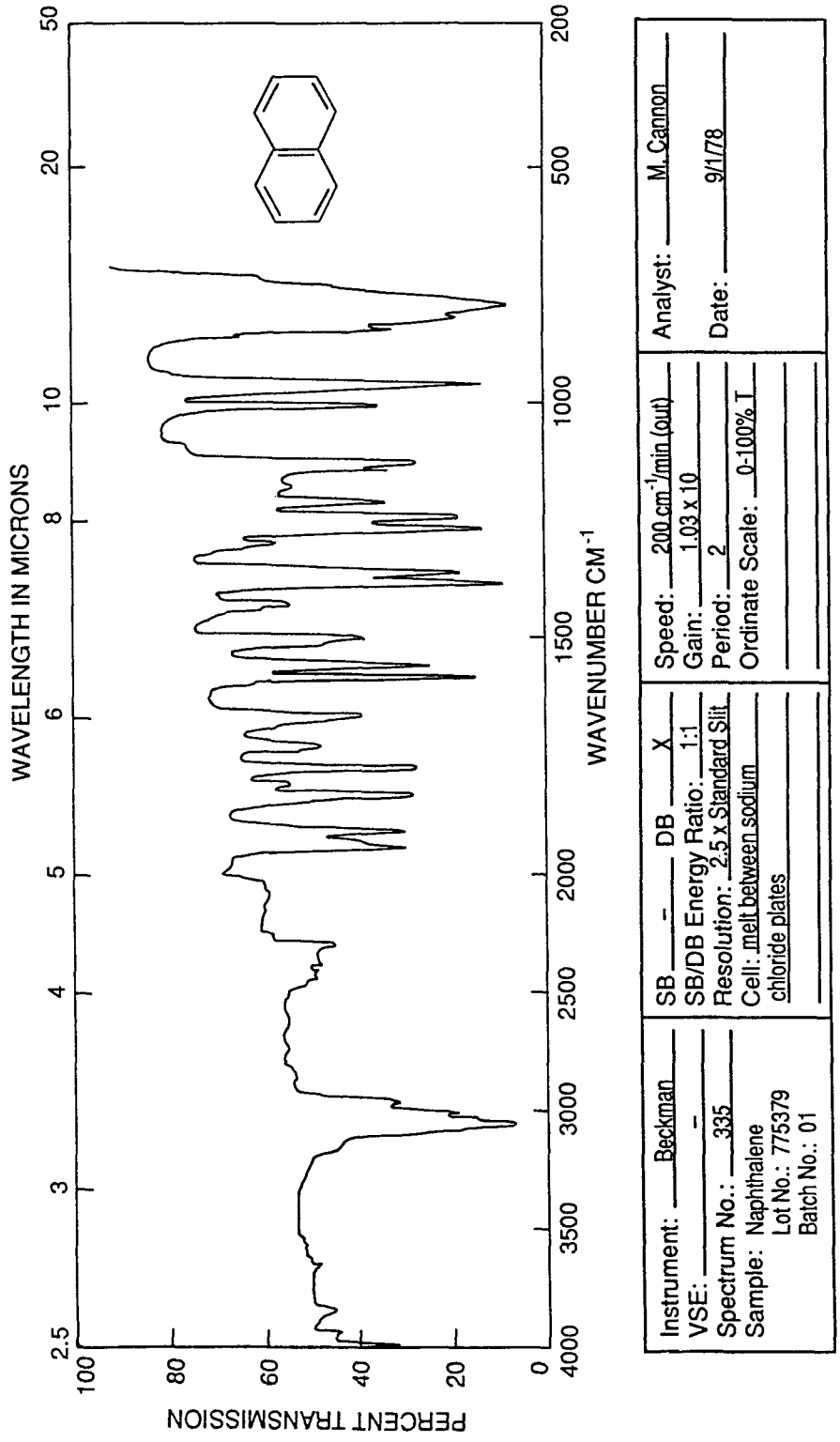

FIGURE E1
Infrared Absorption Spectrum of Naphthalene

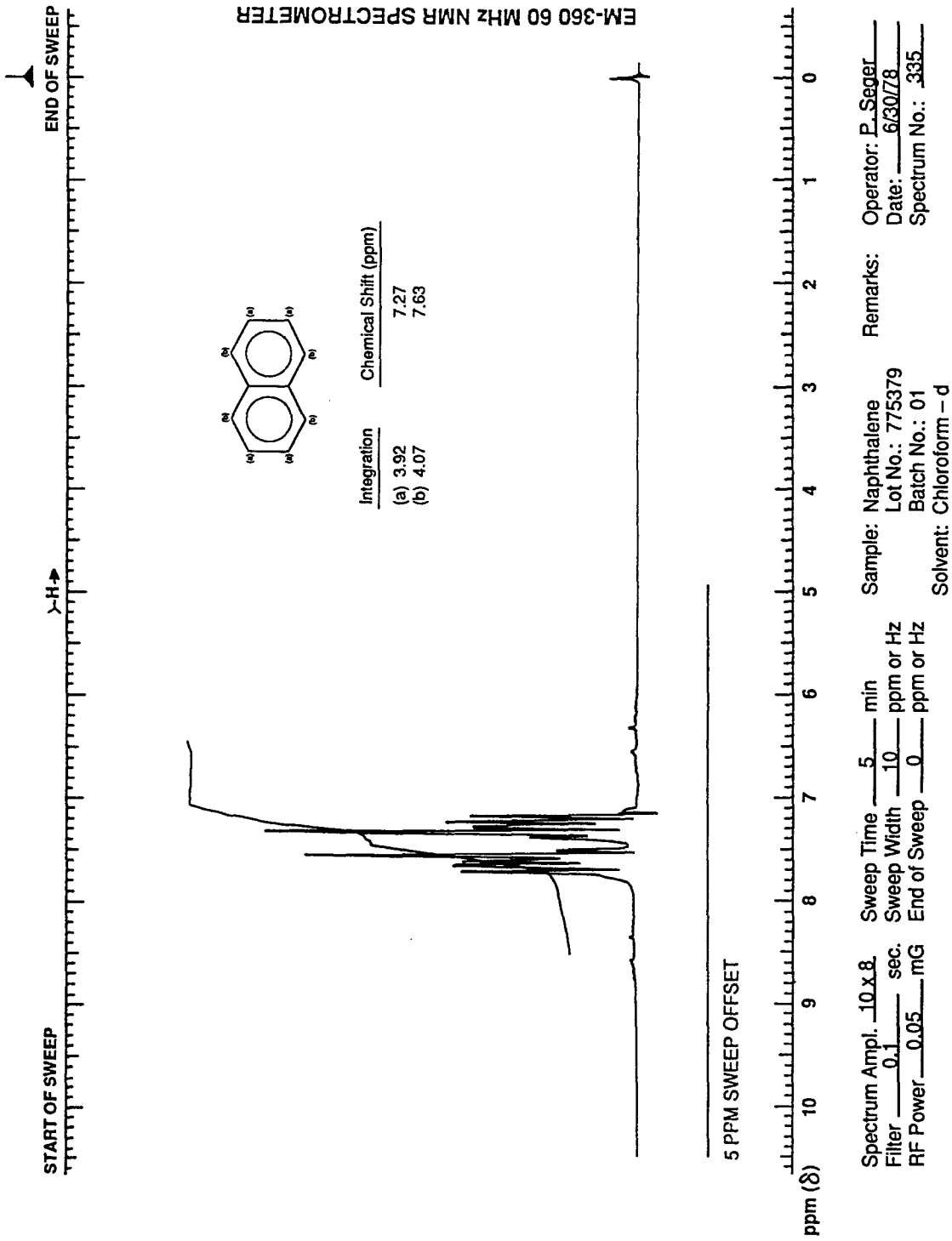

FIGURE E2
Nuclear Magnetic Resonance Spectrum of Naphthalene

TABLE E1
Analysis of Weekly Chamber Concentrations for Mice in the 2-Year Inhalation Studies of Naphthalene

Range	Number of Weeks Exposures Within Specified Concentration		
	10 ppm	30 ppm (Chamber #3)	30 ppm (Chamber #4)
>110%	2	0	0
90%-110%	95	100	99
<90%	7	4	5
Highest reading	11.2	31.0	30.6
Lowest reading	5.5[a]	25.2	24.4[b]

[a] Second lowest: 8.5 ppm
[b] Second lowest: 26.3 ppm

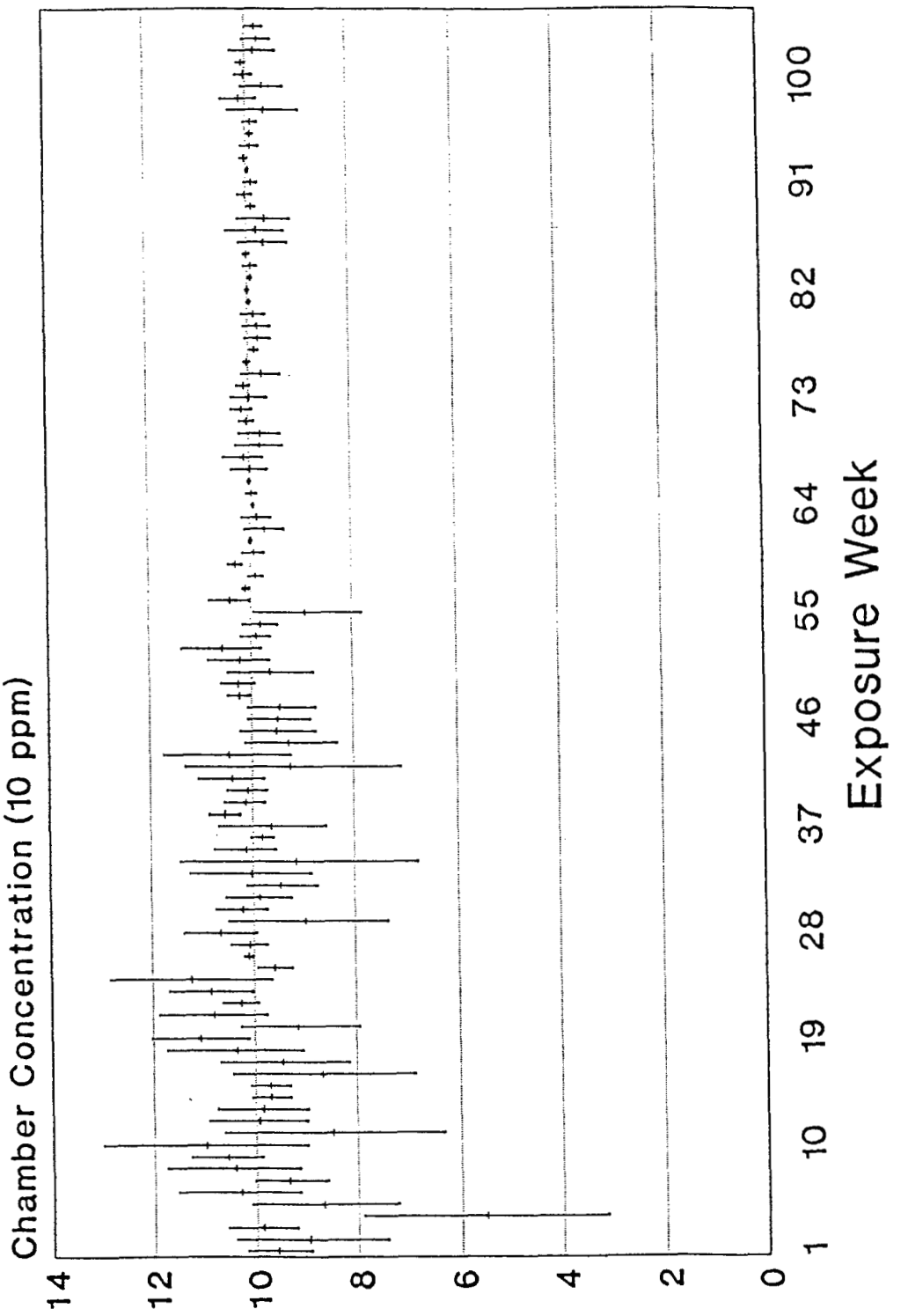

FIGURE E3
Weekly Mean Concentration and Standard Deviation in the 10 ppm Naphthalene Mice Exposure Chamber for the 2-Year Studies

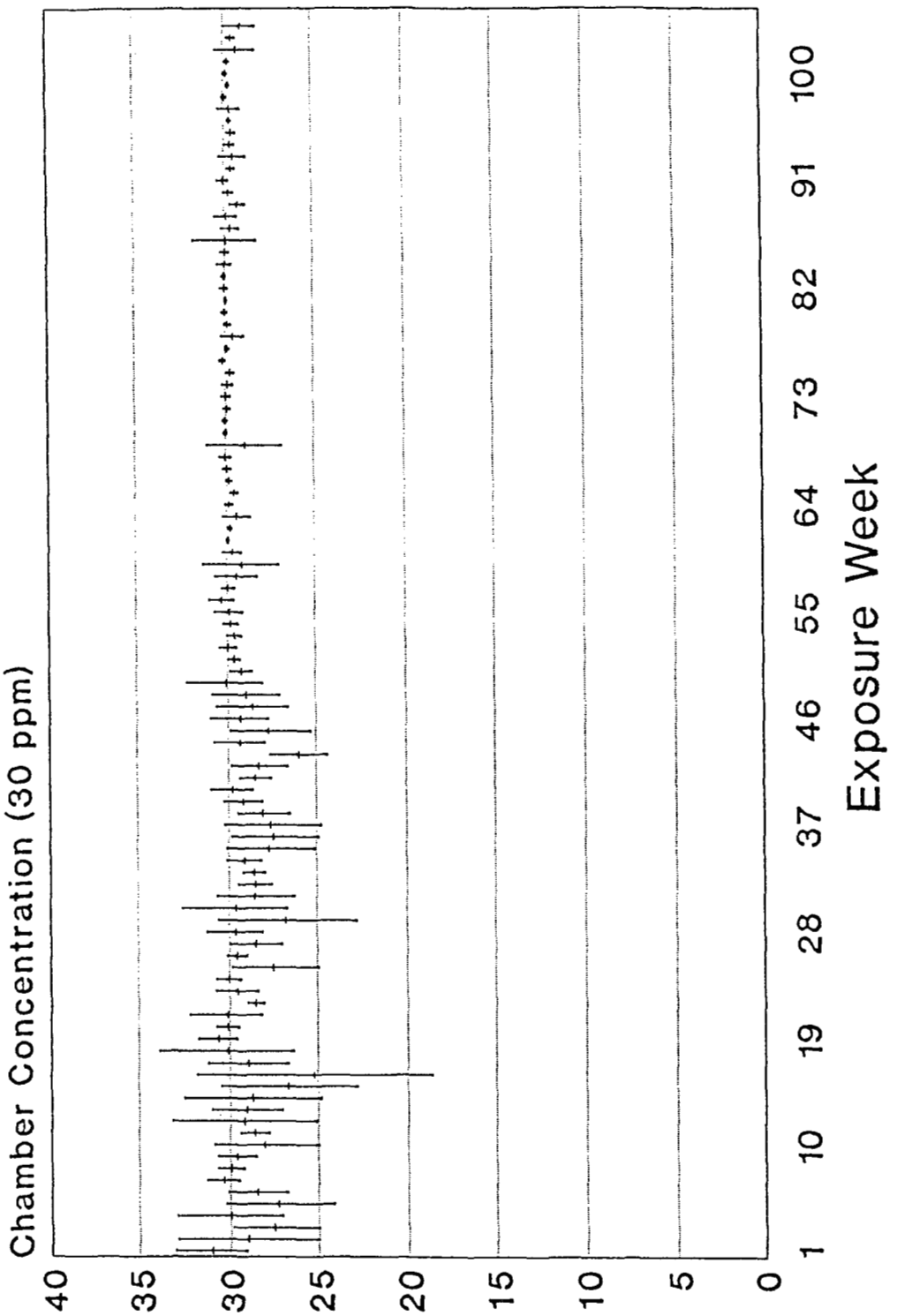

FIGURE E4
Weekly Mean Concentration and Standard Deviation in the 30 ppm Naphthalene Mice Exposure Chamber (Study Chamber 3) for the 2-Year Studies

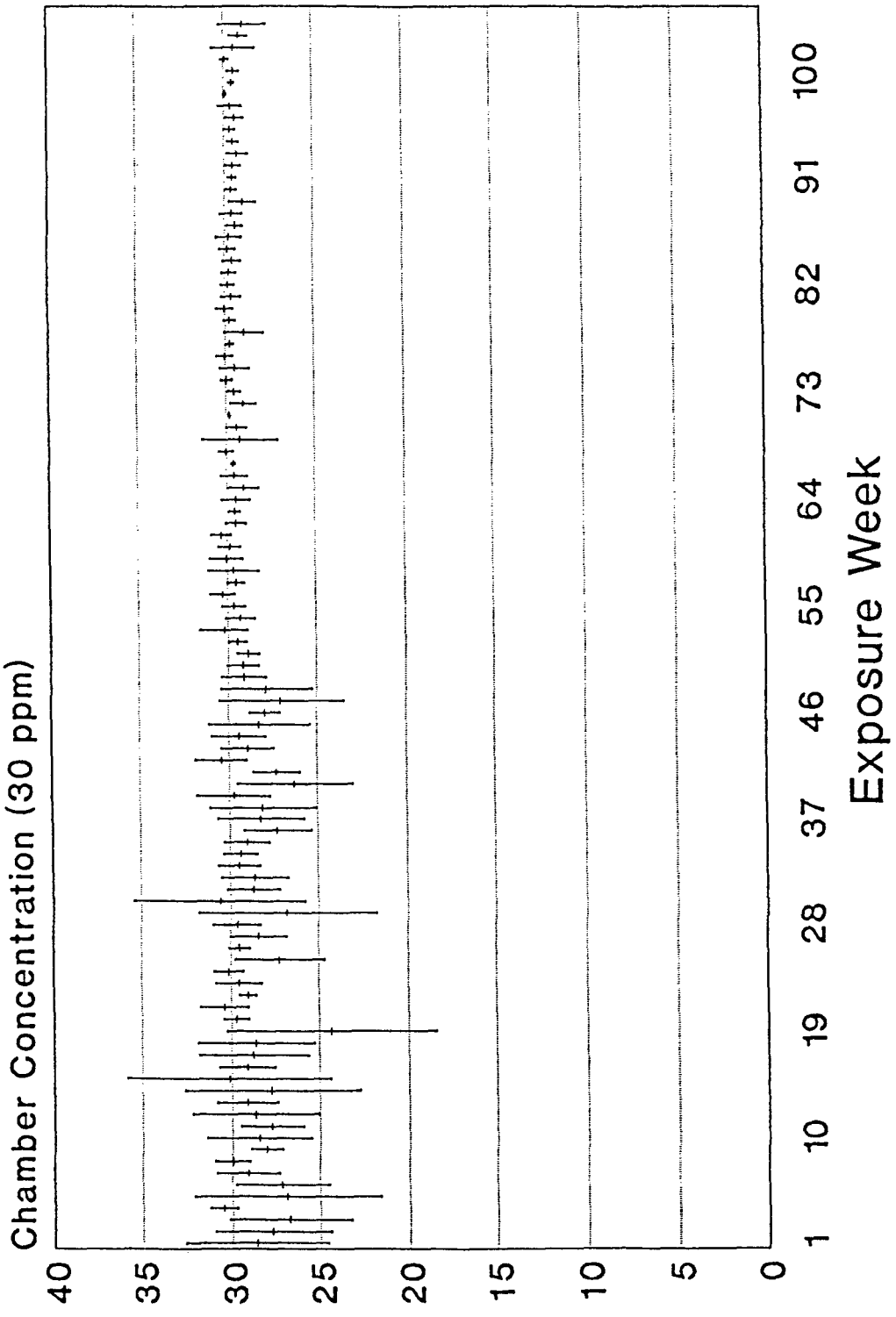

FIGURE E5
Weekly Mean Concentration and Standard Deviation in the 30 ppm Naphthalene Mice Exposure Chamber (Study Chamber 4) for the 2-Year Studies

APPENDIX F
INGREDIENTS AND VITAMINS AND MINERALS IN NIH-31 RAT AND MOUSE RATION

TABLE F1
Ingredients of NIH-31 Rat and Mouse Ration[a]

Ingredients[b]	Percent by Weight
Ground #2 yellow shelled corn	21.0
Ground whole wheat	35.5
Soybean meal (49% protein)	5.00
Fish meal (60% protein)	9.00
Wheat middlings	10.00
Alfalfa meal (dehydrated, 17% protein)	2.0
Corn gluten meal (60% protein)	2.0
Soy oil	1.5
Dried brewer's yeast	1.00
Dicalcium phosphate	1.5
Ground limestone	0.5
Salt	0.5
Premixes (vitamin and mineral)	0.5

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

TABLE F2
Vitamins and Minerals in NIH-31 Rat and Mouse Ration[a]

	Amount	Source
Vitamins		
A	20,000,000 IU	Stabilized vitamin A palmitate or acetate
D_3	3,800,000 IU	D-activated animal sterol
K_3	2.0 g	Menadione
d-α-Tocopheryl acetate	15,000 IU	
Choline	700 g	Choline chloride
Folic acid	1.0 g	
Niacin	20.0 g	
d-Pantothenic acid	25.0 g	*d*-Calcium pantothenate
Riboflavin	5.0 g	
Thiamine	65.0 g	Thiamine mononitrate
B_{12}	14,000 μg	
Pyridoxine	2.0 g	Pyridoxine hydrochloride
Biotin	120.0 mg	*d*-Biotin
Minerals		
Iron	60.0 g	Iron sulfate
Manganese	100.0 g	Manganous oxide
Zinc	10.0 g	Zinc oxide
Copper	4.0 g	Copper sulfate
Iodine	1.5 g	Calcium iodate
Cobalt	0.4 g	Cobalt carbonate
Magnesium	400 g	

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

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

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TR No.	CHEMICAL
338	Erythromycin Stearate
339	2-Amino-4-nitrophenol
340	Iodinated Glycerol
341	Nitrofurantoin
342	Dichlorvos
343	Benzyl Alcohol
344	Tetracycline Hydrochloride
345	Roxarsone
346	Chloroethane
347	D-Limonene
348	*a*-Methyldopa Sesquihydrate
349	Pentachlorophenol
350	Tribromomethane
351	*p*-Chloroaniline Hydrochloride
352	N-Methylolacrylamide
353	2,4-Dichlorophenol
354	Dimethoxane
355	Diphenhydramine Hydrochloride
356	Furosemide
357	Hydrochlorothiazide
358	Ochratoxin A
359	8-Methoxypsoralen
360	N,N-Dimethylaniline
361	Hexachloroethane
362	4-Vinyl-1-Cyclohexene Diepoxide
363	Bromoethane (Ethyl Bromide)
364	Rhodamine 6G (C.I. Basic Red 1)
365	Pentaerythritol Tetranitrate
366	Hydroquinone
367	Phenylbutazone
368	Nalidixic Acid
369	Alpha-Methylbenzyl Alcohol
370	Benzofuran
371	Toluene
372	3,3'-Dimethoxybenzidine Dihydrochloride
373	Succinic Anhydride
374	Glycidol
375	Vinyl Toluene
376	Allyl Glycidyl Ether
377	*o*-Chlorobenzalmalononitrile
378	Benzaldehyde
379	2-Chloroacetophenone
380	Epinephrine Hydrochloride
381	*d*-Carvone
382	Furfural
385	Methyl Bromide
386	Tetranitromethane
387	Amphetamine Sulfate
388	Ethylene Thiourea
389	Sodium Azide
390	3,3'-Dimethylbenzidine Dihydrochloride
391	Tris(2-chloroethyl) Phosphate
392	Chlorinated Water and Chloraminated Water
393	Sodium Fluoride
395	Probenecid
396	Monochloroacetic Acid
399	Titanocene Dichloride
405	C.I. Acid Red 114
406	γ-Butyrolactone
407	C.I. Pigment Red 3
415	Polysorbate 80

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