NATIONAL TOXICOLOGY PROGRAM
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TOXICOLOGY AND CARCINOGENESIS STUDIES OF MARINE DIESEL FUEL AND JP-5 NAVY FUEL

(CAS NO. 8008-20-6)

IN B6C3F$_1$ MICE

(DERMAL STUDIES)

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

NATIONAL TOXICOLOGY PROGRAM

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

The NTP is made up of four charter DHHS agencies: the National Cancer Institute (NCI), National Institutes of Health; the National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health; the National Center for Toxicological Research (NCTR), Food and Drug Administration; and the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS.

NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS STUDIES OF MARINE DIESEL FUEL AND JP-5 NAVY FUEL

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IN B6C3F$_1$ MICE

(DERMAL STUDIES)

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

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

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

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

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

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

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

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

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

These NTP Technical Reports are available for sale from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161 (703-487-4650). Single copies of this Technical Report are available without charge (and while supplies last) from the NTP Public Information Office, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709.

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ABSTRACT

Toxicology and carcinogenesis studies were conducted by applying marine diesel fuel or JP-5 navy fuel to clipped dorsal interscapular skin of male and female B6C3F$_1$ mice to determine both systemic and dermal effects. Doses for the 2-year studies were set by conducting 14-day and 13-week studies. Doses of 2,000-40,000 mg/kg marine diesel fuel were applied neat in the 14-day studies; in the 13-week studies, doses of 250-4,000 mg/kg marine diesel fuel in acetone were applied with a dose volume of 0.1 ml. Doses of 5,000-40,000 mg/kg JP-5 navy fuel in ethanol were applied in the 14-day studies with a dose volume of 0.5 ml; in the 13-week studies, doses of 500-8,000 mg/kg JP-5 navy fuel in acetone were applied with a dose volume of 0.2 ml. For the 2-year studies, doses were selected which did not cause deaths, decrease body weight gain, or produce excessive dermatitis in the 14-day or 13-week studies. Two-year studies were conducted by administering marine diesel fuel or JP-5 navy fuel by dermal application to groups of 49 or 50 male and 50 female B6C3F$_1$ mice at doses of 0, 250, or 500 mg/kg in an acetone vehicle with a dose volume of 0.1 ml.

Both sexes of mice dosed with 500 mg/kg marine diesel fuel (84-week exposure) and female mice dosed with 500 mg/kg JP-5 navy fuel (90-week exposure) were killed early because of excessive irritation and ulceration at the site of application and to prevent the spread of infection. Survival rates at those times were 26/50 males and 29/50 females dosed with marine diesel fuel and 17/50 females dosed with JP-5 navy fuel. Survival rates at the end of the studies (104 weeks) were reduced ($P<0.01$) in low dose female mice receiving marine diesel fuel (40/50 in vehicle controls compared with 12/50 in the low dose group) or with JP-5 navy fuel (44/50 in vehicle controls compared with 33/50 in the low dose group). Body weight gain was decreased below that of the vehicle controls after week 30 in all groups of mice receiving marine diesel fuel and in both sexes of mice receiving the high dose of JP-5 navy fuel.

There was a marked increase in the incidence of chronic dermatitis in mice receiving marine diesel fuel or JP-5 navy fuel. Chronic dermatitis was defined as a composite lesion of epidermal histopathologic changes generally consisting of acanthosis, hyperkeratosis, and in some instances necrosis and ulceration of the overlying epidermis. Dermal changes frequently included fibrosis, increased amounts of melanin, and the presence of acute and chronic inflammatory cell infiltrates. A dose-related, proportional increase in the severity of the lesions was twofold to threefold greater in the dosed groups than in the vehicle controls. The average degree of severity of the lesions was judged to be minimal in the vehicle controls, mild in the low dose groups, and moderate in the high dose groups of mice dosed with marine diesel fuel or JP-5 navy fuel. There were similar responses at the site of inguinal skin to which the chemicals had migrated after application, but the degree of severity of the lesions was judged to be minimal to mild in the vehicle control and dosed groups of mice.

Squamous cell papillomas or carcinomas (combined) occurred with a positive trend ($P<0.05$) at the site of application in male mice administered marine diesel fuel (vehicle control, 0/49; low dose, 0/49; high dose, 3/49). The total numbers of mice with squamous cell papillomas or carcinomas (combined) both for the site of application and the adjacent inguinal skin were 1/50, 2/49, and 3/50 for the vehicle control, low dose, and high dose groups of male mice and 0/50, 1/45, and 2/48 for female mice. There are no NTP historical data for B6C3F$_1$ mice that received acetone by dermal application. The NTP historical incidence of squamous cell papillomas or carcinomas (combined) in untreated male and female B6C3F$_1$ mice is 0.3%-0.4% in over 3,500 observations.

Marine diesel fuel was not mutagenic in *Salmonella typhimurim* strains TA98, TA100, TA1535, or TA1537, and JP-5 navy fuel was not mutagenic in strains TA97, TA98, TA100, or TA1535 in the presence or absence of Aroclor 1254-induced male Sprague-Dawley rat or male Syrian hamster S9 when tested according to the preincubation protocol.

Audits of the experimental data were conducted for these 2-year studies on marine diesel fuel and JP-5 navy fuel. No data discrepancies were found that influenced the final interpretations.

Under the conditions of these 2-year dermal studies, marine diesel fuel at doses of 250 and 500 mg/kg resulted in dose-related increased incidences of squamous cell neoplasms of the skin (primarily carcinomas), providing *equivocal evidence of carcinogenicity** for male and female B6C3F$_1$ mice. The sensitivity for detecting systemic carcinogenicity in female mice dosed with marine diesel fuel was reduced by poor survival. Under the conditions of these 2-year dermal studies, JP-5 navy fuel at doses of 250 and 500 mg/kg provided *no evidence of carcinogenicity* for male and female B6C3F$_1$ mice.

*Categories of evidence of carcinogenicity are defined in the Note to the Reader on page 2. The public discussion regarding the interpretative conclusions is summarized on pages 14-15.

CONTRIBUTORS

The NTP Technical Report on the Toxicology and Carcinogenesis Studies of Marine Diesel Fuel and JP-5 Navy Fuel is based on the 2-year studies of marine diesel fuel that began in January 1981 and ended in January 1983 and on the 2-year studies of JP-5 navy fuel that began in December 1980 and ended in December 1982 at Litton Bionetics, Inc.

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The members of the Peer Review Panel who evaluated the draft Technical Report on marine diesel fuel and JP-5 navy fuel on August 14, 1985, are listed below. Panel members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, Panel members have five major responsibilities: (a) to ascertain that all relevant literature data have been adequately cited and interpreted, (b) to determine if the design and conditions of the NTP studies were appropriate, (c) to ensure that the Technical Report presents the experimental results and conclusions fully and clearly, (d) to judge the significance of the experimental results by scientific criteria, and (e) to assess the evaluation of the evidence of carcinogenicity and other observed toxic responses.

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SUMMARY OF PEER REVIEW COMMENTS ON THE TOXICOLOGY AND CARCINOGENESIS STUDIES OF MARINE DIESEL FUEL AND JP-5 NAVY FUEL

On August 14, 1985, the draft Technical Report on the toxicology and carcinogenesis studies of marine diesel fuel and JP-5 navy fuel received peer review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The review meeting was held in the Conference Center, Building 101, South Campus, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.

Dr. M. Dieter, NTP, began the discussion with a summary of the study design, results, and proposed conclusions (equivocal evidence of carcinogenicity for mice receiving marine diesel fuel; no evidence of carcinogenicity for mice receiving JP-5 navy fuel).

Dr. Tannenbaum, a principal reviewer, considered the studies flawed, primarily for two reasons. First, the high degree of ulceration, especially in mice dosed with marine diesel fuel, led to early termination of high dose groups and made the interpretation of the results difficult. Also, the design did not allow for development of data on whether the fuels were tumor promoters. Second, Dr. Tannenbaum stated that studies conducted on materials that are poorly defined chemically were difficult to evaluate because the materials evaluated may not be representative and it is often unclear which component caused the toxic response.

As a second principal reviewer, Dr. Perera agreed with the proposed conclusions for marine diesel fuel in female mice and for JP-5 navy fuel in male and female mice. She suggested that the conclusion for marine diesel fuel in male mice be changed to some evidence of carcinogenicity based on a significant positive trend for squamous cell papillomas or squamous cell carcinomas at the site of application and at the site of application combined with the inguinal skin. There was also a positive trend and a significant increase in hepatocellular adenomas or carcinomas in the high dose group, which are supported by a positive trend and a significant increase in hepatocellular carcinomas in high dose female mice. Dr. Dieter said that the liver tumors were not emphasized due to the overlap with historical control values. Dr. Perera said that the reduced survival rates should be mentioned in the Abstract.

As a third principal reviewer, Dr. Crowley stated that he agreed with the conclusions proposed for JP-5 navy fuel in male and female mice but did not agree with the conclusions for mice administered marine diesel fuel. He suggested a change to no evidence of carcinogenicity based on the use of the incidental tumor test, which showed no difference between control and high dose male mice with the small numbers of tumors involved. There was no statistical analysis presented for female mice. Dr. Dieter said that the number of tumors for females exposed to marine diesel fuel was somewhat low for statistical analysis, but these would be included in the text [page 49]. An analysis was done combining benign and malignant tumors (seven of nine were carcinomas) and tumors from both the site of application and the site of chemical migration. The conclusion of equivocal evidence of carcinogenicity was based partly on statistically significant trends by the life table and incidental tumor tests in male mice. Dr. J. Huff, NIEHS, mentioned that the background rate for these neoplasms was quite low.

In other discussion, Dr. Purchase said that analysis should have been conducted for polycyclic aromatic hydrocarbons. Dr. Dieter replied that this might be done retrospectively [page 22] and could help explain why there were tumor responses with the marine diesel fuel and not the JP-5 navy fuel. Dr. Purchase asked whether the animals that had tumors also had ulcers. If so, the studies should more properly be described as studies wherein repeated trauma was applied to damaged skin. Dr. Dieter said that an analysis of the relationship between ulcers and tumors would be made and added to the report. [See page 57.] He reported that there were significant numbers of animals with dermatitis and ulceration in the parallel JP-5 navy fuel studies and yet there were no skin tumors, so a correlation does not exist. Dr. Hook pointed out that the NTP states that the results obtained are

specific for the conditions of those studies. Dr. Mirer commented that there is a body of data, primarily in male rats, showing kidney toxicity and tumors arising from exposure to petroleum hydrocarbons. He asked why the fuels were not studied in rats. Dr. Dieter replied that an earlier gavage study in rats had been terminated, since the gavage route was considered inappropriate, and at the Aerospace Medical Research Laboratory, there is an ongoing inhalation study in rats with JP-5 navy fuel.

Dr. Tannenbaum moved that the conclusions as written, equivocal evidence of carcinogenicity for male and female mice administered marine diesel fuel and no evidence of carcinogenicity for male and female mice exposed to JP-5 navy fuel, be accepted. Dr. Purchase seconded the motion. In the ensuing discussion, there seemed to be a consensus that the incidental tumor test rather than the life table test was the most appropriate statistical test. In the marine diesel fuel studies, there were no statistically significant differences among groups with the use of the incidental tumor test, and Dr. Crowley stated that the conclusion should be no evidence of carcinogenicity. Dr. G. Boorman, NIEHS, responded that the conclusion of equivocal evidence of carcinogenicity was based in part on the fact that seven of the nine tumors were squamous cell carcinomas, tumors that occur only rarely in control mice. The motion was approved by nine affirmative votes to two negative votes (Dr. Crowley and Dr. Purchase).

I. INTRODUCTION

I. INTRODUCTION

Marine diesel fuel and JP-5 navy fuel are complex mixtures whose compositions vary widely between sources and even between lots, depending on their refining history and boiling point range (Bingham et al., 1979). The samples used in the present studies were mixtures of petroleum-derived products and, according to the suppliers, contained 13% aliphatics and 87% aromatics (marine diesel fuel) or 84% aliphatics and 16% aromatics (JP-5 navy fuel). Marine diesel fuel is a common industrial and military fuel. JP-5 navy fuel is a jet fuel used exclusively by the U.S. Navy and is characterized as "fuel, aviation, turbine engine." The National Cancer Institute nominated these military and industrial fuels for carcinogenicity studies because of the potential exposure of armed forces personnel.

In 1980, an estimated 800 million metric tons of petroleum was refined in the United States--450 and 350 million metric tons of domestic crude and imported crude, respectively (Cuddihy et al., 1980). About 40% of the total was converted into gasoline and 20% into middle distillate gas, oil, and diesel fuel. An additional 30-50 million metric tons of diesel fuel will be needed annually in the future if all other competing uses of this fuel remain at their current levels. An estimated 10-20 million gallons of petroleum oil served as a vehicle for agricultural sprays between 1965 and 1969 (Kay, 1973).

Polynuclear aromatic hydrocarbons are well recognized as causative tumorigenic constituents in petroleum hydrocarbons (Bingham et al., 1979). There is documentation of skin tumors in C3H or CFW mice after dermal application of industrial fuel oil at 20 mg or 100 mg, three times per week. The tumor incidences cited were 94% at 36 weeks and 97% at 25 weeks with an average latency period for tumor induction between 16 and 17 weeks (API, 1959). Comparable information for JP-5 navy fuel has not been reported. Two recent studies reported the carcinogenic potential of oils derived from petroleum hydrocarbons after long-term dermal application to mice. An acid/earth refined naphthenic spindle oil was applied at a volume of 0.25 ml twice a week for 22 weeks to female CF_1 mice and then discontinued (Doak et al., 1983). The total volume of oil delivered was 11.0 ml. Two papillomas and 4 squamous cell carcinomas were found among 27 mice, with development of the first 2-mm tumor occurring at 9 weeks on test. Of the 13 tumors observed in 50 mice dosed once a week for 22 weeks and then once every 2 weeks for 78 weeks, 4 were sloughed and 7 were papillomas, 1 was a squamous cell carcinoma, and 1 was a sebaceous gland adenoma. Of the 5 tumors observed in 50 mice dosed at a volume of 0.25 ml twice a week for 22 weeks with oil diluted 1:1 and then once a week at a volume of 0.25 ml for 78 weeks, 1 was sloughed, 1 was a papilloma, and 3 were squamous cell carcinomas that required 27 weeks for development. Each dosing schedule resulted in the same total volume of 33.4 ml of neat oil delivered to the mice over 78 weeks.

Additional carcinogenicity studies were conducted by giving Swiss mice dermal applications of medicinal-grade oil or crude oil, refined to yield a homogeneous series with increasing concentration of polyaromatic hydrocarbons, at a volume of 0.05 ml two times a week for 12 months (Gradiski et al., 1983). There was a definitive tumorigenic effect associated with the polyaromatic hydrocarbon study material on the skin, including increased incidences of papillomas, keratoacanthomas, squamous cell carcinomas, and fibrosarcomas. The time-to-tumor development was also associated with the polyaromatic hydrocarbon concentration.

Bingham et al. (1979) have reviewed the epidemiologic evidence between 1920-1970 associating skin cancer with heavy and constant exposure to petroleum hydrocarbons. An increased incidence of skin cancer was reported in workers who used high-speed machinery with lubricating oils derived from shale oil, coal tar, or petroleum. Significantly greater rates of primary carcinoma of the scrotal skin occurred in workers employed in screwcutting; the lesion was attributed to the polyaromatic hydrocarbon concentration in the oils used for machine lubrication. Additional epidemiologic evidence was obtained from cotton-mule spinners, who had high incidences of scrotal and other skin cancers caused by groin-level spray of lubricants from high-speed cotton spindles. No such increase was observed in wool-mule spinners, whose spindles operate at slower speeds. Spinning mules have since been virtually eliminated.

Exposure at 150 or 750 mg/m^3 JP-5 navy fuel or marine diesel fuel by inhalation for 90 days

resulted in toxic nephropathy in male but not in female F344 rats (Bruner, 1983). Approximately 20 months after cessation of this exposure, lesions consistent with progressive nephropathy common to old rats were noted; they were more prevalent in dosed male rats than in dosed female or control rats. In addition, cellular debris in the medullary tubules and mild to moderate multifocal papillary hyperplasia of pelvic urothelium along the surface of the renal papillus occurred in male rats only. No primary renal cell tumors occurred in animals exposed to JP-5 navy fuel or marine diesel fuel, but 1-year inhalation exposure at 100 ppm JP-10 cruise missile fuel (tricyclodecane) or 30 or 150 mg/m^3 RJ-5 (endo-endo-dihydro(norbornadiene)) resulted in nine primary renal cell tumors in male rats from each of the the high dose groups from each experiment. There were no significantly increased incidences of renal cell tumors in females, and one renal cell tumor was seen in controls in these experiments; the studies were terminated 1 year after exposure. These findings were regarded as biologically significant, since the nephropathy was identical to that caused by the 90-day exposure to the other petroleum hydrocarbon fuels and since the background incidence of primary kidney tumors in male rats has been reported as 0.5% by the National Cancer Institute (Chu et al., 1981).

Nephrotoxicity also resulted from the dermal application of JP-5 navy fuel, JP-8 jet fuel, and marine diesel fuel when applied three times per week for 60 weeks to C3Hf/Bd mice of either sex (Easley et al., 1982). By the end of the experiment, 44/136 dosed mice had extensive renal cortical degeneration that consisted of atrophied and degenerating nephrons supported by an intact reticulum with a high incidence of papillary necrosis. The percentage of renal lesions in mice dosed with marine diesel fuel was 21/106 (20%) compared with 23/208 (11%) in mice dosed with the jet fuels. In contrast to the inhalation studies in which renal nephrosis was more prevalent in male rats than in female rats exposed to petroleum hydrocarbon fuels, dermally exposed female mice showed a greater incidence of renal lesions, regardless of the dose or type of fuel, than did male mice (total incidence of renal lesions: female mice--38/146, 26%; male mice--6/168, 4%).

Teratologic studies were performed (under contract to the American Petroleum Institute [API]) with female (CRL:COBS CD [SD] BR) rats that were mated and exposed to airborne fuel oil (type unspecified), diesel fuel (analysis unknown), or jet fuel A with a boiling point range of 325°-540° F containing 17.9% total aromatic and 82.1% total saturated compounds (Litton Bionetics, Inc., 1979a,b,c). The concentrations used in each study, 0, 100, or 400 ppm, were verified during the exposures. No chemically induced terata, variation in sex ratio, embryo toxicity, or inhibition of fetal growth and development were reported.

Litton Bionetics, Inc., performed a comprehensive series of mutagenesis and cellular genotoxicity studies for the API, testing diesel fuel (1978, 1981), JP-5 navy fuel (1977), and jet fuel A (1980). Hazleton Laboratories America performed in vitro and in vivo mutagenicity studies on jet fuel A, also for the API (1979). The in vitro tests included the Ames microbial mutagenesis assay, mouse lymphoma cell mutagenesis assay, and cytotoxicity tests in Chinese hamster ovary cells; in vivo tests included rat bone marrow cytogenetic effects, a dominant lethal assay in CD-1 mice, and tests for chromosomal aberrations in plants. Marine diesel fuel was clastogenic in the rat bone marrow cytogenetics test. Both fuels gave negative results in each of the in vitro tests, were not positive in the mouse dominant lethal assay, and did not cause chromosomal aberrations in plants.

In NTP tests, marine diesel fuel was not mutagenic in *Salmonella typhimurium* strains TA98, TA100, TA1535, or TA1537; JP-5 navy fuel was not mutagenic in strains TA97, TA98, TA100, or TA1535 in the presence or absence of Aroclor 1254-induced male Sprague-Dawley rat or male Syrian hamster S9 when tested according to a preincubation protocol (Appendixes G and H).

Marine diesel fuel and JP-5 navy fuel were applied dermally to B6C3F$_1$ mice to determine the toxicity and potential carcinogenicity of these fuels after short- and long-term exposure. Military personnel and industrial workers may encounter dermal exposure to petroleum hydrocarbon fuels during production, transfer, storage, or refueling operations. Another common route of

exposure, inhalation, was used in studies by the Department of Defense (MacNaughton and Uddin, 1984; Bruner, 1984) and by the American Petroleum Institute (Litton Bionetics, 1978, 1979a,b,c, 1980, 1981; Hazleton Laboratories America, 1979).

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF MARINE DIESEL FUEL AND JP-5 NAVY FUEL

Marine Diesel Fuel

JP-5 Navy Fuel

Reanalysis of the Aromatic Content of Marine Diesel Fuel and JP-5 Navy Fuel

PREPARATION AND CHARACTERIZATION OF DOSE MIXTURES

Marine Diesel Fuel

JP-5 Navy Fuel

SINGLE-ADMINISTRATION STUDIES

Marine Diesel Fuel

FOURTEEN-DAY STUDIES

Marine Diesel Fuel

JP-5 Navy Fuel

THIRTEEN-WEEK STUDIES

Marine Diesel Fuel

JP-5 Navy Fuel

TWO-YEAR STUDIES

Study Design

Source and Specifications of Animals

Animal Maintenance

Clinical Examinations and Pathology

Statistical Methods

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF MARINE DIESEL FUEL AND JP-5 NAVY FUEL

Marine Diesel Fuel

Marine diesel fuel (petroleum-derived) was obtained in one lot (lot no. 9110L) from Wright Patterson Air Force Base. According to information from the supplier, marine diesel fuel is a mixture of hydrocarbons containing 12.7% paraffins, 43.7% naphthalenes, and 43.6% aromatic compounds. Purity and identity analyses were conducted at Midwest Research Institute (Appendix I). Infrared, ultraviolet/visible, and nuclear magnetic resonance spectra were consistent with the manufacturer's specifications of a mixture of aromatic and aliphatic hydrocarbons, although the data from the analytical chemistry laboratory indicate a lower aromatic content than that indicated by the manufacturer. Capillary column gas chromatography indicated that there were more than 200 components in the study material.

Marine diesel fuel was stable for 2 weeks at temperatures as high as 60° C. Marine diesel fuel was stored at 4° C. Results of periodic reanalyses of the bulk chemical by infrared spectroscopy and capillary gas chromatography indicated no notable degradation of the chemical throughout the studies (Appendix I).

JP-5 Navy Fuel

JP-5 navy fuel (petroleum derived), a specially refined kerosene, was obtained in one lot (lot no. WP8477) from Wright Patterson Air Force Base and was labeled "fuel, aviation, turbine engine." According to information from the supplier, JP-5 navy fuel is a mixture of hydrocarbons containing 52.8% cycloparaffins, 30.8% paraffins, 15.9% aromatics, and 0.5% olefins. Purity and identity analyses were conducted at Midwest Research Institute (Appendix J). Infrared, ultraviolet/visible, and nuclear magnetic resonance (NMR) spectra were consistent with the stated composition. Capillary gas chromatography indicated that there were more than 150 components in the study material.

JP-5 navy fuel was stored at 4° C. Results of periodic reanalyses of the bulk chemical by infrared spectroscopy and capillary gas chromatography indicated no notable degradation of the chemical throughout the studies (Appendix J).

Reanalysis of the Aromatic Content of Marine Diesel Fuel and JP-5 Navy Fuel

The aromatic content of marine diesel fuel was significantly higher than that of JP-5 navy fuel when determined by proton-NMR and carbon-13 NMR, as well as by an American Society for Testing and Materials (ASTM) elution chromatography method. The aromatic content cannot be determined precisely by the NMR methods because of uncertainties in the operational definition used by the petroleum industry for aromatic content of petroleum products. The ASTM method can be used to estimate the relative aromatic content of the two fuels. Although this method cannot identify individual components, marine diesel fuel was found to contain 10-20 times as much aromatics as JP-5 navy fuel, a finding that is in agreement with the information from the supplier of the fuels.

PREPARATION AND CHARACTERIZATION OF DOSE MIXTURES

Marine Diesel Fuel

A stability study was performed at the analytical chemistry laboratory on dose mixtures of marine diesel fuel in ethanol (50% v/v). This study showed the ethanol dose formulation to be stable 7 days at 25° C. In addition, the study laboratory performed a stability study of marine diesel fuel in acetone at levels ranging from 50 to 200 mg/ml. The results of this study indicated that acetone mixtures were stable for up to 47 days at room temperature.

For the single-administration studies, marine diesel fuel was mixed with 95% ethanol (Table 1). For the 14-day studies, marine diesel fuel was applied as the neat chemical. For the 13-week and 2-year studies, marine diesel fuel was mixed with reagent-grade acetone (Appendix K). Dose mixtures of marine diesel fuel in acetone were stored at room temperature for no longer than 7 days. Periodic analyses of marine diesel fuel in acetone were performed by the study and analytical chemistry laboratories to determine if

TABLE 1. PREPARATION AND STORAGE OF DOSE MIXTURES IN THE DERMAL STUDIES OF MARINE DIESEL FUEL (a) AND JP-5 NAVY FUEL (b)

	Single-Administration Studies	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
Preparation	MDF dissolved in 95% ethanol to make solutions of the appropriate concentration (v/v)	MDF--chemical used neat; JP-5--the solutions prepared in graduated cylinder with 95% ethanol and mixed for 30 sec	The appropriate amount of MDF or JP-5 added to graduated cylinders and acetone added to reach the desired volume. The solutions mixed by inversion until a uniform solution was obtained	Same as 13-week studies
Maximum Storage Time	Not stored	MDF--N/A; JP-5--the solutions prepared on 1/24/79 and used throughout the studies	7 days	14 days
Storage Conditions	Not stored	Room temperature		Room temperature

(a) MDF
(b) JP-5

the dose mixtures contained the correct concentrations of marine diesel fuel (Appendix M). Because 46/48 mixtures analyzed were within ± 10% of the target concentration, it is estimated that dose mixtures were prepared within specifications 95% of the time (Table 2; Appendix M).

JP-5 Navy Fuel

A stability study was performed at the analytical chemistry laboratory on dose mixtures of JP-5 navy fuel in ethanol (50% v/v). This study showed that the ethanol dose mixtures were stable for 7 days at 25° C. In addition, the study laboratory performed a stability study of JP-5 navy fuel in acetone at concentrations ranging from 50 to 200 mg/ml. The results of this study indicated that the acetone formulations were stable for up to 52 days at room temperature.

No single-administration studies of JP-5 navy fuel were performed. For the 14-day studies, JP-5 navy fuel was mixed with 95% ethanol (Table 1). For the 13-week and 2-year studies, JP-5 navy fuel was mixed with reagent-grade acetone (Appendix N).

Dose mixtures of JP-5 navy fuel in acetone were stored at room temperature for no longer than 2 weeks. Periodic analyses of JP-5 navy fuel in acetone were performed by the study and analytical laboratories to determine if the dose mixtures contained the correct concentrations of JP-5 navy fuel (Appendix O). Because 50/55 mixtures analyzed were within ± 10% of the target concentration, it is estimated that dose mixtures were prepared within specifications 91% of the time (Table 2; Appendix P).

SINGLE-ADMINISTRATION STUDIES

Marine Diesel Fuel

Male and female B6C3F$_1$ mice were obtained from Charles River Breeding Laboratories and were held for 4 weeks before the studies began. Groups of five male and five female mice were administered a single 0.5-ml dermal application of 5,000, 10,000, 20,000, 30,000, or 40,000 mg/kg marine diesel fuel in 95% ethanol to the clipped dorsal interscapular region. No controls were used in these studies.

TABLE 2. SUMMARY OF RESULTS OF ANALYSIS OF DOSE MIXTURES IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL AND JP-5 NAVY FUEL

	Marine Diesel Fuel	JP-5 Navy Fuel
Mean of percent of target concentration	98.5	100.0
Standard deviation	3.3	5.02
Number of samples	48	55
Number of samples more than 10% different from target concentration	2	5

Mice were housed five per cage and received water (acidified to pH 2.5) and feed ad libitum. Details of animal maintenance are presented in Table 3. The mice were observed twice per day and weighed on the day of dosing. Necropsies were not performed.

FOURTEEN-DAY STUDIES

Marine Diesel Fuel

Male and female B6C3F$_1$ mice were obtained from Charles River Breeding Laboratories and were held for 2 weeks before the studies began. Groups of five male and five female mice were given dermal applications of marine diesel fuel for 14 consecutive days. Each day, mice received applications of 2,000, 4,000, 8,000, 20,000, or 40,000 mg/kg of 100% marine diesel fuel to the clipped dorsal interscapular region. Controls were untreated.

Mice were housed five per cage and received water (acidified to pH 2.5) and feed ad libitum. Details of animal maintenance are presented in Table 3. The mice were observed twice per day and were weighed on days 0 and 14 or 15. A necropsy was performed on all animals. Skin from the site of application was examined microscopically.

JP-5 Navy Fuel

Male and female B6C3F$_1$ mice were obtained from Charles River Breeding Laboratories and were held for 2 weeks before the studies began. Groups of five male and five female mice were given 0.5-ml dermal applications of JP-5 navy fuel in 95% ethanol for 14 consecutive days. Each day, mice received applications of 0, 5,000, 10,000, 20,000, 30,000, or 40,000 mg/kg JP-5 navy fuel to the clipped dorsal interscapular region. Conditions of animal maintenance were the same as those given for marine diesel fuel.

THIRTEEN-WEEK STUDIES

Thirteen-week studies were conducted to evaluate the cumulative toxic effects of repeated administrations of marine diesel fuel and JP-5 navy fuel and to determine the doses to be used in the 2-year studies.

Marine Diesel Fuel

Four- to six-week-old male and female B6C3F$_1$ mice were obtained from Charles River Breeding Laboratories and observed for 15 days before the studies began. Groups of 10 mice of each sex were given dermal applications (to the clipped dorsal interscapular area) of 0.1 ml of 0, 250, 500, 1,000, 2,000, or 4,000 mg/kg marine diesel fuel in acetone, 5 days per week for 13 weeks.

Mice were housed five per cage in polycarbonate cages. Diets consisting of NIH 07 Rat and Mouse Ration pellets and water (acidified with hydrochloric acid to pH 2.5 for bacterial control) were available ad libitum. Animals were checked twice per day; moribund animals were killed. Animal weights were recorded weekly. Further experimental details are summarized in Table 3. At the end of the 13-week studies, survivors were killed. A necropsy was performed on all animals except those excessively autolyzed or cannibalized. Tissues and groups examined histologically are listed in Table 3.

JP-5 Navy Fuel

Four- to six-week-old male and female B6C3F$_1$ mice were obtained from Charles River Breeding Laboratories and observed for 15 days before the studies began. Groups of 10 mice of each sex

TABLE 3. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE DERMAL STUDIES OF MARINE DIESEL FUEL (a) AND JP-5 NAVY FUEL (b)

	Single-Administration Studies	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
EXPERIMENTAL DESIGN				
Size of Study Group	5 males and 5 females: the single-administration study was conducted for MDF only	5 males and 5 females	10 males and 10 females	49 or 50 males and 50 females
Doses	MDF--5,000,10,000, 20,000, 30, 000, or 40,000 mg/kg MDF in 95% ethanol applied dermally to the clipped dorsal interscapular region (40,000 mg/kg dose applied as the neat chemical); dose vol--0.5 ml	MDF--0, 2,000, 4,000, 8,000, 20,000, or 40,000 mg/kg of neat MDF; JP-5--0, 5,000, 10,000, 20,000, 30,000, or 40,000 mg/kg in 95% ethanol; dose vol--0.5 ml; both substances applied by dermal application to the clipped dorsal interscapular region	MDF--0, 250, 500, 1,000, 2,000, or 4,000 mg/kg in acetone (4,000 mg/kg dose applied as the neat chemical); dose vol--0.1 ml; JP-5--0, 500, 1,000, 2,000, 4,000, or 8,000 mg/kg in acetone (8,000 mg/kg dose was applied as the neat chemical); dose vol--0.2 ml except during wk 2 (0.22 ml) and 3 (0.23ml); both substances applied by dermal application to the clipped dorsal interscapular region	0, 250, or 500 mg/kg MDF or JP-5 in acetone by dermal application to the clipped dorsal interscapular region; dose vol--0.1 ml
Date of First Dose	12/6/78	MDF--4/12/79; JP-5--1/25/79	MDF--12/27/79; JP-5--1/30/80	MDF--1/14/81; JP-5--12/11/80
Date of Last Dose	N/A	MDF--4/25/79; JP-5--2/7/79	MDF--3/26/80; JP-5--4/29/80	MDF--8/20/82 for high dose, 1/7/83 for the others; JP-5--8/23/82 for high dose females, 12/3/82 for the others
Duration of Dosing	Single dose	14 consecutive d	5 d/wk for 13 wk	MDF--high dose, 84 wk; JP-5--high dose females, 90 wk; all others 5 d/wk for 103 wk
Type and Frequency of Observation	Observed 1 × d; weighed on day of dosing	Observed 2 × d; 1 × d for signs of toxicity; weighed on d 0 and 14 (JP-5) and d 15 (MDF)	Observed 2 × d; weighed 1 × wk	Observed 2 × d; clinically examined 1 × 4 wk; weighed 1 × wk for 13 wk and 1 × 4 wk thereafter

TABLE 3. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE DERMAL STUDIES OF MARINE DIESEL FUEL AND JP-5 NAVY FUEL (Continued)

	Single-Administration Studies	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
Necropsy and Histologic Examination	Necropsy not performed	Necropsy performed on all animals; skin from the site of application was examined microscopically	Necropsy performed on all animals; histologic examination performed on the following tissues of the vehicle control and 8,000 mg/kg groups and on all animals dying before the end of the studies: gross lesions and tissue masses, mandibular or mesenteric lymph node, salivary gland, sternebrae, femur or vertebrae including marrow, thyroid gland, parathyroids, small intestine, colon, liver, prostate/testes or ovaries/uterus, lungs and mainstem bronchi, skin from the site of application, gallbladder, heart, esophagus, stomach, brain, thymus, trachea, pancreas, spleen, kidneys, adrenal glands, urinary bladder, pituitary gland, spinal cord (if neurologic signs present), eyes (if abnormal), and mammary gland. The skin, spleen, and liver of all groups were examined microscopically.	Necropsy and histologic examination performed on all animals; the following tissues were examined: gross lesions and tissue masses, mandibular and mesenteric lymph nodes, salivary gland, sternebrae including marrow, thyroid gland, parathyroids, liver, urinary bladder, prostate/testes/seminal vesicles or ovaries/uterus, lungs and mainstem bronchi, gallbladder, skin from the site of application and inguinal skin, thigh muscle, costochondral junction (rib), larynx, nasal cavity, heart, esophagus, brain, thymus, trachea, pancreas, spleen, kidneys, adrenal glands, pituitary gland, eyes, mammary gland, spinal cord, sciatic nerve, stomach, cecum, duodenum, ileum, jejunum, colon, and rectum
ANIMALS AND ANIMAL MAINTENANCE				
Strain and Species	$B6C3F_1$ mice	$B6C3F_1$ mice	$B6C3F_1$ mice	$B6C3F_1$ mice
Animal Source	Charles River Breeding Laboratories (Portage, MI)	Same as single-administration studies	Same as single-administration studies	Charles River Breeding Laboratories (Kingston, NY)
Study Laboratory	Litton Bionetics, Inc.	Litton Bionetics, Inc.	Litton Bionetics, Inc.	Litton Bionetics, Inc.
Method of Animal Identification	Toe clip and ear notch	MDF--ear punch and toe clip; JP-5--toe clip and ear notch	Toe clip and ear notch	Ear punch and toe clip

TABLE 3. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE DERMAL STUDIES OF MARINE DIESEL FUEL AND JP-5 NAVY FUEL (Continued)

	Single-Administration Studies	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
Time Held Before Study	4 wk	2 wk	2 wk	2 wk
Age When Placed on Study	Approximately 9 wk	MDF--7-8 wk; JP-5--7-8 wk	6-8 wk	8 wk
Age When Killed	Approximately 11 wk	MDF--9-10 wk; JP-5--9-10 wk	19-21 wk	MDF--high dose, 92 wk; other groups, 112 wk; JP-5--high dose females, 97 wk; other groups, 113 wk
Necropsy or Kill Dates	Not available	MDF--4/27/79; JP-5--2/8/79	MDF--3/27/80-3/28/80; JP-5--4/30/80-5/1/80	MDF--high dose, 8/27/82; others, 1/17/83-1/18/83; JP-5--high dose females, 8/30/82; others, 12/13/82-12/15/82
Method of Animal Distribution	Computer randomization to cages and to dose groups	Same as single-administration studies	Animals were assigned to weight distribution classes, then to groups according to a table of random numbers	Same as 13-wk studies
Feed	Purina Laboratory Chow® (Ralston Purina Co., St. Louis, MO); available ad libitum	Purina Laboratory Chow® pellets (Ralston Purina Co., St. Louis, MO); available ad libitum	NIH 07 Rat and Mouse Ration (Zeigler Bros., Gardners, PA); available ad libitum	Same as 13-wk studies
Bedding	Hardwood chips (Lab Products, Inc., Garfield, NY, and Rochelle Park, NY)	Ab-sorb-dri heat-treated hardwood chips (Lab Products, Inc., Garfield, NY, and Rochelle Park, NY)	Same as 14-d studies	Ab-sorb-dri heat-treated hardwood chips (Lab Products, Inc., Garfield, NY, and Rochelle Park, NY) used until 9/23/81; SANI-CHIPS, hardwood chips (P.J. Murphy Forest Products Corp., Rochelle Park, NJ) used for the remainder of the studies
Water	Tap water in bottles acidified to pH 2.5 with HCl for bacterial control; available ad libitum	Same as single-administration studies	Same as single-administration studies	Same as single-administration studies
Cages	Polycarbonate (Lab Products, Inc., Garfield, NY, and Rochelle Park, NY)	Same as single-administration studies	Same as single-administration studies	Polycarbonate (Lab Products, Inc., Garfield, NY, and Rochelle Park, NY, and Hazleton Systems, Aberdeen, MD)

TABLE 3. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE DERMAL STUDIES OF MARINE DIESEL FUEL AND JP-5 NAVY FUEL (Continued)

	Single-Administration Studies	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
Cage Filters	Nonwoven filter sheets (Snow Filtration Co., Cincinnati, OH)	Nonwoven polyester filter sheets (Snow Filtration Co., Cincinnati, OH)	MDF--nonwoven polyester filter sheets (Snow Filtration Co., Cincinnati, OH); JP-5--nonwoven filter paper (Snow Filtration Co., Cincinnati, OH)	Same as 14-d studies
Animals per Cage	5	5	5	5
Other Chemicals on Study in the Same Room	None	None	None	None
Animal Room Environment	Temp--74° ± 2° F; hum--30%-70%; fluorescent light 12 h/d; 15 room air changes/h	Same as single-administration studies	Same as single-administration studies	Same as single-administration studies except 12-15 room air changes/h

(a) MDF
(b) JP-5

were given dermal applications (to the clipped dorsal interscapular area) of 0, 500, 1,000, 2,000, 4,000, or 8,000 mg/kg in acetone, 5 days per week for 13 weeks. The 8,000 mg/kg dose was applied as the neat chemical. Conditions of animal maintenance were the same as those given for marine diesel fuel.

TWO-YEAR STUDIES

Study Design

Groups of 49 or 50 mice of each sex were administered 0, 250, or 500 mg/kg marine diesel fuel in acetone by dermal application to the clipped dorsal interscapular region, 5 days per week for 103 weeks (84 weeks for high dose male and high dose female mice). Groups of 50 mice of each sex were administered 0, 250, or 500 mg/kg JP-5 navy fuel in acetone by dermal application to the clipped dorsal interscapular region, 5 days per week for 103 weeks (90 weeks for high dose female mice).

Source and Specifications of Animals

The male and female B6C3F$_1$ (C57BL/6N, female, × C3H/HeN MTV$^-$, male) mice used in these studies were produced under strict barrier conditions at Charles River Breeding Laboratories under a contract to the Carcinogenesis Program. Breeding stock for the foundation colony at the production facility originated at the National Institutes of Health Repository.

Mice shipped for study were progeny of defined microflora-associated parents that were transferred from isolators to barrier-maintained rooms. Mice were shipped to the study laboratory at 5.5 weeks of age (marine diesel fuel) and 6 weeks of age (JP-5 navy fuel). The mice were quarantined at the study facility for 15 days (marine diesel fuel) and 2 weeks (JP-5 navy fuel). Thereafter, a complete necropsy was performed on five animals of each sex to assess their health status. The mice were placed on study at 8 weeks of age. The health of the animals was monitored during the course of the studies according to the protocols of the NTP Sentinel Animal Program (Appendix R).

A quality control skin grafting program has been in effect since early 1978 to monitor the genetic integrity of the inbred mice used to produce the hybrid B6C3F$_1$ study animal. In

mid-1981, data were obtained that showed incompatibility between the NIH C3H reference colony and the C3H colony from a Program supplier. In August 1981, inbred parental lines of mice were further tested for genetic integrity via isozyme and protein electrophoresis profiles that demonstrate phenotype expressions of known genetic loci.

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

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

Animal Maintenance

Mice were clipped with electric clippers once per week. Mice were housed five per cage in polycarbonate cages. Feed and water (acidified with hydrochloric acid to pH 2.5 for bacterial control) were available ad libitum. Details of animal maintenance are summarized in Table 3.

Clinical Examinations and Pathology

All animals were observed twice daily, and clinical signs were recorded once per week. Body weights by cage were recorded once per week for the first 13 weeks of the studies and once per month thereafter. Mean body weights were calculated for each group. Moribund animals were killed, as were animals that survived to the end of the study. A necropsy was performed on all animals, including those found dead unless they were excessively autolyzed or cannibalized. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study in each group.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Tissues examined microscopically are listed in Table 3.

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

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

Statistical Methods

Data Recording: Data on this experiment were recorded in the Carcinogenesis Bioassay Data System (Linhart et al., 1974). The data elements include descriptive information on the chemicals, animals, experimental design, survival,

body weight, and individual pathologic results, as recommended by the International Union Against Cancer (Berenblum, 1969).

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

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

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

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

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

The high dose group of female mice that received JP-5 navy fuel and the high dose groups of males and females that received marine diesel fuel were killed early because of ulcer formation at the site of dermal application. Thus, the early termination date (week 90 for females that received JP-5 navy fuel and week 84 for male and female mice that received marine diesel fuel) was regarded as the end of the study for the life table analyses.

Incidental Tumor Analyses--The second method of analysis assumed that all tumors of a given type observed in animals that died before the end of the study were "incidental"; i.e., they were merely observed at necropsy in animals dying of an unrelated cause. According to this approach, the proportions of tumor-bearing animals in dosed and vehicle control groups of male mice administered JP-5 navy fuel were compared in each of five time intervals: weeks 0-52, weeks 53-78, weeks 79-92, week 93 to the week before the terminal-kill period, and the terminal-kill period. The other groups were compared in three time intervals: weeks 0-52, week 53 to the week before the early high dose termination, and the week of high dose termination through the terminal kill of the vehicle control and low dose groups. The denominators

of these proportions were the number of animals on which a necropsy actually examined for tumors during the time interval. The individual time interval comparisons were then combined by the previously described method to obtain a single overall result. (See Haseman, 1984, for the computational details of both methods.)

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

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

III. RESULTS

SINGLE-ADMINISTRATION STUDIES

Marine Diesel Fuel

FOURTEEN-DAY STUDIES

Marine Diesel Fuel

JP-5 Navy Fuel

THIRTEEN-WEEK STUDIES

Marine Diesel Fuel

JP-5 Navy Fuel

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

SINGLE-ADMINISTRATION STUDIES

Marine Diesel Fuel

None of the mice died before the end of the studies. No compound-related signs of toxicity were observed.

FOURTEEN-DAY STUDIES

Marine Diesel Fuel

All the mice that received 20,000 or 40,000 mg/kg marine diesel fuel died before the end of the studies (Table 4). Control male mice lost weight, and none of the male mice in the other groups gained weight. Female mice that received 8,000 mg/kg gained no weight. Skin lesions in all groups of dosed mice were similar and were characterized by moderate acanthosis, parakeratosis, and hyperkeratosis and were accompanied by moderate mixed cellular inflammatory infiltrate in the upper dermis.

JP-5 Navy Fuel

All the mice that received 40,000 mg/kg JP-5 navy fuel and all female mice that received 30,000 mg/kg JP-5 navy fuel died before the end of the studies (Table 5). Mice that received 10,000 mg/kg or more JP-5 navy fuel lost weight. Compound-related effects at the site of application were scaly skin and hair loss. Microscopically, the skin lesions were characterized by acanthosis, hyperkeratosis, and acute or subacute inflammation.

TABLE 4. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE FOURTEEN-DAY DERMAL STUDIES OF MARINE DIESEL FUEL

Dose (mg/kg)	Survival (a)	Mean Body Weights (grams) Initial	Final	Change	Final Weight Relative to Controls (percent)
MALE					
0	5/5	23	21	− 2	--
2,000	5/5	24	23	− 1	110
4,000	5/5	24	24	0	114
8,000	5/5	24	21	− 3	100
20,000	(b) 0/5	24	(c)	(c)	(c)
40,000	(d) 0/5	24	(c)	(c)	(c)
FEMALE					
0	5/5	18	19	+ 1	--
2,000	5/5	17	19	+ 2	100
4,000	5/5	17	18	+ 1	95
8,000	5/5	18	18	0	95
20,000	(e) 0/5	18	(c)	(c)	(c)
40,000	(f) 0/5	17	(c)	(c)	(c)

(a) Number surviving/number initially in group
(b) Day of death: all 12
(c) No data are presented due to the 100% mortality in this group.
(d) Day of death: all 8
(e) Day of death: all 7
(f) Day of death: all 9

TABLE 5. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE FOURTEEN-DAY DERMAL STUDIES OF JP-5 NAVY FUEL

Dose (mg/kg)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Vehicle Controls (percent)
MALE					
0	5/5	24.0 ± 0.7	24.6 ± 1.2	+ 0.6 ± 0.7	--
5,000	5/5	22.4 ± 1.1	23.0 ± 0.8	+ 0.6 ± 0.5	93.5
10,000	5/5	23.2 ± 0.7	21.4 ± 0.7	− 1.8 ± 0.2	87.0
20,000	5/5	23.6 ± 1.1	22.6 ± 1.4	− 1.0 ± 0.5	91.9
30,000	5/5	22.2 ± 0.6	18.8 ± 0.4	− 3.4 ± 0.2	76.4
40,000	(d) 0/5	21.2 ± 1.0	(e)	(e)	(e)
FEMALE					
0	5/5	18.2 ± 0.2	20.2 ± 0.4	+ 2.0 ± 0.3	--
5,000	5/5	18.2 ± 0.7	20.2 ± 1.1	+ 2.0 ± 0.6	100.0
10,000	5/5	18.0 ± 0.6	16.8 ± 0.6	− 1.2 ± 0.2	83.2
20,000	5/5	18.0 ± 0.8	16.0 ± 0.4	− 2.0 ± 0.8	79.2
30,000	(d) 0/5	18.2 ± 0.9	(e)	(e)	(e)
40,000	(f) 0/5	16.8 ± 0.4	(e)	(e)	(e)

(a) Number surviving/number initially in group
(b) Initial mean group body weight ± standard error of the mean
(c) Mean body weight change of the survivors ± standard error of the mean
(d) Day of death: all 9
(e) No data are presented due to the 100% mortality in this group.
(f) Day of death: 6, 6, 6, 7, 7

THIRTEEN-WEEK STUDIES

Marine Diesel Fuel

Five of 10 female mice that received 4,000 mg/kg marine diesel fuel died during week 4 due to accidental dehydration (Table 6). No other deaths occurred. Final mean body weights of male mice that received 500, 1,000, 2,000, or 4,000 mg/kg marine diesel fuel were 8%-13% lower than that of the vehicle controls. Final mean body weights of female mice were not adversely affected by marine diesel fuel. An increased severity of mild chronic active dermatitis was observed at the site of application for the group that received 4,000 mg/kg marine diesel fuel.

Dose Selection Rationale: Based on body weight changes and the incidence and severity of dermatitis observed in the 13-week studies, doses selected for mice for the 2-year studies were 250 and 500 mg/kg marine diesel fuel, administered in acetone 5 days per week by dermal application.

JP-5 Navy Fuel

Five of 10 males that received 8,000 mg/kg JP-5 navy fuel died (Table 7). The distribution of other deaths is given in Table 7. The final mean body weight of male mice that received 8,000 mg/kg was 7% lower than that of the vehicle controls. The final mean body weights of female mice were not affected by JP-5 navy fuel. Slight to moderate splenic extramedullary hematopoiesis, slight hepatic karyomegaly, and increased severity of dermatosis were considered to be compound related (Table 8).

Dose Selection Rationale: Based on the severity of the dermatitis observed in the 13-week studies, doses selected for mice for the 2-year studies were 250 and 500 mg/kg JP-5 navy fuel, administered in acetone 5 days per week by dermal application.

TABLE 6. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE THIRTEEN-WEEK DERMAL STUDIES OF MARINE DIESEL FUEL

Dose (mg/kg)	Survival (a)	Mean Body Weights (grams) Initial	Final	Change	Final Weight Relative to Vehicle Controls (percent)
MALE					
0	10/10	25.6	34.7	+ 9.1	--
250	10/10	23.6	33.9	+10.3	97.7
500	10/10	24.2	31.7	+ 7.5	91.4
1,000	10/10	25.1	31.8	+ 6.7	91.6
2,000	10/10	26.1	31.5	+ 5.4	90.8
4,000	10/10	25.3	30.1	+ 4.8	86.7
FEMALE					
0	10/10	17.7	24.3	+ 6.6	--
250	10/10	17.5	24.4	+ 6.9	100.4
500	10/10	17.6	25.4	+ 7.8	104.5
1,000	10/10	17.8	25.9	+ 8.1	106.6
2,000	10/10	18.5	26.1	+ 7.6	107.4
4,000	(b) 5/10	17.9	25.2	+ 7.3	103.7

(a) Number surviving/number initially in group
(b) Deaths judged accidental

TABLE 7. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE THIRTEEN-WEEK DERMAL STUDIES OF JP-5 NAVY FUEL

Dose (mg/kg)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Vehicle Controls (percent)
MALE					
0	10/10	24.5 ± 0.8	32.3 ± 1.0	+7.8 ± 0.3	--
500	10/10	24.5 ± 0.3	34.0 ± 0.7	+9.5 ± 0.5	105.3
1,000	10/10	24.3 ± 0.6	32.4 ± 0.8	+8.1 ± 0.4	100.3
2,000	10/10	23.9 ± 0.6	30.9 ± 0.8	+7.0 ± 0.5	95.7
4,000	(d) 9/10	24.7 ± 0.7	30.6 ± 0.7	+6.3 ± 0.3	94.7
8,000	(e) 5/10	25.3 ± 0.5	30.1 ± 1.0	+4.5 ± 0.3	93.2
FEMALE					
0	10/10	19.6 ± 0.3	25.0 ± 0.6	+5.4 ± 0.4	--
500	10/10	19.4 ± 0.3	26.0 ± 0.5	+6.6 ± 0.3	104.0
1,000	10/10	18.9 ± 0.3	25.7 ± 0.4	+6.8 ± 0.3	102.8
2,000	(f) 6/10	19.2 ± 0.2	25.5 ± 0.5	+6.4 ± 0.3	102.0
4,000	(g) 5/10	19.0 ± 0.3	26.1 ± 0.9	+7.0 ± 0.6	104.4
8,000	10/10	19.2 ± 0.3	25.7 ± 0.3	+6.5 ± 0.2	102.8

(a) Number surviving/number initially in group
(b) Initial group body weight ± standard error of the mean. Subsequent calculations are based on those animals surviving to the end of the study.
(c) Mean body weight change of the survivors ± standard error of the mean
(d) Week of death: 11
(e) Week of death: all 3
(f) Week of death: 4, 4, 5, 5
(g) Week of death: all 12

TABLE 8. INCIDENCES OF MICE WITH SELECTED LESIONS IN THE THIRTEEN-WEEK DERMAL STUDIES OF JP-5 NAVY FUEL

Site: Lesion	Dose (mg/kg)					
	Vehicle Control	500	1,000	2,000	4,000	8,000
MALE						
Skin, application site: Dermatosis						
Incidence (a)	0/10	10/10	10/10	10/10	10/10	10/10
Average severity (b)	--	2.3	3.1	3.1	3.5	3.6
Skin, nonapplication site: Dermatosis						
Incidence	1/9	9/10	10/10	10/10	10/10	9/9
Average severity	1.0	1.4	1.8	2.8	3.0	2.3
Spleen: Extramedullary hematopoiesis						
Incidence	0/10	1/10	6/10	8/10	10/10	8/8
Average severity	--	2.0	2.2	2.5	2.5	2.1
Liver: Karyomegaly						
Incidence	0/10	3/10	5/10	9/10	6/10	8/10
FEMALE						
Skin, application site: Dermatosis						
Incidence	1/10	10/10	10/10	9/9	10/10	10/10
Average severity	1.0	1.9	2.8	3.4	3.9	3.6
Skin, nonapplication site: Dermatosis						
Incidence	1/10	8/10	10/10	10/10	10/10	9/9
Average severity	1.0	1.1	2.0	2.6	3.3	3.0
Spleen: Extramedullary hematopoiesis						
Incidence	1/10	2/10	7/10	6/9	10/10	9/9
Average severity	2.0	2.0	2.3	2.5	3.0	2.9
Liver: Karyomegaly						
Incidence	0/10	2/10	8/10	7/10	5/10	8/10

(a) Incidence equals the number of animals with lesions out of the total number of animals examined microscopically.
(b) Lesions were graded for severity as follows: 1 = minimal; 2 = slight; 3 = mild; 4 = moderate; 5 = marked.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Marine Diesel Fuel: Mean body weights of high dose male mice were more than 5% lower than those of the vehicle controls after week 28 and 9%-23% lower after week 40 (Table 9 and Figure 1). Mean body weights of low dose male mice were 5%-15% lower than those of the vehicle controls after week 60. Mean body weights of high dose female mice were more than 5% lower than those of the vehicle controls after week 28 and 15%-20% lower after week 72. Mean body weights of low dose female mice were 5%-19% lower than those of the vehicle controls after week 40.

JP-5 Navy Fuel: Mean body weights of high dose male mice were 5% lower than those of the vehicle controls after week 32 and 14%-22% lower after week 76 (Table 10 and Figure 2). Final mean body weights of high dose female mice were 7% lower than those of the vehicle controls after week 32 and 13%-25% lower after week 60.

TABLE 9. MEAN BODY WEIGHTS AND SURVIVAL OF MICE IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL

Weeks on Study	Vehicle Control		250 mg/kg			500 mg/kg		
	Av Wt (grams)	No. of Survivors	Av Wt (grams)	Wt (percent of veh controls)	No. of Survivors	Av Wt (grams)	Wt (percent of veh controls)	No. of Survivors
MALE								
0	23.1	50	22.9	99	50	22.5	97	50
1	24.2	50	24.6	102	50	24.5	101	50
2	25.6	50	26.0	102	50	25.4	99	50
3	26.6	50	26.9	101	49	26.7	100	50
4	27.3	50	27.5	101	49	27.4	100	50
5	28.1	50	28.4	101	49	27.4	98	49
6	28.4	50	29.4	104	49	29.1	102	49
7	29.2	50	29.8	102	49	29.5	101	49
8	29.8	50	30.7	103	49	30.8	103	49
9	30.3	50	31.2	103	49	30.8	102	49
10	30.5	50	31.3	103	49	30.8	101	49
11	31.3	49	32.0	102	49	31.9	102	49
12	31.8	49	33.2	104	49	32.1	101	49
13	32.2	49	33.3	103	49	32.4	101	49
16	32.9	49	33.1	101	48	32.2	98	49
20	35.2	48	35.2	100	48	34.3	97	49
24	36.4	48	36.4	100	48	34.8	96	49
28	38.0	48	38.1	100	48	36.1	95	49
32	37.9	48	37.4	99	48	35.5	94	49
36	38.2	45	37.4	98	48	35.2	92	49
40	39.0	44	37.4	96	47	35.2	90	47
44	39.1	44	37.6	96	46	35.5	91	47
48	39.3	43	37.4	95	46	34.7	88	47
52	38.1	43	37.2	98	46	34.6	91	47
56	38.3	43	37.0	97	45	33.5	87	44
60	38.6	42	36.4	94	45	32.4	84	44
64	38.7	41	36.7	95	45	33.1	86	42
68	39.1	40	36.6	94	44	32.4	83	41
72	40.6	39	37.7	93	44	32.8	81	34
76	40.1	38	37.1	93	43	31.9	80	30
80	40.5	36	36.8	91	40	31.0	77	28
84	40.6	36	36.4	90	38	31.1	77	26
88	40.2	36	36.3	90	34	--	--	--
92	40.1	35	34.7	87	30	--	--	--
96	40.1	35	34.7	87	27	--	--	--
100	40.4	32	34.3	85	23	--	--	--
104	39.0	30	33.4	86	19	--	--	--
FEMALE								
0	18.2	50	18.3	101	50	17.9	98	50
1	19.0	50	20.0	105	45	19.5	103	50
2	20.1	50	20.7	103	45	20.6	102	50
3	21.1	50	21.2	100	45	21.1	100	50
4	21.4	50	21.2	99	45	21.4	100	50
5	21.9	50	22.1	101	44	22.1	101	50
6	22.3	50	23.3	104	44	23.2	104	50
7	23.0	50	23.5	102	44	23.5	102	50
8	23.6	50	24.0	102	44	23.6	100	50
9	24.0	50	24.0	100	44	24.0	100	50
10	23.8	50	24.2	102	44	24.2	102	50
11	24.3	50	24.4	100	44	24.6	101	50
12	24.4	50	24.7	101	44	24.6	101	50
13	24.8	50	24.9	100	44	25.2	102	49
16	25.2	50	25.1	100	44	25.0	99	49
20	27.2	49	26.7	98	43	27.0	99	49
24	28.6	49	28.7	100	43	27.8	97	49
28	30.3	49	29.7	98	43	28.9	95	49
32	30.5	49	28.9	95	43	28.8	94	48
36	30.4	49	29.0	95	43	28.7	94	46
40	31.4	49	29.4	94	43	29.2	93	43
44	31.8	49	30.0	94	43	29.6	93	43
48	32.4	49	30.3	94	43	29.8	92	43
52	32.1	49	30.3	94	43	29.8	93	42
56	32.2	49	30.5	95	42	29.9	93	41
60	32.5	49	30.2	93	42	29.7	91	40
64	33.3	49	30.8	92	42	30.7	92	40
68	33.7	49	30.7	91	41	30.8	91	39
72	37.1	48	32.5	88	35	31.3	84	37
76	36.4	48	32.8	90	31	31.1	85	35
80	37.4	48	32.1	86	27	31.1	83	32
84	37.8	48	31.8	84	22	30.3	80	28
88	38.4	48	31.7	83	21	--	--	--
92	37.8	46	31.3	83	18	--	--	--
96	37.9	45	31.8	84	16	--	--	--
100	39.0	43	31.6	81	14	--	--	--
104	37.8	40	31.4	83	12	--	--	--

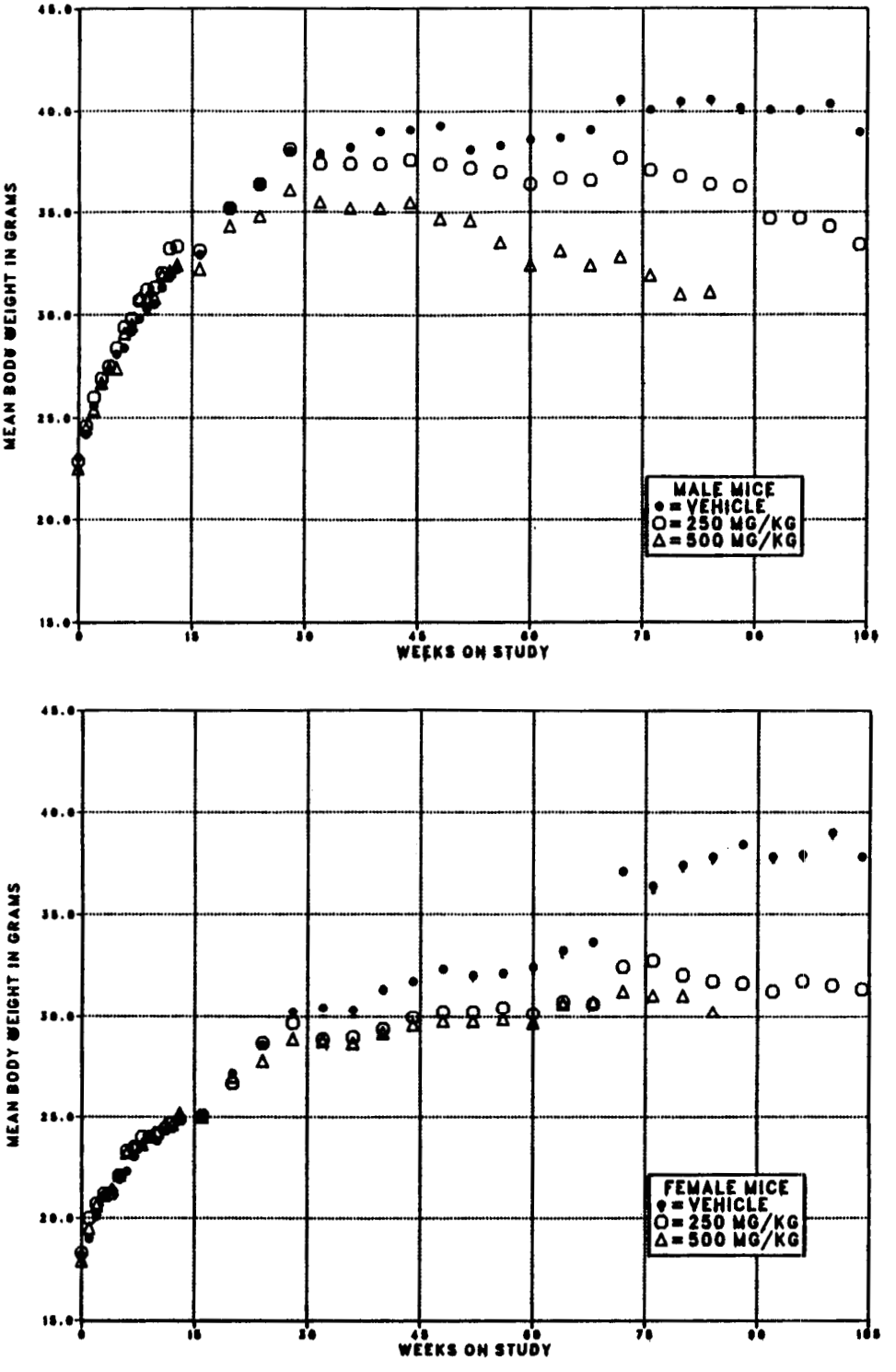


FIGURE 1. GROWTH CURVES FOR MICE ADMINISTERED MARINE DIESEL FUEL BY DERMAL APPLICATION FOR TWO YEARS

TABLE 10. MEAN BODY WEIGHTS AND SURVIVAL OF MICE IN THE TWO-YEAR DERMAL STUDIES OF JP-5 NAVY FUEL

Weeks on Study	Vehicle Control		250 mg/kg			500 mg/kg		
	Av Wt (grams)	No. of Survivors	Av Wt (grams)	Wt (percent of veh controls)	No. of Survivors	Av Wt (grams)	Wt (percent of veh controls)	No. of Survivors
MALE								
0	23.2	50	23.2	100	50	22.9	99	50
1	24.0	50	24.0	100	50	24.0	100	50
2	25.9	50	25.9	100	50	26.2	101	49
3	26.8	50	26.9	100	50	26.6	99	49
4	28.8	50	28.1	98	50	28.3	98	49
5	29.4	50	28.8	98	50	29.7	101	49
6	30.1	50	30.2	100	50	29.7	99	49
7	30.7	50	30.6	100	50	30.3	99	49
8	30.0	50	30.4	101	50	30.4	101	49
9	31.0	50	31.2	101	50	30.3	98	49
10	31.8	50	31.5	99	50	31.7	100	49
11	32.5	50	32.2	99	50	32.0	98	49
12	32.3	50	32.7	101	50	32.6	101	49
13	33.1	49	33.5	101	50	33.1	100	49
16	33.9	49	34.3	101	50	33.5	99	49
20	34.8	48	35.3	101	50	34.2	98	49
24	37.0	48	38.0	103	50	36.4	98	49
28	37.1	47	38.6	104	50	36.2	98	49
32	38.3	47	39.4	103	50	36.3	95	48
36	39.1	47	40.5	104	50	36.5	93	48
40	39.4	47	40.6	103	50	36.5	93	48
44	39.2	47	40.6	104	50	35.2	90	47
48	39.2	47	40.1	102	50	35.6	91	47
52	38.7	47	39.5	102	50	35.7	92	47
56	38.9	47	39.7	102	50	35.4	91	47
60	38.9	47	39.3	101	50	35.3	91	47
64	38.2	47	38.1	100	50	34.1	89	47
68	38.3	46	38.1	99	50	34.6	90	47
72	38.5	46	39.2	102	49	34.6	90	47
76	39.8	45	39.2	98	47	34.4	86	47
80	39.8	45	38.7	97	47	33.8	85	46
84	39.9	44	38.3	96	43	32.3	81	44
88	40.0	43	38.9	97	43	32.1	80	37
92	40.5	43	38.9	96	41	32.4	80	36
96	39.7	41	37.8	95	39	31.5	79	35
100	39.3	41	38.0	97	36	31.2	79	33
104	38.8	36	37.1	96	33	30.3	78	28
FEMALE								
0	18.7	50	19.6	105	50	19.3	103	50
1	19.1	50	19.6	103	50	19.5	102	50
2	20.4	50	20.9	102	50	21.3	104	47
3	20.6	50	21.3	103	50	21.9	106	47
4	21.9	48	22.9	105	49	22.7	104	47
5	22.4	48	23.5	105	49	24.0	107	47
6	23.0	48	23.9	104	49	24.3	106	47
7	23.5	48	24.4	104	49	24.4	104	47
8	23.5	48	24.1	103	49	24.6	105	47
9	23.6	48	24.6	104	49	24.9	106	47
10	24.1	48	25.0	104	49	25.4	105	47
11	24.3	48	25.4	105	49	25.8	106	47
12	24.2	48	25.7	106	49	25.9	107	47
13	25.1	48	25.9	103	49	26.3	105	47
16	25.5	48	26.0	102	49	26.0	102	46
20	26.3	48	27.2	103	49	26.9	102	46
24	28.3	48	29.4	104	49	28.1	99	46
28	29.6	48	30.7	104	49	28.5	96	45
32	30.9	48	31.4	102	49	28.8	93	45
36	32.5	48	33.6	103	49	29.2	90	45
40	33.8	48	33.8	100	49	29.9	88	44
44	34.3	48	34.0	99	48	30.5	89	44
48	34.0	48	33.8	99	48	30.1	89	44
52	33.2	48	33.0	99	48	30.4	92	44
56	33.3	48	33.4	100	48	30.3	91	44
60	34.4	48	34.1	99	47	29.9	87	42
64	33.6	48	33.8	101	47	29.2	87	40
68	34.5	48	34.0	99	47	29.9	87	39
72	35.5	48	34.7	98	47	30.4	86	39
76	36.2	48	35.3	98	47	30.0	83	38
80	36.9	48	35.4	96	47	29.8	81	28
84	37.4	48	35.7	95	47	29.0	78	22
88	38.6	48	37.1	96	44	28.9	75	19
92	40.3	47	37.4	93	40	--	--	--
96	38.6	46	36.9	96	39	--	--	--
100	39.8	45	36.3	91	36	--	--	--
104	39.3	44	34.7	88	33	--	--	--

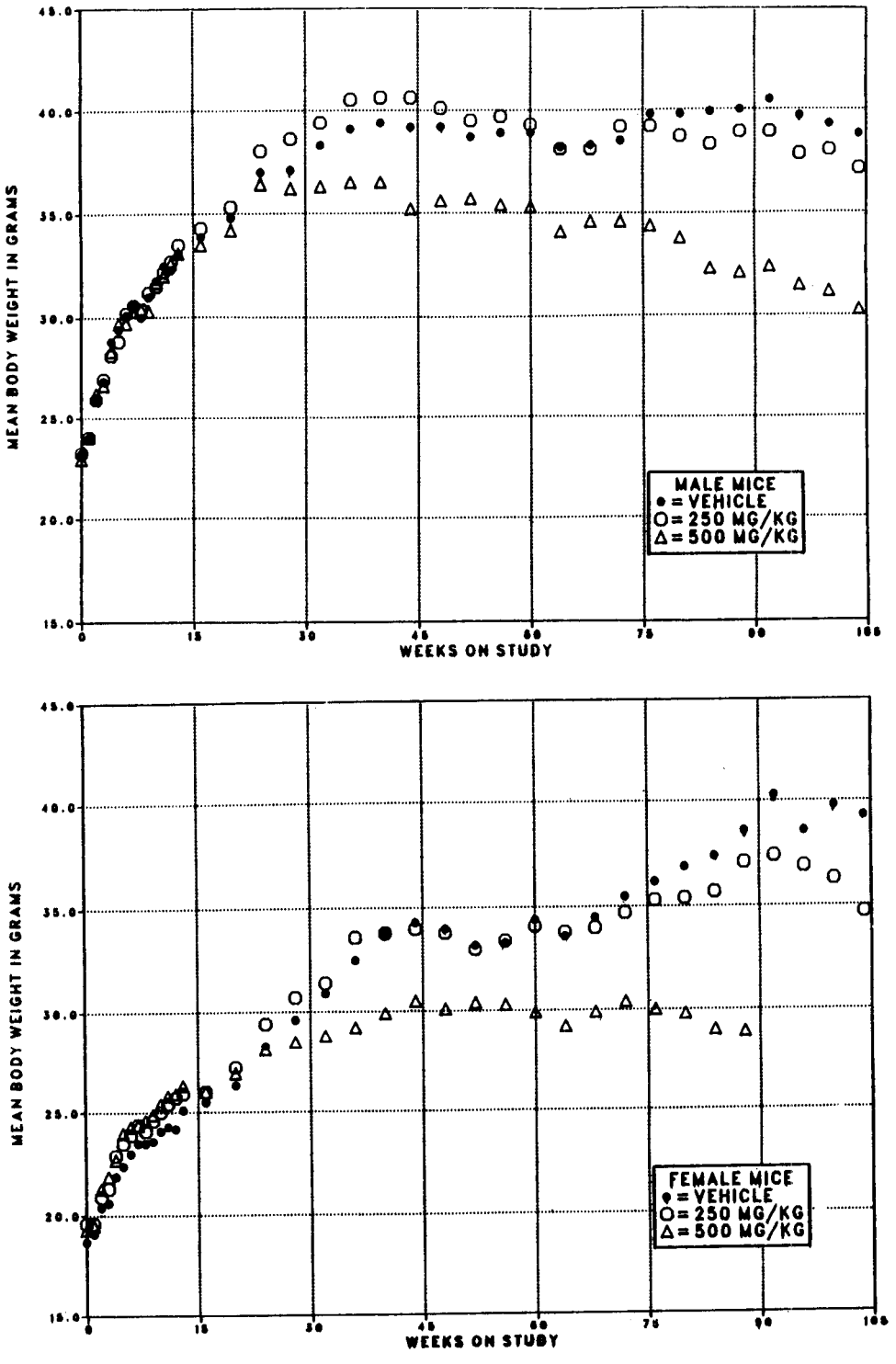


FIGURE 2. GROWTH CURVES FOR MICE ADMINISTERED JP-5 NAVY FUEL BY DERMAL APPLICATION FOR TWO YEARS

Survival

Marine Diesel Fuel: Estimates of the probabilities of survival for male and female mice administered marine diesel fuel at the doses used in these studies and those of the vehicle controls are shown in the Kaplan and Meier curves in Figure 3. The survival of both dosed groups of female mice (the low dose after week 67 and the high dose after week 58) was significantly lower than that of the vehicle controls (Table 11). Because of severe ulceration of the skin, all high dose mice were killed at week 84.

JP-5 Navy Fuel: Estimates of the probabilities of survival for male and female mice administered JP-5 navy fuel at the doses used in these studies and those of the vehicle controls are shown in the Kaplan and Meier curves in Figure 4. The survival of both dosed groups of female mice was significantly lower than that of the vehicle controls (the low dose after week 97 and the high dose after week 57) (Table 12). The high dose group of female mice was killed at week 90. Survival of male mice was not affected by administration of JP-5 navy fuel.

Pathology and Statistical Analyses of Results

This section describes the significant or noteworthy changes in the incidences of mice with neoplastic or nonneoplastic lesions of the skin, liver, hematopoietic system, multiple organs, and urinary bladder in the studies of marine diesel fuel and of the skin, liver, hematopoietic system, kidney, adrenal gland, spleen, axillary lymph node, multiple organs, and bone marrow in the studies of JP-5 navy fuel.

Histopathologic findings on neoplasms in mice in the marine diesel fuel studies are summarized in Appendix A (Tables A1 and A2); Appendix A (Tables A3 and A4) also gives the survival and tumor status for individual male and female mice. Histopathologic findings on neoplasms in mice in the JP-5 navy fuel studies are summarized in Appendix B (Tables B1 and B2); Appendix B (Tables B3 and B4) also gives the survival and tumor status for individual male and female mice.

Findings on nonneoplastic lesions in the studies of marine diesel fuel are summarized in Appendix C (Tables C1 and C2). Findings on nonneoplastic lesions in the studies of JP-5 navy fuel are summarized in Appendix D (Tables D1 and D2).

Appendix E (Tables E1 and E2) contains the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups in the marine diesel fuel studies. Appendix E (Tables E3 and E4) also contains the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups in the JP-5 navy fuel studies. The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes).

The high dose group of female mice that received JP-5 navy fuel and the high dose groups of males and females that received marine diesel fuel were killed early because of ulceration at the site of dermal application. For statistical purposes, the early termination date (week 90 for females that received JP-5 navy fuel and week 84 for male and female mice that received marine diesel fuel) was regarded as the end of the study for all analyses; the week of first tumor observation, however, is the week that the tumor was actually first observed. All animals dying during the first week of the study were excluded from the calculation of tumor incidences and the corresponding statistical analyses.

TABLE 11. SURVIVAL OF MICE IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL

	Vehicle Control	250 mg/kg	500 mg/kg
MALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	19	27	24
Accidentally killed	1	1	0
Animals missexed	0	1	0
Killed at termination	30	(d) 20	(e) 26
Died during termination period	0	1	0
Survival P values (c)	0.003	0.219	0.075
FEMALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	10	37	20
Accidentally killed	0	1	1
Killed at termination	40	12	(e) 29
Survival P values (c)	<0.001	<0.001	<0.001

(a) Terminal-kill period: week 105
(b) Includes animals killed in a moribund condition
(c) The result of the life table trend test is in the vehicle control column, and the results of the life table pairwise comparisons with the vehicle controls are in the dosed columns.
(d) Includes two animals killed at week 99
(e) Early termination at week 84

TABLE 12. SURVIVAL OF MICE IN THE TWO-YEAR DERMAL STUDIES OF JP-5 NAVY FUEL

	Vehicle Control	250 mg/kg	500 mg/kg
MALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	14	17	21
Accidentally killed	0	0	1
Killed at termination	36	33	28
Survival P values (c)	0.172	0.662	0.204
FEMALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	4	15	33
Accidentally killed	0	1	0
Animals missing	2	1	0
Killed at termination	44	33	(d) 17
Survival P values (c)	<0.001	0.009	<0.001

(a) Terminal-kill period: week 105
(b) Includes animals killed in a moribund condition
(c) The result of the life table trend test is in the vehicle control column, and the results of the life table pairwise comparisons with the vehicle controls are in the dosed columns.
(d) Early termination at week 90

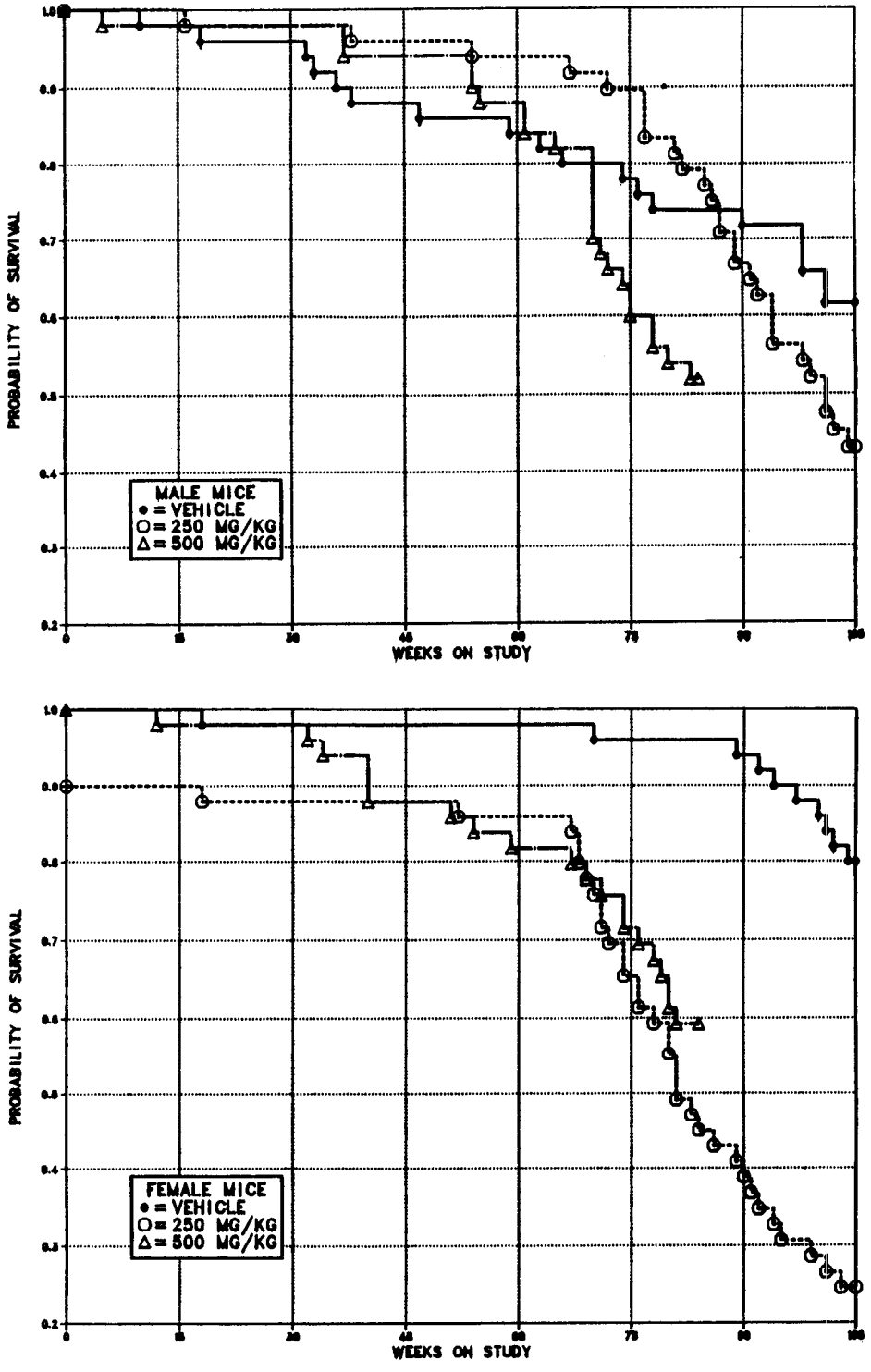
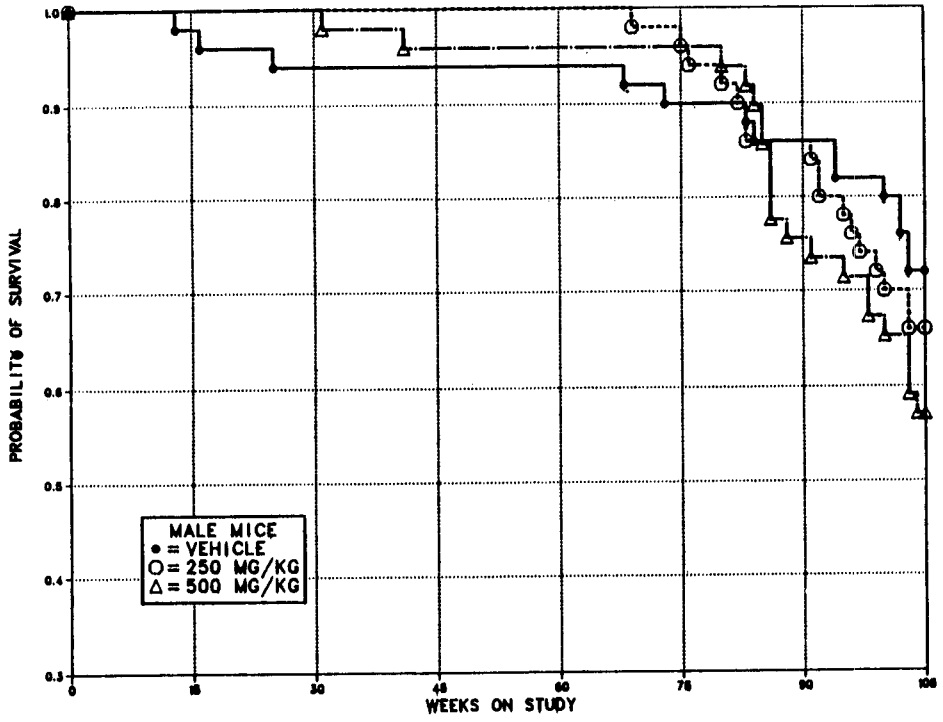


FIGURE 3. KAPLAN-MEIER SURVIVAL CURVES FOR MICE ADMINISTERED MARINE DIESEL FUEL BY DERMAL APPLICATION FOR TWO YEARS



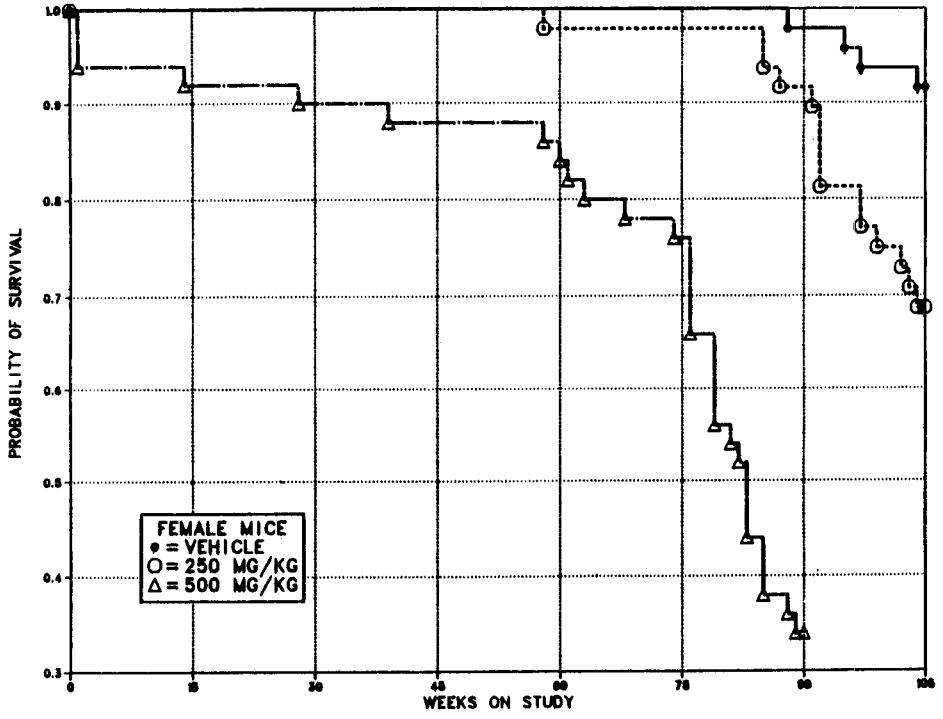


FIGURE 4. KAPLAN-MEIER SURVIVAL CURVES FOR MICE ADMINISTERED JP-5 NAVY FUEL BY DERMAL APPLICATION FOR TWO YEARS

Skin, Marine Diesel Fuel: Ulcers and chronic dermatitis in both males and females were observed at increased incidences at the site of dermal application and at the inguinal skin site, to which the dose mixture migrated after application (Table 13). Chronic dermatitis consisted of hyperplasia of the epithelium (acanthosis) with accumulation of keratin on the surface (hyperkeratosis) and acute to chronic inflammation of the dermis. Fibroplasia was frequently associated with the ulcers that developed. The incidence and severity of chronic dermatitis were increased in dosed mice at the site of application and at the inguinal site (Tables 14 and 15).

Squamous cell papillomas or squamous cell carcinomas (combined) at the site of application in male mice occurred with a significant positive trend (Tables 13 and 16). A squamous cell papilloma of the skin (inguinal skin site) was observed in 1/50 male vehicle controls, and squamous cell carcinomas were observed in 2/49 males in the high dose group. At the application site in females, squamous cell carcinomas were observed in 0/50 vehicle control, 1/50 low dose, and 2/48 high dose animals.

Skin, JP-5 Navy Fuel: Ulcers and chronic dermatitis were observed at increased incidences in dosed mice at both the application site and the inguinal skin site, to which the dose mixture migrated after application (Tables 17-19). The skin lesions were similar to those occurring in mice dosed with marine diesel fuel. The lesion consisted of necrosis of the epithelium with excoriation and ulceration and subsequent acanthosis. Microscopically, the ulceration extended deep into the dermis in severely affected animals. The chronic dermatitis varied in severity from mild chronic inflammation of the dermis to superficial and deep suppuration.

No neoplasia was observed at necropsy or microscopically at the site of application for dosed or vehicle control animals. A squamous cell carcinoma was observed at the inguinal skin site for 1/50 females in the high dose group.

TABLE 13. INCIDENCES OF MICE WITH SELECTED LESIONS IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL

Site/Lesion	Vehicle Control	250 mg/kg	500 mg/kg (a)
MALE			
Skin, application site			
Ulcer	1/49	25/49	36/49
Squamous cell papilloma	0/49	0/49	1/49
Squamous cell carcinoma	0/49	0/49	2/49
Squamous cell papilloma or carcinoma	0/49	0/49	3/49
Skin, inguinal site (b)			
Ulcer	0/50	6/49	7/50
Squamous cell papilloma	1/50	0/49	0/50
Squamous cell carcinoma	0/50	2/49	0/50
Liver			
Hematopoiesis	0/50	3/48	1/49
Hepatocellular adenoma	5/50	10/48	10/49
Hepatocellular carcinoma	5/50	9/48	5/49
Hepatocellular adenoma or carcinoma	9/50	17/48	14/49
Spleen			
Hematopoiesis	9/50	14/48	40/49
Multiple organs			
Amyloidosis	0/50	6/49	1/50
Axillary lymph node			
Plasmacytosis	0/42	1/42	18/40
Urinary bladder			
Lymphocytic inflammatory infiltrate	7/49	6/46	18/49
FEMALE			
Skin, application site			
Ulcer	0/50	27/45	39/48
Squamous cell carcinoma	0/50	1/45	2/48
Skin, inguinal site (b)			
Ulcer	0/50	8/45	5/50
Liver			
Hematopoiesis	1/50	5/45	9/50
Hepatocellular adenoma	4/50	2/45	2/50
Hepatocellular carcinoma	0/50	2/45	3/50
Hepatocellular adenoma or carcinoma	4/50	4/45	5/50
Spleen			
Hematopoiesis	5/50	24/44	34/50
Multiple organs			
Amyloidosis	1/50	23/45	23/50
Axillary lymph node			
Plasmacytosis	1/50	6/39	24/44
Urinary bladder			
Lymphocytic inflammatory infiltrate	4/50	15/42	15/49

(a) Early termination at week 84
(b) Adjacent skin site to which the dose mixture migrated after application

TABLE 14. INCIDENCE AND SEVERITY OF CHRONIC DERMATITIS AT THE SITE OF APPLICATION IN MICE IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL (a)

	Vehicle Control	250 mg/kg	500 mg/kg
MALE			
Number of animals with dermatitis	3	40	47
Total sections of skin evaluated	50	50	48
Percent with dermatitis	6.0	80.0	97.9
Mean severity of lesion	1.53	2.97	3.29
FEMALE			
Number of animals with dermatitis	26	44	46
Total sections of skin evaluated	50	48	47
Percent with dermatitis	52.0	91.7	97.9
Mean severity of lesion	1.33	3.12	3.27

(a) Severity: 1 = minimal; 2 = mild; 3 = moderate; 4 = marked

TABLE 15. INCIDENCE AND SEVERITY OF CHRONIC DERMATITIS AT THE INGUINAL SKIN SITE IN MICE IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL (a)

	Vehicle Control	250 mg/kg	500 mg/kg
MALE			
Number of animals with dermatitis	2	15	20
Total sections of control skin evaluated	49	47	49
Percent with dermatitis	4.1	31.9	40.8
Mean severity of lesion	2.00	1.60	2.55
FEMALE			
Number of animals with dermatitis	2	18	19
Total sections of control skin evaluated	49	44	49
Percent with dermatitis	4.1	40.9	38.8
Mean severity of lesion	2.00	2.27	2.31

(a) Severity: 1 = minimal; 2 = mild; 3 = moderate; 4 = marked

TABLE 16. ANALYSIS OF SKIN TUMORS IN MICE IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL (a)

	Vehicle Control	250 mg/kg	500 mg/kg (b)
MALE			
Application Site: Squamous Cell Papilloma			
Overall Rates	0/49 (0%)	0/49 (0%)	1/49 (2%)
Application Site: Squamous Cell Carcinoma			
Overall Rates	0/49 (0%)	0/49 (0%)	2/49 (4%)
Application Site: Squamous Cell Papilloma or Carcinoma			
Overall Rates	0/49 (0%)	0/49 (0%)	3/49 (6%)
Adjusted Rates	0.0%	0.0%	11.5%
Terminal Rates	0/30 (0%)	0/19 (0%)	3/26 (12%)
Week of First Observation			84
Life Table Tests	P=0.019	(c)	P=0.073
Incidental Tumor Tests	P=0.019	(c)	P=0.073
Integumentary System (d): Squamous Cell Papilloma or Carcinoma			
Overall Rates	1/50 (2%)	2/49 (4%)	3/50 (6%)
Adjusted Rates	2.8%	5.3%	11.5%
Terminal Rates	1/30 (3%)	1/19 (5%)	3/26 (12%)
Week of First Observation	105	101	84
Life Table Tests	P=0.130	P=0.519	P=0.196
Incidental Tumor Tests	P=0.130	P=0.519	P=0.196
FEMALE			
Application Site (e): Squamous Cell Carcinoma			
Overall Rates	0/50 (0%)	1/45 (2%)	2/48 (4%)
Adjusted Rates	0.0%	4.3%	6.1%
Terminal Rates	0/40 (0%)	1/12 (8%)	1/29 (3%)
Week of First Observation		84	74
Life Table Tests	P=0.090	P=0.353	P=0.160
Incidental Tumor Tests	P=0.122	P=0.353	P=0.359

(a) The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes).
(b) The terminal rates for these groups are based on the the number of animals alive when the studies were terminated at week 84. Life table analyses regarded week 84 as the end of study for all groups.
(c) No P value is reported because no tumors were observed in the 250 mg/kg and vehicle control groups.
(d) Combined sites: application site and adjacent inguinal skin site to which dose mixture migrated after application
(e) No skin tumors were seen at the adjacent inguinal skin site in female mice.

TABLE 17. INCIDENCES OF MICE WITH SELECTED LESIONS IN THE TWO-YEAR DERMAL STUDIES OF JP-5 NAVY FUEL

Site/Lesion	Vehicle Control	250 mg/kg	500 mg/kg (a)
MALE			
Skin, application site			
Ulcer	2/48	11/50	27/49
Skin, inguinal site (b)			
Ulcer	2/50	5/50	13/49
Papilloma	0/50	1/50	0/49
Squamous cell carcinoma	0/50	0/50	1/49
Liver			
Amyloid	2/50	2/50	22/49
Kidney			
Amyloid	3/50	2/49	23/49
Adrenal cortex			
Amyloid	0/50	0/49	5/49
Spleen			
Amyloid	2/49	2/49	8/48
Multiple organs			
Amyloid	0/50	0/50	9/49
Bone marrow			
Granulocytic hyperplasia	1/47	0/47	8/48
FEMALE			
Skin, application site			
Ulcer	0/48	14/48	27/47
Skin, inguinal site (b)			
Ulcer	0/48	3/49	14/47
Squamous cell carcinoma	0/48	0/49	1/47
Liver			
Amyloid	0/48	1/49	11/47
Kidney			
Amyloid	0/48	1/49	12/47
Adrenal cortex			
Amyloid	0/48	0/49	2/46
Spleen			
Amyloid	0/48	1/47	6/47
Multiple organs			
Amyloid	0/48	0/49	17/47
Bone marrow			
Granulocytic hyperplasia	0/48	1/44	14/43
Axillary lymph node			
Hyperplasia	0/47	0/45	7/44

(a) Week of termination: high dose males--week 105; high dose females--week 90; all other groups--week 105.
(b) Adjacent skin site to which the dose mixture migrated after application

TABLE 18. INCIDENCE AND SEVERITY OF CHRONIC DERMATITIS AT THE SITE OF APPLICATION IN MICE IN THE TWO-YEAR DERMAL STUDIES OF *JP-5* NAVY FUEL

	Vehicle Control	250 mg/kg	500 mg/kg (a)
MALE			
Number of animals with dermatitis	22	49	49
Total sections of skin evaluated	49	50	50
Percent with dermatitis	44.9	98.0	98.0
Mean severity of lesion (b)	1.41	2.29	3.45
FEMALE			
Number of animals with dermatitis	15	48	46
Total sections of skin evaluated	47	49	49
Percent with dermatitis	31.9	97.9	93.9
Mean severity of lesion (b)	1.00	2.60	3.20

(a) Week of termination: high dose males--week 105; high dose females--week 90; all other groups--week 105
(b) Severity: 1 = minimal; 2 = mild; 3 = moderate; 4 = marked

TABLE 19. INCIDENCE AND SEVERITY OF CHRONIC DERMATITIS AT THE INGUINAL SKIN SITE IN MICE IN THE TWO-YEAR DERMAL STUDIES OF *JP-5* NAVY FUEL

	Vehicle Control	250 mg/kg	500 mg/kg (a)
MALE			
Number of animals with dermatitis	3	31	36
Total sections of control skin evaluated	48	50	49
Percent with dermatitis	6.3	62.0	73.5
Mean severity of lesion (b)	1.00	1.77	2.39
FEMALE			
Number of animals with dermatitis	10	41	44
Total sections of control skin evaluated	47	48	49
Percent with dermatitis	21.3	85.4	89.8
Mean severity of lesion (b)	1.10	2.05	2.39

(a) Week of termination: high dose males--week 105; high dose females--week 90; all other groups--week 105
(b) Severity: 1 = minimal; 2 = mild; 3 = moderate; 4 = marked

Liver, Marine Diesel Fuel: Hematopoiesis was observed at increased incidences in dosed female mice (Table 13). Hepatocellular adenomas and hepatocellular adenomas or carcinomas (combined) in male mice occurred with significant positive trends by the life table test, and the incidence of hepatocellular adenomas or carcinomas (combined) in the high dose group of male mice was significantly greater than those in the vehicle controls by the life table test (Table 20).

Liver, JP-5 Navy Fuel: Amyloid was found at increased incidences in high dose male and high dose female mice (Table 17).

Hematopoietic System and Multiple Organs, Marine Diesel Fuel: Increased incidences of splenic extramedullary hematopoiesis and plasmacytosis of the axillary lymph node in dosed mice of each sex and amyloidosis (of multiple organs) in dosed females were considered to be the consequence of severe dermatitis and ulceration of the skin (Table 13).

Hematopoietic System, JP-5 Navy Fuel: Malignant lymphomas in male mice occurred with a significant negative trend, and the incidence in the high dose group was significantly lower than that in the vehicle controls. The incidence of malignant lymphomas in low dose female mice was significantly greater than that in the vehicle controls (Table 21).

Urinary Bladder, Marine Diesel Fuel: The incidences of inflammatory infiltrates in the urinary bladder were increased in high dose males and dosed females (Table 13).

Kidney, Adrenal Cortex, Spleen, or Multiple Organs, JP-5 Navy Fuel: Amyloid was observed at increased incidences in the kidney, adrenal cortex, spleen, and multiple organs of high dose male mice and in the spleen, kidney, and multiple organs of high dose female mice (Table 17). The amyloid was generally of minimal to mild severity and was considered to be the consequence of the severe dermatitis and ulceration of the skin.

Bone Marrow, JP-5 Navy Fuel: Granulocytic hyperplasia was observed at an increased incidence in high dose mice (Table 17).

Axillary Lymph Node, JP-5 Navy Fuel: Hyperplasia was observed at an increased incidence in high dose female mice (Table 17).

TABLE 20. ANALYSIS OF HEPATOCELLULAR TUMORS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL

	Vehicle Control	250 mg/kg	500 mg/kg (a)
Adenoma			
Overall Rates	5/50 (10%)	10/48 (21%)	10/49 (20%)
Adjusted Rates	13.5%	26.1%	32.0%
Terminal Rates	3/30 (10%)	5/19 (26%)	7/26 (27%)
Week of First Observation	76	77	61
Life Table Tests	P=0.034	P=0.152	P=0.052
Incidental Tumor Tests	P=0.100	P=0.150	P=0.134
Carcinoma			
Overall Rates	5/50 (10%)	9/48 (19%)	5/49 (10%)
Hepatocellular Adenoma or Carcinoma (b)			
Overall Rates	9/50 (18%)	17/48 (35%)	14/49 (29%)
Adjusted Rates	23.5%	41.1%	46.3%
Terminal Rates	5/30 (17%)	8/19 (42%)	11/26 (42%)
Week of First Observation	66	67	61
Life Table Tests	P=0.035	P=0.080	P=0.048
Incidental Tumor Tests	P=0.162	P=0.071	P=0.134

(a) The terminal rates for these groups are based on the the number of animals alive when the studies were terminated at week 84. Life table analyses regarded week 84 as the end of study for all groups.
(b) There are no historical data for B6C3F$_1$ mice administered acetone by dermal application in NTP studies; historical incidence in untreated controls in NTP studies (mean ± SD): 540/1,784 (30% ± 8%).

TABLE 21. ANALYSIS OF MALIGNANT LYMPHOMAS IN MICE IN THE TWO-YEAR DERMAL STUDIES OF JP-5 NAVY FUEL

	Vehicle Control	250 mg/kg	500 mg/kg
MALE (a)			
Overall Rates	8/50 (16%)	3/50 (6%)	1/49 (2%)
Adjusted Rates	20.7%	8.3%	3.4%
Terminal Rates	6/36 (17%)	2/33 (6%)	0/28 (0%)
Week of First Observation	94	92	104
Life Table Tests	P=0.020N	P=0.132N	P=0.043N
Incidental Tumor Tests	P=0.008N	P=0.088N	P=0.027N
FEMALE (b)			
Overall Rates	7/48 (15%)	19/49 (39%)	(c) 5/47 (11%)
Adjusted Rates	14.6%	41.2%	20.3%
Terminal Rates	4/44 (9%)	12/33 (36%)	2/17 (12%)
Week of First Observation	88	85	76
Life Table Tests	P=0.064	P=0.004	P=0.270
Incidental Tumor Tests	P=0.551	P=0.010	P=0.347N

(a) There are no historical data for $B6C3F_1$ mice administered acetone by dermal application in NTP studies; historical incidence in untreated male controls in NTP studies (mean ± SD): 217/1,791 (12% ± 7%).
(b) There are no historical data for $B6C3F_1$ mice administered acetone by dermal application in NTP studies; historical incidence in untreated female controls in NTP studies (mean ± SD): 481/1,791 (27% ± 10%).
(c) The terminal rates for these groups are based on the the number of animals alive when the studies were terminated at week 84. Life table analyses regarded week 84 as the end of study for all groups.

IV. DISCUSSION AND CONCLUSIONS

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There was little toxicologic information to be gleaned from the short-term studies. Single-administration studies were performed with marine diesel fuel but not with JP-5 navy fuel, and no toxicity occurred. In the 14-day studies, marine diesel fuel was applied neat at 2,000-40,000 mg/kg in 0.025-0.50 ml but JP-5 navy fuel was given as a 95% ethanol mixture at doses of 5,000-40,000 mg/kg in 0.5 ml. For the 13-week studies, marine diesel fuel was applied at doses of 250-4,000 mg/kg in acetone, whereas JP-5 navy fuel was applied at doses of 500-8,000 mg/kg in acetone. Mortality occurred at the higher doses in each phase of the short-term studies, except for the single-administration studies. Although the doses selected for the 2-year studies were below those that produced deaths or body weight changes, in the 13-week studies there was a 100% incidence of dermatitis, graded (on a scale of 1-5) as 3 (mild) in the marine diesel fuel and 2 (slight) in the JP-5 navy fuel studies.

The frequency and duration of administration of the fuels to the skin proved to be excessive. The 5 days per week dosing regimen resulted in progressive and dose-related irritation, dermatitis, inflammation, and finally ulceration at the site of application, in the worst cases extending down each side in a saddle-shaped lesion. Chronic inflammation and acanthosis occurred in almost all the mice dosed with marine diesel fuel, and ulcers were present in about 50% of the low dose and 75% of the high dose groups. Dosing with JP-5 navy fuel resulted in a much lower incidence of chronic inflammation and half as many ulcers as in the marine diesel fuel-dosed mice.

Clinical observations prompted the decision to terminate the high dose groups of both sexes of mice dosed with marine diesel fuel at week 84 of exposure, and the high dose group of female mice dosed with JP-5 navy fuel at week 90. This action was taken to prevent the spread of possible infection and because of excessive irritation at the site of application. The remaining dose groups were carefully monitored and an aggressive moribund-kill program instituted, based on lack of body weight gain, animal sensitivity to application of the chemical, the degree of skin irritation, and ulcer formation.

Previous studies of petroleum hydrocarbons by the dermal route of application employed a dosing regimen of three times per week or fewer, and durations of dosing as short as 6 and up to 24 months (API, 1959; Doak et al., 1983; Gradiski et al., 1983; Holland et al., 1981). These studies evaluated the tumorigenic responses of industrial fuel oil, acid/earth refined naphthenic spindle oil, medicinal-grade oil, crude oil, synthetic petroleums, and natural petroleums in the mouse strains C3H, CFW, and CF1, Swiss mice, and C3Hf/Bd mice. In each of these studies, there were tumorigenic effects on the skin, as shown by the occurrence of squamous cell papillomas, squamous cell carcinomas, and other tumors of the integumentary system.

Holland et al. (1981) did not observe significant differences when skin tumor data were analyzed separately for each sex and thus reported estimations and comparisons on pooled data. They concluded that three synthetic petroleums were capable of inducing skin neoplasms within a 2-year exposure period and that under comparable exposure conditions a composite sample of five natural petroleums was noncarcinogenic.

Several other mouse skin studies were performed at the Kettering Laboratory, University of Cincinnati, under the contract sponsorship of the American Petroleum Institute (MacFarland et al., 1982). Data from one of those studies indicated that a variety of petroleum hydrocarbons induced skin tumorigenicity in male C3H mice, including crude oils, aromatic fractions, and coal tar (Stemmer and Barkley, 1982). The importance of the vehicle solvent on the latency period of tumor induction and the types of developing tumors was emphasized. Coal tar application resulted in the appearance of squamous cell carcinomas with the shortest latency period ever recorded at the Kettering Laboratory.

Lewis et al. (1982) found that crude oil fractions were moderately carcinogenic, that distillate fractions boiling below 120° F or above 1,070° F were inactive, that all fractions boiling between 120° F and 700° F showed low carcinogenic activity, and that the fraction boiling between 700° F and 1,070° F was potently carcinogenic. These studies used male C3H mice and 50 mg

undiluted materials applied twice a week for a minimum of 18 months.

The carcinogenic potencies of crude oils and hydrotreated shale oils were compared in studies performed at Kettering Laboratory in which South Louisiana and Kuwait crude oils were applied twice per week for 80 weeks and animals were observed for another 40 weeks. Other studies sponsored by the Department of Energy were conducted at Los Alamos National Laboratories in which mice were dosed three times per week with oil or shale diluted in mixtures of cyclohexane:acetone (30:70) for 78 weeks and observed 22 more weeks (Coomes and Hazer, 1982). Analyses of these studies indicated that crude oils exhibited a broad range of carcinogenic potencies and that hydrotreatment reduced the carcinogenic potency of raw shale oil, which was more potent than the crude oils. Each of these studies reviewed above also used benzo(a)pyrene-dosed mice as positive controls.

In the present studies, a large percentage of vehicle control mice dosed with the acetone vehicle were diagnosed as having skin lesions, characterized as chronic dermatitis and consisting of acanthosis, hyperkeratosis, and in some instances necrosis and ulceration of the overlying epidermis. Dermal changes frequently included fibrosis, increased amounts of melanin, and the presence of acute and chronic inflammatory cell infiltrates. The percentage of vehicle controls with dermatitis varied widely, the range being 6.0%-52.0% (see Tables 14, 15, 18, and 19). Despite this variance, there was at least a twofold increase in the incidence of dermatitis in mice dosed with marine diesel fuel or JP-5 navy fuel in acetone and a dose-related, proportional increase in the severity of the lesions, which was twofold to threefold greater in dosed groups compared with vehicle controls.

There was also an increase in the incidence of dermatitis in the untreated, inguinal skin region caused by migration of JP-5 navy fuel and marine diesel fuel after application. The incidences of these lesions in the inguinal skin site were twofold to threefold greater in groups dosed with JP-5 navy fuel compared with those in groups dosed with marine diesel fuel, and although the degree of severity of the lesions was proportional to dose in the JP-5 navy fuel groups, there were no differences in severity as a result of dosing with marine diesel fuel.

In this report, the incidence of squamous cell tumors is divided between the site of application and the inguinal skin site, between papillomas and carcinomas, and between sexes. The dermal studies reviewed above reported lists of skin tumors resulting from exposure to various mixtures of petroleum hydrocarbons irrespective of site of application, type, and in some instances sex (API, 1959; Doak et al., 1983; Gradiski et al., 1983; Holland et al., 1981; Bingham et al., 1979). Consolidating the neoplastic skin lesions in the present studies by this procedure yields results comparable to those of other petroleum hydrocarbon dermal studies (Table 22).

There was no particular association between the presence of ulcers and the incidence of squamous cell papillomas or carcinomas, irrespective of whether tumors occurred at the site of application or the inguinal site. Of all mice dosed with marine diesel fuel, 51%-73% of each group exhibited skin ulcers at the site of application; only five of these animals had tumors at the same site. Of the seven mice with squamous cell carcinomas, there were five with ulcers and two without ulcers; in the two mice with squamous cell papillomas, one occurred with an ulcer and the other without an ulcer.

The historical incidences of squamous cell papillomas (0.1%-0.2%) or squamous cell carcinomas (0.3%) in untreated male and female control $B6C3F_1$ mice are negligible, based on 1,791 male and 1,791 female mice examined grossly. When the integumentary system is considered as a whole, there were more sarcomas in male than in female mice but no sex differences in the incidences of squamous cell tumors, basal cell neoplasms, keratoacanthomas, or lipomas in those untreated control mice (Haseman et al., 1984a).

Seven NTP dermal studies--on tetrachlorodibenzodioxin (TCDD), 2-chloroethanol, hamamelis water, hexachlorodibenzodioxin, selenium sulfide, Selsun®, and TCDD plus dimethylbenz(a)anthracene (DMBA)--were reviewed by Haseman et al. (1984b). These studies used a variety of mouse strains, including $B6C3F_1$, Swiss-Webster, Swiss CD-1, and ICR Swiss, and employed a dose regimen of three times per

TABLE 22. INCIDENCES OF SKIN TUMORS IN MICE IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL AND JP-5 NAVY FUEL

	Marine Diesel Fuel			JP-5 Navy Fuel		
	Vehicle Control	250 mg/kg	500 mg/kg	Vehicle Control	250 mg/kg	500 mg/kg
MALE						
Tumors observed at site of application						
Squamous cell papilloma	(a) 0/49	0/49	1/49	0/48	0/50	0/49
Squamous cell carcinoma	0/49	0/49	2/49	0/48	0/50	0/49
Tumors observed at inguinal skin site (b)						
Squamous cell papilloma	1/50	0/49	0/50	0/50	(c) 1/50	0/49
Squamous cell carcinoma	0/50	2/49	0/50	0/50	(d) 0/50	1/49
Total papillomas and carcinomas, site of application and inguinal skin						
	1	2	3	0	1	1
FEMALE						
Tumors observed at site of application						
Squamous cell papilloma	0/50	0/45	0/48	0/48	0/48	0/47
Squamous cell carcinoma	0/50	1/45	2/48	0/48	0/48	0/47
Tumors observed at inguinal skin site (b)						
Squamous cell papilloma	0/50	0/45	0/50	0/48	0/49	0/47
Squamous cell carcinoma	0/50	0/45	0/50	0/48	0/49	1/47
Total papillomas and carcinomas, site of application and inguinal skin						
	0	1	2	0	0	1
MALE AND FEMALE						
Total papillomas and carcinomas, site of application and inguinal skin						
	1	3	5	0	1	2

(a) Number of tumors found/number of animals examined
(b) Adjacent skin site to which dose mixture migrated after application
(c) Papillioma, NOS
(d) An undifferentiated carcinoma was observed.

week, except for hamamelis water, which was applied five times per week. Of these studies, five were negative, one was judged inadequate, and TCDD was found to be equivocal in male mice and positive in female mice, inducing fibrosarcomas of the integumentary system.

Another consistent response to dermal application of these two fuels was an increase in the percentage of female mice undergoing lactogenesis proportional to dose of JP-5 navy fuel or marine diesel fuel. This response was evident at both the site of application and inguinal skin and was independent of the incidence of dermatitis. Lactogenesis was characterized by the presence of abundant secretory material within individual mammary gland acini and by increased height and number of secretory cells in the individual glands. There were galactoceles in a few of the mice that had been dosed with JP-5 navy fuel. This response has not been reported in the literature and might serve as a sensitive endpoint for petroleum hydrocarbon exposure in females. Because of the conditions of these studies, early death, toxicity, and migration of the chemical beyond the site of application, it is uncertain whether lactogenesis represents a local or systemic response to petroleum hydrocarbons or whether these fuels affected the secretion, delivery, or mechanism of action of the family of hormones involved in the process of lactogenesis.

Nephrotoxicity was the other nonneoplastic lesion reported in C3Hf/Bd mice after dermal application of marine diesel fuel or JP-5 navy fuel (Easley et al., 1982). The nature of the lesions (atrophied and degenerating nephrons and papillary necrosis) supported the premise that chronic ischemia had occurred. In that study, marine diesel fuel caused more severe nephrotoxicity, and female mice were affected preferentially. Nephrotoxicity was not observed in the present studies. Renal papillary necrosis was rarely seen in females (vehicle control, 0/50; low dose, 2/50; high dose, 1/50) or males (vehicle control, 0/48; low dose, 1/48; high dose, 0/49) after dosing with marine diesel fuel. After dosing with JP-5 navy fuel, the incidence of papillary necrosis in males (vehicle control, 0/50; low dose, 0/49; high dose, 5/50) or females (vehicle control, 0/48; low dose, 0/49; high dose, 2/50) was associated with a high incidence of renal amyloidosis. Amyloid, an immune complex deposition seen in the glomerular tufts, cortical interstitium, and papillus, was observed microscopically in male mice (vehicle control, 3/50; low dose, 2/49; high dose, 23/50) and female mice (vehicle control, 0/48; low dose, 1/49; high dose, 12/50). The presence of amyloid suggested a chronic antigenic stimulation by the mice in response to the dermal ulcerations at the site of application. There were only two renal neoplasms, a tubular cell adenocarcinoma in a male vehicle control and a tubular cell adenoma in a low dose male that had been dosed dermally with JP-5 navy fuel, and none in mice dosed with marine diesel fuel.

Unleaded gasoline vapor did induce kidney tumors in F344 rats and $B6C3F_1$ mice after inhalation exposure for 6 hours per day, 5 days per week for 103-113 weeks (MacFarland et al., 1984). This study began with 100 animals per sex, species, and dose group, but 40 animals per dose group were killed for examination before study termination. Final death rates were not given; statistical considerations included life table adjustments.

Renal carcinomas or sarcomas occurred in a dose-related fashion in male rats exposed to gasoline at 67, 292, or 2,056 ppm; there was one renal sarcoma in a female rat from the intermediate dose group (MacFarland et al., 1984). The incidences of renal carcinomas or adenomas (combined) were 0, 1, 4, and 7 in the control, low, medium, and high dose groups of male rats. In female mice, there were dose-related increases in the incidences of hepatocellular neoplasms and also two renal tumors in the high dose group. The incidences of hepatocellular neoplasms in female mice were 14%, 19%, 21%, and 48% in the control, low, medium, and high dose groups. Some hepatocellular neoplasms in male and female mice metastasized to the lungs.

The present studies reported actual and survival-adjusted incidences of hepatocellular adenomas and adenomas or carcinomas (combined) in male mice dosed with marine diesel fuel. These results are not interpreted to be of biologic significance, even though there were positive trends based on the life table tests. It is doubtful whether these neoplasms were responsible for early deaths; moreover, there was only one instance where a marginally significant incidence

(P=0.048) in adenomas or carcinomas (combined) was greater than that in vehicle controls; this result occurred when life table analysis was used, an analytic method that presumes these tumors were directly or indirectly the cause of death. The overall incidence of hepatocellular adenomas or carcinomas (combined) was 18% in the vehicle controls, compared with the historical rate of hepatocellular adenomas or carcinomas (combined) of 30% in untreated control male $B6C3F_1$ mice.

The incidence of malignant lymphomas was increased in low dose female mice in the JP-5 navy fuel study. However, the increased incidence is not regarded as biologically significant, since the incidence in the high dose group was not increased and in male mice there were negative trends. The incidence in the low dose group of female mice (39%) was above the mean of historical untreated control incidences reported for lymphomas (27%) and within the reported range (10%-62%) in untreated control female $B6C3F_1$ mice.

The negative NTP results obtained for mutagenicity in Salmonella are consistent with those reported by others for both marine diesel fuel and JP-5 navy fuel (Litton, 1978, 1981). However, in a Hazleton study (1979), another aviation fuel, jet fuel A, was reported to be mutagenic in the mouse lymphoma cell assay. This fuel was not mutagenic in a mouse dominant lethal assay conducted by Litton Bionetics, Inc. (1980). Both jet fuel A and marine diesel fuel were reported to induce bone marrow cytogenetic effects in rats (Hazleton, 1979; Litton, 1978, 1981). Therefore, these fuels showed some evidence of genetic toxicity in eukaryotic cells but were uniformly negative in prokaryotic organisms.

The experimental and tabulated data for the NTP Technical Report on marine diesel fuel and JP-5 navy fuel were examined for accuracy, consistency, and compliance with Good Laboratory Practice requirements. As summarized in Appendix S, the audit revealed no major problems with the conduct of the studies or with the collection and documentation of the experimental data. No discrepancies were found that influenced the final interpretation of the results of these studies.

Conclusions: Under the conditions of these 2-year dermal studies, marine diesel fuel at doses of 250 and 500 mg/kg resulted in dose-related increased incidences of squamous cell neoplasms of the skin (primarily carcinomas), providing *equivocal evidence of carcinogenicity** for male and female $B6C3F_1$ mice. The sensitivity for detecting systemic carcinogenicity in female mice dosed with marine diesel fuel was reduced by poor survival. Under the conditions of these 2-year dermal studies, JP-5 navy fuel at doses of 250 and 500 mg/kg provided *no evidence of carcinogenicity* for male and female $B6C3F_1$ mice.

*Categories of evidence of carcinogenicity are defined in the Note to the Reader on page 2. The public discussion regarding the interpretative conclusions is summarized on pages 14-15.

V. REFERENCES

V. REFERENCES

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APPENDIX A

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	50
INTEGUMENTARY SYSTEM			
#Skin paint site	(49)	(49)	(49)
Squamous cell papilloma			1 (2%)
Squamous cell carcinoma			2 (4%)
Sarcoma, NOS		1 (2%)	
Fibrosarcoma	1 (2%)	1 (2%)	1 (2%)
Fibrosarcoma, invasive			1 (2%)
*Skin	(50)	(49)	(50)
Squamous cell papilloma	1 (2%)		
Squamous cell carcinoma		2 (4%)	
*Subcutaneous tissue	(50)	(49)	(50)
Fibroma	3 (6%)		
Fibrosarcoma	10 (20%)	4 (8%)	2 (4%)
RESPIRATORY SYSTEM			
#Lung	(50)	(49)	(49)
Hepatocellular carcinoma, metastatic	1 (2%)		
Alveolar/bronchiolar adenoma	4 (8%)	5 (10%)	2 (4%)
Alveolar/bronchiolar carcinoma		2 (4%)	
HEMATOPOIETIC SYSTEM			
*Multiple organs	(50)	(49)	(50)
Malignant lymphoma, NOS	5 (10%)	4 (8%)	
Malignant lymphoma, histiocytic type		1 (2%)	
#Lymph node	(42)	(42)	(40)
Fibrosarcoma, metastatic			1 (3%)
#Inguinal lymph node	(42)	(42)	(40)
Fibrosarcoma, metastatic	1 (2%)		
#Liver	(50)	(48)	(49)
Malignant lymphoma, NOS			1 (2%)
CIRCULATORY SYSTEM			
#Liver	(50)	(48)	(49)
Hemangioma	2 (4%)		
Hemangiosarcoma	2 (4%)	2 (4%)	2 (4%)
DIGESTIVE SYSTEM			
#Liver	(50)	(48)	(49)
Hepatocellular adenoma	5 (10%)	10 (21%)	10 (20%)
Hepatocellular carcinoma	5 (10%)	9 (19%)	5 (10%)
#Forestomach	(48)	(46)	(49)
Squamous cell papilloma		2 (4%)	
#Cecum	(49)	(47)	(49)
Adenocarcinoma, NOS	1 (2%)		
*Rectum	(50)	(49)	(50)
Adenocarcinoma, NOS	1 (2%)		
*Intramuscular anal gland	(50)	(49)	(50)
Cystadenoma, NOS	1 (2%)		

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
URINARY SYSTEM			
#Kidney	(50)	(48)	(49)
Fibrosarcoma, metastatic		1 (2%)	
ENDOCRINE SYSTEM			
#Pituitary intermedia	(48)	(45)	(45)
Adenoma, NOS	1 (2%)		
#Adrenal	(49)	(48)	(49)
Pheochromocytoma	3 (6%)		
#Adrenal/capsule	(49)	(48)	(49)
Adenoma, NOS	1 (2%)		
#Thyroid	(47)	(46)	(44)
Follicular cell adenoma	1 (2%)		
REPRODUCTIVE SYSTEM			
None			
NERVOUS SYSTEM			
None			
SPECIAL SENSE ORGANS			
*Harderian gland	(50)	(49)	(50)
Adenoma, NOS	3 (6%)	1 (2%)	
MUSCULOSKELETAL SYSTEM			
None			
BODY CAVITIES			
*Mesentery	(50)	(49)	(50)
Hepatocellular carcinoma, invasive		1 (2%)	
ALL OTHER SYSTEMS			
None			
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Natural death	13	14	5
Moribund sacrifice	6	14	19
Scheduled sacrifice		2	26
Terminal sacrifice	30	18	
Accidentally killed, nda	1	1	
Animal missexed		1	

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
Total animals with primary tumors**	30	31	19
Total primary tumors	50	44	26
Total animals with benign tumors	16	17	10
Total benign tumors	25	18	13
Total animals with malignant tumors	22	22	12
Total malignant tumors	25	26	13
Total animals with secondary tumors##	2	2	2
Total secondary tumors	2	2	2

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

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
#Skin paint site	(50)	(50)	(48)
Squamous cell carcinoma		1 (2%)	2 (4%)
*Subcutaneous tissue	(50)	(50)	(50)
Sarcoma, NOS	1 (2%)		
Neurofibrosarcoma		1 (2%)	
Fibrosarcoma	2 (4%)		1 (2%)
RESPIRATORY SYSTEM			
#Lung	(50)	(50)	(50)
Adenocarcinoma, NOS, metastatic	1 (2%)		
Alveolar/bronchiolar adenoma			1 (2%)
Alveolar/bronchiolar carcinoma		1 (2%)	
HEMATOPOIETIC SYSTEM			
*Multiple organs	(50)	(50)	(50)
Malignant lymphoma, NOS	8 (16%)	3 (6%)	3 (6%)
Malignant lymphoma, histiocytic type	2 (4%)		1 (2%)
Malignant lymphoma, mixed type	2 (4%)		
#Spleen	(50)	(49)	(50)
Malignant lymphoma, NOS	1 (2%)		
#Mesenteric lymph node	(50)	(43)	(44)
Malignant lymphoma, NOS		1 (2%)	
#Axillary lymph node	(50)	(43)	(44)
Malignant lymphoma, NOS			1 (2%)
#Liver	(50)	(50)	(50)
Malignant lymphoma, NOS	1 (2%)		
CIRCULATORY SYSTEM			
#Spleen	(50)	(49)	(50)
Hemangiosarcoma	1 (2%)		
#Liver	(50)	(50)	(50)
Hemangiosarcoma	2 (4%)		
DIGESTIVE SYSTEM			
#Liver	(50)	(50)	(50)
Hepatocellular adenoma	4 (8%)	2 (4%)	2 (4%)
Hepatocellular carcinoma		2 (4%)	3 (6%)
#Forestomach	(49)	(46)	(50)
Squamous cell papilloma	2 (4%)	1 (2%)	
#Pylorus	(49)	(46)	(50)
Adenomatous polyp, NOS			1 (2%)
#Cecum	(50)	(41)	(48)
Leiomyoma	1 (2%)		
URINARY SYSTEM			
None			

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#Anterior pituitary	(49)	(48)	(46)
Adenoma, NOS	5 (10%)	2 (4%)	1 (2%)
#Adrenal/capsule	(50)	(49)	(50)
Adenoma, NOS		1 (2%)	
#Pancreatic islets	(50)	(48)	(50)
Islet cell adenoma	1 (2%)		
REPRODUCTIVE SYSTEM			
*Mammary gland	(50)	(50)	(50)
Adenoma, NOS		1 (2%)	
Adenocarcinoma, NOS	1 (2%)		
#Uterus	(50)	(50)	(50)
Endometrial stromal polyp	3 (6%)		
#Cervix uteri	(50)	(50)	(50)
Leiomyosarcoma			1 (2%)
#Uterus/endometrium	(50)	(50)	(50)
Adenocarcinoma, NOS	1 (2%)		
#Ovary	(50)	(47)	(49)
Papillary cystadenoma, NOS		1 (2%)	
Granulosa cell tumor		1 (2%)	
NERVOUS SYSTEM			
None			
SPECIAL SENSE ORGANS			
*Harderian gland	(50)	(50)	(50)
Adenoma, NOS	1 (2%)		
MUSCULOSKELETAL SYSTEM			
None			
BODY CAVITIES			
None			
ALL OTHER SYSTEMS			
*Multiple organs	(50)	(50)	(50)
Fibrosarcoma, metastatic	1 (2%)		
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Natural death	5	19	8
Moribund sacrifice	5	18	12
Scheduled sacrifice			29
Terminal sacrifice	40	12	
Accidentally killed, nda		1	1

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
Total animals with primary tumors**	29	14	16
Total primary tumors	39	18	17
Total animals with benign tumors	16	6	5
Total benign tumors	17	8	5
Total animals with malignant tumors	20	8	11
Total malignant tumors	22	9	12
Total animals with secondary tumors##	2		
Total secondary tumors	2		
Total animals with tumors uncertain--benign or malignant		1	
Total uncertain tumors		1	

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

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL: VEHICLE CONTROL

ANIMAL NUMBER	04611	04811	04814	04837	04841	04840	04813	04842	04825	04838	04919	04932	04916	04923	04904	04943	04949	04907	04908	04901	04902	04903	04905	04906
WEEKS ON STUDY	01100	01808	03832	03833	03836	03838	04847	05959	06863	06606	07070	07474	07676	07878	09090	09898	09898	09898	10101	10108	10105	10205	10305	10505
INTEGUMENTARY SYSTEM																								
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
Fibrosarcoma																								
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																								
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																								
Fibrosarcoma											X		X	X	X	X	X		X					
RESPIRATORY SYSTEM																								
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic																			X					
Alveolar/bronchiolar adenoma												X												
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																								
Bone marrow	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	−	−	+	+	−	−	+	−	−	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma, metastatic																X								
Thymus	−	+	+	+	−	−	−	+	+	−	+	+	+	−	−	−	+	+	+	+	+	+	−	+
CIRCULATORY SYSTEM																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																								
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma												X								X				
Hepatocellular carcinoma										X									X	X				
Hemangioma															X									
Hemangiosarcoma																					X		X	
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	−	−	+	+	−	−	+	+	−	−	+	+	+	+	+	+	+	−	+	+	+	+	+	+
Large intestine	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																								
Rectum	N	N	N	N	N	N	N	N	N	N	N	N	N	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																					X			
Cystadenoma, NOS																							X	
URINARY SYSTEM																								
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																								
Pituitary	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																							X	
Adrenal	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																							X	
Pheochromocytoma												X												
Thyroid	+	+	+	+	+	−	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+
Follicular cell adenoma																								
Parathyroid	−	−	+	−	−	−	+	+	−	−	+	+	−	+	+	−	−	+	−	+	+	+	−	+
REPRODUCTIVE SYSTEM																								
Mammary gland	N	N	N	N	+	N	N	N	N	N	+	N	N	N	N	+	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																								
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																								
ALL OTHER SYSTEMS																								
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, NOS																					X			X

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

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: VEHICLE CONTROL (Continued)

ANIMAL NUMBER	0009	0010	0012	0015	0017	0018	0020	0021	0022	0024	0026	0027	0028	0029	0030	0031	0033	0034	0035	0036	0039	0044	0045	0047	0050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibrosarcoma					X																					1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Squamous cell papilloma											X															1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroma					X											X	X									3
Fibrosarcoma	X						X											X								10
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic																										1
Alveolar/bronchiolar adenoma									X								X	X								4
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Fibrosarcoma, metastatic																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	41
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma									X						X										X	5
Hepatocellular carcinoma											X						X									5
Hemangioma																		X								2
Hemangiosarcoma																										2
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, NOS																X										1
Rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenocarcinoma, NOS																										1
Cystadenoma, NOS																										1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma, NOS																										1
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma, NOS																										1
Pheochromocytoma											X						X									3
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Follicular cell adenoma																	X									1
Parathyroid	+	+	+	+	−	−	+	+	−	+	−	+	−	+	+	+	−	+	−	−	+	+	+	+	+	30
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenoma, NOS			X				X														X					3
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malignant lymphoma, NOS		X																X	X							5

* Animals necropsied

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL: LOW DOSE

ANIMAL NUMBER	03 2	01 6	02 9	03 5	04 8	04 7	00 8	03 1	03 4	04 1	01 3	00 9	00 7	00 1	00 3	03 7	01 5	01 7	01 1	03 9	00 2	03 0	03 6	00 6	01 2
WEEKS ON STUDY	00 3	01 6	03 8	04 0	05 4	08 7	07 2	07 7	07 7	07 7	08 1	08 2	08 5	08 6	08 7	08 7	08 9	08 9	09 1	09 2	09 4	09 4	09 4	09 8	09 9
INTEGUMENTARY SYSTEM																									
Skin paint site	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																									
Fibrosarcoma																									
Skin	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Subcutaneous tissue	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																				X			X		
RESPIRATORY SYSTEM																									
Lungs and bronchi	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma								X											X						
Alveolar/bronchiolar carcinoma														X											
Trachea	S	+	+	+	+	−	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	S	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	−	+	+	+	+
Spleen	S	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
Lymph nodes	S	+	−	−	+	+	−	+	−	−	+	+	+	+	−	+	+	+	−	+	+	+	+	+	+
Thymus	S	−	+	−	−	−	+	−	−	+	−	+	+	−	−	−	+	+	−	+	+	+	−	+	+
CIRCULATORY SYSTEM																									
Heart	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	S	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+
Liver	S	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma										X							X							X	
Hepatocellular carcinoma						X					X	X										X			
Hemangiosarcoma																X									
Bile duct	S	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	S	+	+	+	N	N	+	+	N	+	N	+	+	N	N	N	N	+	+	+	+	+	+	+	+
Pancreas	S	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
Esophagus	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	S	+	+	+	+	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																						X			
Small intestine	S	+	+	+	+	−	+	+	−	+	+	−	+	−	−	+	+	+	+	+	+	+	+	+	+
Large intestine	S	+	+	+	+	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	S	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma, metastatic																				X					
Urinary bladder	S	+	+	+	+	−	+	+	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	S	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal	S	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
Thyroid	S	+	+	+	−	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+
Parathyroid	S	+	+	−	−	−	−	−	−	+	−	−	−	−	−	+	+	+	+	−	−	−	−	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	S	+	N	+	N	+	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	+	N	N
Testis	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	S	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Harderian gland	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																									
BODY CAVITIES																									
Mesentery	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Hepatocellular carcinoma, invasive																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, NOS																	X				X	X			
Malig. lymphoma, histiocytic type																		X							

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

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

ANIMAL NUMBER	0 1 4	0 2 6	0 1 8	0 4 9	0 3 3	0 3 8	0 0 4	0 0 5	0 1 0	0 1 9	0 2 0	0 2 1	0 2 2	0 2 3	0 2 4	0 2 5	0 2 7	0 2 8	0 4 0	0 4 2	0 4 3	0 4 4	0 4 5	0 4 6	0 5 0	TOTAL:
WEEKS ON STUDY	0 9 9	0 9 9	1 0 1	1 0 1	1 0 2	1 0 4	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	TISSUES / TUMORS
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sarcoma, NOS		X																								1
Fibrosarcoma								X																		1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*49
Squamous cell carcinoma			X							X																2
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*49
Fibrosarcoma	X							X																		4
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma								X		X								X								5
Alveolar/bronchiolar carcinoma						X																				2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	48
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	42
Thymus	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	35
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Hepatocellular adenoma			X			X			X							X			X		X				X	10
Hepatocellular carcinoma						X	X		X					X				X								9
Hemangiosarcoma									X																	2
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*49
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Squamous cell papilloma																		X								2
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
Kidney	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Fibrosarcoma, metastatic																										1
Urinary bladder	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ENDOCRINE SYSTEM																										
Pituitary	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	45
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Parathyroid	-	+	-	+	-	-	+	-	+	+	+	+	+	+	+	+	+	-	+	+	-	-	+	+	+	26
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	*49
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Adenoma, NOS													X													1
BODY CAVITIES																										
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Hepatocellular carcinoma, invasive																		X								1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Malignant lymphoma, NOS				X																						4
Malig. lymphoma, histiocytic type																										1

* Animals necropsied

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL: HIGH DOSE

ANIMAL NUMBER	01 18	02 21	02 25	04 42	04 45	01 14	00 02	03 34	01 17	00 03	00 07	00 09	01 10	01 11	01 19	02 22	04 40	02 20	02 23	03 01	00 01	00 08	01 16	03 36	00 04
WEEKS ON STUDY	00 05	03 77	03 77	05 54	05 54	05 55	06 61	06 61	06 65	07 70	07 70	07 70	07 70	07 70	07 70	07 11	07 72	07 74	07 75	07 75	07 78	07 78	08 80	08 33	08 84
INTEGUMENTARY SYSTEM																									
Skin paint site	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Firosarcoma												X													
Fibrosarcoma, invasive						X																			
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma						X								X											
RESPIRATORY SYSTEM																									
Lungs and bronchi	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Trachea	−	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
Spleen	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	−	−	−	+	−	+	−	+	−	+	+	+	+	−	+	+	+	+	+	−	−	+	−	+	+
Fibrosarcoma, metastatic												X													
Thymus	−	+	+	−	+	+	+	+	−	+	+	−	+	+	+	−	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	−	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+
Liver	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma								X	X			X													
Hepatocellular carcinoma																									
Hemangiosarcoma																X									
Malignant lymphoma, NOS																									
Bile duct	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	−	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	−	+	+	+	+	+	+	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid	−	+	+	+	+	+	+	+	−	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	−	+	+	−	+	−	−	+	−	−	−	+	−	−	+	+	−	+	−	−	−	−	−	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

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

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

ANIMAL NUMBER	00 05	00 06	01 12	01 13	01 15	02 24	02 26	02 27	02 28	02 29	03 31	03 32	03 33	03 35	03 37	03 38	03 39	04 41	04 43	04 44	04 46	04 47	04 48	04 49	05 50	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	08 4	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Squamous cell papilloma																	X									1
Squamous cell carcinoma	X																							X		2
Fibrosarcoma																										1
Fibrosarcoma, invasive																										1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibrosarcoma																										2
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma									X	X																2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	40
Fibrosarcoma, metastatic																										1
Thymus	+	+	+	+	−	+	+	+	−	+	+	−	+	+	+	+	+	+	−	+	−	+	+	+	+	40
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular adenoma							X		X	X						X	X	X						X		10
Hepatocellular carcinoma							X	X			X								X	X						5
Hemangiosarcoma	X																									2
Malignant lymphoma, NOS													X													1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder & common bile duct	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	45
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thyroid	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	44
Parathyroid	−	+	−	+	−	+	+	+	+	−	+	+	+	+	+	+	−	−	+	+	+	+	−	+	−	27
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49

*Animals necropsied

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL: VEHICLE CONTROL

ANIMAL NUMBER	0004	0050	0043	0049	0033	0016	0028	0027	0019	0013	0001	0002	0003	0005	0006	0007	0008	0009	0010	0011	0012	0014	0015	0017	0018
WEEKS ON STUDY	018	070	089	092	094	097	100	101	102	104	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
INTEGUMENTARY SYSTEM																									
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS								X																	
Fibrosarcoma																									X
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic					X																				
Trachea	−	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−
Hemangiosarcoma																									
Malignant lymphoma, NOS																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma															X										X
Hemangiosarcoma																									
Malignant lymphoma, NOS																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma												X								X					
Small intestine	+	+	+	+	+	−	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyoma																									
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+
Adenoma, NOS					X							X									X	X			
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid	−	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	−	−	+	−	−	+	−	−	−	+	+	+	+	−	+	+	+	+	+	−	+	+	−	−	−
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																		X							
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS					X																				
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Endometrial stromal polyp									X				X				X								
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Fibrosarcoma, metastatic																									
Malignant lymphoma, NOS						X	X																		
Malig. lymphoma, histiocytic type																									
Malignant lymphoma, mixed type																									

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

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: VEHICLE CONTROL (Continued)

ANIMAL NUMBER	020	021	022	023	024	025	026	029	030	031	032	034	035	036	037	038	039	040	041	042	044	045	046	047	048	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS																										1
Fibrosarcoma					X																					2
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, NOS, metastatic																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+		47
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma													X													1
Malignant lymphoma, NOS															X											1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	46
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma															X					X						4
Hemangiosarcoma									X				X													2
Malignant lymphoma, NOS								X																		1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Squamous cell papilloma																										2
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyoma												X														1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma, NOS							X																			5
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	47
Parathyroid	+	+	+	+	+	+	–	–	+	–	–	+	–	+	+	+	+	+	+	+	+	–	–	+	–	30
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islet cell adenoma																										1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenocarcinoma, NOS																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, NOS												X														1
Endometrial stromal polyp																										3
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenoma, NOS																								X		1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Fibrosarcoma, metastatic					X																					1
Malignant lymphoma, NOS		X															X		X				X	X	X	8
Malig. lymphoma, histiocytic type							X					X														2
Malignant lymphoma, mixed type													X							X						2

* Animals necropsied

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL: LOW DOSE

ANIMAL NUMBER	02121	02223	02424	02525	00303	02828	01111	04505	00101	04404	04808	01414	01313	03404	01909	01505	04303	03505	04707	01212	00006	00808	00404	03232
WEEKS ON STUDY	00000	00000	00000	00000	00004	01818	05212	06787	06868	06868	06809	07701	07701	07711	07722	07744	07746	07768	07788	07780	08800	08801	08811	08181
INTEGUMENTARY SYSTEM																								
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																								
Subcutaneous tissue	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neurofibrosarcoma																							X	
RESPIRATORY SYSTEM																								
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma														X										
Trachea	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																								
Bone marrow	−	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	−	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	−	+
Malignant lymphoma, NOS																								
Thymus	+	+	+	+	−	+	+	+	−	+	+	−	+	+	+	+	−	+	−	+	+	−	−	+	−
CIRCULATORY SYSTEM																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																								
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																								
Hepatocellular carcinoma																								
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	+	+	N	+	+	+	N	+	+	N	+	+	+	+	N	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																								
Small intestine	−	−	+	−	−	+	−	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+
Large intestine	−	+	−	+	+	−	−	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																								
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	−	−	−	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																								
Pituitary	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																								
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+
Adenoma, NOS																						X		
Thyroid	−	−	+	+	+	+	+	−	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
Parathyroid	−	−	−	+	+	+	−	−	−	+	+	−	+	−	−	−	+	−	−	−	−	−	−	+
REPRODUCTIVE SYSTEM																								
Mammary gland	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	N	+	+
Adenoma, NOS																								
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papillary cystadenoma, NOS																								
Granulosa cell tumor																								
NERVOUS SYSTEM																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																								
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, NOS																							X	

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

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

ANIMAL NUMBER	0037	0039	0038	0029	0030	0031	0118	0117	0002	0033	0041	0026	0049	0005	0007	0009	0010	0016	0020	0027	0038	0040	0042	0046	0050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	0081	0083	0084	0086	0089	0090	0091	0092	0094	0095	0099	1001	1003	1005	1005	1005	1005	1005	1005	1005	1005	1005	1005	1005	1005	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma													X													1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Neurofibrosarcoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Spleen	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph nodes	−	+	+	+	+	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Malignant lymphoma, NOS									X																	1
Thymus	−	−	+	+	−	+	−	+	+	−	−	−	+	+	−	+	+	−	+	+	+	+	+	−	+	32
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma														X							X					2
Hepatocellular carcinoma						X		X																		2
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	N	N	N	N	+	+	+	+	+	+	N	N	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	−	+	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Squamous cell papilloma							X																			1
Small intestine	−	−	−	+	−	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	37
Large intestine	−	−	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	41
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	−	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	43
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	48
Adenoma, NOS																X			X							2
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma, NOS																										1
Thyroid	−	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	44
Parathyroid	−	−	+	+	−	−	+	+	−	−	−	−	+	−	+	+	+	+	+	+	−	+	+	−	+	22
REPRODUCTIVE SYSTEM																										
Mammary gland	N	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	N	+	+	*50
Adenoma, NOS														X												1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Ovary	−	+	+	+	+	+	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	47
Papillary cystadenoma, NOS														X												1
Granulosa cell tumor								X																		1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malignant lymphoma, NOS			X								X															3

* Animals necropsied

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL: HIGH DOSE

ANIMAL NUMBER	037	005	002	015	016	018	019	038	044	048	023	006	008	032	050	047	041	014	013	040	001	003	004	007	009
WEEKS ON STUDY	012	032	034	034	040	040	040	051	054	059	067	069	071	074	074	076	078	079	080	080	081	084	084	084	084
INTEGUMENTARY SYSTEM																									
Skin paint site	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+
Squamous cell carcinoma															X										
Fibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Trachea	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	−	+	−	+	−	+	+	−	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+
Malignant lymphoma, NOS																									
Thymus	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	−	+	−
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	−	+	+	+	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																X			X						
Hepatocellular carcinoma																							X		
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS																					X				
Small intestine	+	−	+	−	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	−	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	+	+	−	−	−	−	−	−	+	+	+	−	+	+	+	−	−	−	−	−	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	N	+	N	+	+	+	+	+	N	+	+	+	N	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, NOS		X																		X					
Malig. lymphoma, histiocytic type																									

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

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

ANIMAL NUMBER	0110	0111	0112	0117	0220	0221	0222	0224	0225	0226	0227	0228	0229	0230	0231	0233	0234	0235	0236	0239	0242	0243	0245	0246	0249	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	084	084	084	084	084	084	084	084	084	084	084	084	084	084	084	084	084	084	084	084	084	084	084	088	084	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Squamous cell carcinoma																									X	2
Fibrosarcoma																							X			1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma		X																								1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Malignant lymphoma, NOS																							X			1
Thymus	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma																										2
Hepatocellular carcinoma																	X							X		3
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenomatous polyp, NOS																										1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	46
Adenoma, NOS					X																					1
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Parathyroid	–	–	+	+	+	–	+	–	+	+	+	+	–	+	–	–	+	+	+	+	+	–	+	–	–	28
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyosarcoma								X																		1
Ovary	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malignant lymphoma, NOS																						X				3
Malig. lymphoma, histiocytic type												X														1

*Animals necropsied

APPENDIX B

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE IN THE TWO-YEAR DERMAL STUDIES OF JP-5 NAVY FUEL

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*Skin	(50)	(50)	(50)
Undifferentiated carcinoma		1 (2%)	
Papilloma, NOS		1 (2%)	
Squamous cell carcinoma			1 (2%)
*Subcutaneous tissue	(50)	(50)	(50)
Sarcoma, NOS	1 (2%)	4 (8%)	1 (2%)
Fibroma	1 (2%)	1 (2%)	
Fibrosarcoma	1 (2%)	3 (6%)	
RESPIRATORY SYSTEM			
#Lung	(50)	(49)	(49)
Hepatocellular carcinoma, metastatic		1 (2%)	1 (2%)
Alveolar/bronchiolar adenoma	3 (6%)	4 (8%)	2 (4%)
Alveolar/bronchiolar carcinoma	2 (4%)	1 (2%)	2 (4%)
Sarcoma, NOS, metastatic		1 (2%)	
HEMATOPOIETIC SYSTEM			
*Multiple organs	(50)	(50)	(50)
Malignant lymphoma, undiffer. type	3 (6%)		
Malignant lymphoma, lymphocytic type	1 (2%)	1 (2%)	
Malignant lymphoma, histiocytic type		1 (2%)	1 (2%)
Malignant lymphoma, mixed type	2 (4%)		
Granulocytic leukemia	1 (2%)		
*Subcutaneous tissue	(50)	(50)	(50)
Mast cell tumor			1 (2%)
#Spleen	(49)	(49)	(49)
Malignant lymphoma, mixed type	1 (2%)		
#Mesenteric lymph node	(43)	(44)	(36)
Malignant lymphoma, histiocytic type		1 (2%)	
#Ileum	(45)	(45)	(48)
Malignant lymphoma, lymphocytic type	1 (2%)		
CIRCULATORY SYSTEM			
*Subcutaneous tissue	(50)	(50)	(50)
Hemangioma			1 (2%)
Hemangiosarcoma	1 (2%)		
#Bone marrow	(47)	(47)	(49)
Hemangioma		1 (2%)	
#Liver	(50)	(50)	(50)
Hemangiosarcoma		4 (8%)	3 (6%)
DIGESTIVE SYSTEM			
#Liver	(50)	(50)	(50)
Hepatocellular adenoma	7 (14%)	6 (12%)	10 (20%)
Hepatocellular carcinoma	10 (20%)	10 (20%)	8 (16%)
Sarcoma, NOS, metastatic		1 (2%)	
#Forestomach	(48)	(49)	(49)
Papilloma, NOS	1 (2%)		
#Duodenum	(45)	(45)	(48)
Adenocarcinoma, NOS		1 (2%)	

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
URINARY SYSTEM			
#Kidney	(50)	(49)	(50)
Tubular cell adenocarcinoma	1 (2%)		
ENDOCRINE SYSTEM			
#Anterior pituitary	(44)	(48)	(46)
Adenoma, NOS			1 (2%)
#Adrenal/capsule	(50)	(49)	(50)
Adenoma, NOS	2 (4%)	1 (2%)	
#Adrenal medulla	(50)	(49)	(50)
Pheochromocytoma	2 (4%)		3 (6%)
REPRODUCTIVE SYSTEM			
None			
NERVOUS SYSTEM			
#Brain	(50)	(50)	(49)
Astrocytoma		1 (2%)	
SPECIAL SENSE ORGANS			
None			
MUSCULOSKELETAL SYSTEM			
None			
BODY CAVITIES			
None			
ALL OTHER SYSTEMS			
None			
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Natural death	10	9	13
Moribund sacrifice	4	8	8
Terminal sacrifice	36	33	28
Accidentally killed, NOS			1

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
Total animals with primary tumors**	30	28	26
Total primary tumors	41	42	34
Total animals with benign tumors	15	9	14
Total benign tumors	16	14	17
Total animals with malignant tumors	22	22	14
Total malignant tumors	25	28	16
Total animals with secondary tumors##		2	1
Total secondary tumors		3	1
Total animals with tumors uncertain--benign or malignant			1
Total uncertain tumors			1

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

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS MISSING	2	1	
ANIMALS NECROPSIED	48	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	48	49	50
INTEGUMENTARY SYSTEM			
#Skin paint site	(48)	(48)	(50)
Squamous cell carcinoma, invasive			1 (2%)
Sarcoma, NOS			1 (2%)
*Skin	(48)	(49)	(50)
Squamous cell carcinoma			1 (2%)
*Subcutaneous tissue	(48)	(49)	(50)
Sarcoma, NOS			1 (2%)
RESPIRATORY SYSTEM			
#Lung	(48)	(48)	(50)
Hepatocellular carcinoma, metastatic	1 (2%)		
Alveolar/bronchiolar carcinoma	3 (6%)	1 (2%)	
HEMATOPOIETIC SYSTEM			
*Multiple organs	(48)	(49)	(50)
Malignant lymphoma, NOS	1 (2%)		1 (2%)
Malignant lymphoma, undiffer. type	1 (2%)	3 (6%)	
Malignant lymphoma, lymphocytic type	2 (4%)	6 (12%)	1 (2%)
Malignant lymphoma, histiocytic type	2 (4%)	6 (12%)	
Malignant lymphoma, mixed type	1 (2%)	3 (6%)	2 (4%)
#Spleen	(48)	(47)	(50)
Malignant lymphoma, undiffer type			1 (2%)
#Mandibular l. node	(47)	(45)	(45)
Carcinoma, NOS, metastatic		1 (2%)	
#Axillary lymph node	(47)	(45)	(45)
Adenosquamous carcinoma, metastatic			1 (2%)
#Kidney	(48)	(49)	(50)
Malignant lymphoma, lymphocytic type		1 (2%)	
CIRCULATORY SYSTEM			
*Subcutaneous tissue	(48)	(49)	(50)
Hemangiosarcoma	1 (2%)		
#Liver	(48)	(49)	(50)
Hemangiosarcoma	1 (2%)	2 (4%)	1 (2%)
DIGESTIVE SYSTEM			
#Liver	(48)	(49)	(50)
Hepatocellular adenoma	2 (4%)	4 (8%)	2 (4%)
Hepatocellular carcinoma	1 (2%)	3 (6%)	2 (4%)
#Forestomach	(48)	(49)	(50)
Papilloma, NOS	1 (2%)	1 (2%)	1 (2%)
#Duodenum	(46)	(45)	(41)
Adenomatous polyp, NOS	1 (2%)		
URINARY SYSTEM			
#Kidney	(48)	(49)	(50)
Tubular cell adenoma		1 (2%)	

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#Anterior pituitary	(46)	(42)	(43)
Carcinoma, NOS		1 (2%)	
Adenoma, NOS	6 (13%)	6 (14%)	
#Adrenal	(48)	(49)	(49)
Cortical adenoma		2 (4%)	
#Adrenal/capsule	(48)	(49)	(49)
Adenoma, NOS	1 (2%)	1 (2%)	
#Adrenal medulla	(48)	(49)	(49)
Pheochromocytoma		1 (2%)	
#Thyroid	(47)	(46)	(46)
Follicular cell adenoma	2 (4%)	1 (2%)	3 (7%)
#Pancreatic islets	(48)	(47)	(50)
Islet cell adenoma	1 (2%)	1 (2%)	
REPRODUCTIVE SYSTEM			
*Mammary gland	(48)	(49)	(50)
Adenocarcinoma, NOS		1 (2%)	
Adenosquamous carcinoma			1 (2%)
#Uterus	(48)	(48)	(49)
Leiomyosarcoma		1 (2%)	
Endometrial stromal polyp	3 (6%)	1 (2%)	
Endometrial stromal sarcoma		1 (2%)	1 (2%)
#Endometrial stroma	(48)	(48)	(49)
Neoplasm, NOS, unc prim or metastatic			1 (2%)
#Ovary	(47)	(48)	(47)
Papillary adenoma	1 (2%)		
Luteoma	1 (2%)		
Granulosa cell tumor		1 (2%)	
Teratoma, NOS	1 (2%)		1 (2%)
NERVOUS SYSTEM			
#Brain/meninges	(48)	(49)	(50)
Carcinoma, NOS, invasive		1 (2%)	
SPECIAL SENSE ORGANS			
*Harderian gland	(48)	(49)	(50)
Adenoma, NOS		1 (2%)	
MUSCULOSKELETAL SYSTEM			
None			
BODY CAVITIES			
None			
ALL OTHER SYSTEMS			
*Multiple organs	(48)	(49)	(50)
Hepatocellular carcinoma, metastatic		1 (2%)	

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Natural death	3	7	20
Moribund sacrifice	1	8	13
Scheduled sacrifice			17
Terminal sacrifice	44	33	
Accidentally killed, nda		1	
Animal missing	2	1	
TUMOR SUMMARY			
Total animals with primary tumors**	23	35	16
Total primary tumors	33	50	21
Total animals with benign tumors	14	16	6
Total benign tumors	19	20	6
Total animals with malignant tumors	12	26	11
Total malignant tumors	13	29	13
Total animals with secondary tumors##	1	3	2
Total secondary tumors	1	3	2
Total animals with tumors uncertain-- benign or malignant	1	1	1
Total uncertain tumors	1	1	1
Total animals with tumors uncertain-- primary or metastatic			1
Total uncertain tumors			1

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

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL: VEHICLE CONTROL

ANIMAL NUMBER	03 35	00 03	02 26	01 12	01 13	03 32	02 25	03 36	04 45	00 01	01 19	02 28	01 14	04 43	00 02	00 04	00 05	00 06	00 07	00 08	00 09	01 10	01 11	01 15	01 16
WEEKS ON STUDY	01 33	01 66	02 25	06 68	07 33	08 33	08 84	09 44	09 44	10 00	10 02	10 22	10 33	10 33	10 51	10 55	10 55	10 55	10 55	10 55	10 55	10 55	10 55	10 55	10 55
INTEGUMENTARY SYSTEM																									
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS							X																		
Fibroma																									X
Fibrosarcoma															X										
Hemangiosarcoma											X														
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Trachea	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	−	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Malignant lymphoma, mixed type																									
Lymph nodes	−	+	−	−	−	+	+	+	+	−	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	−	−	+	+	+	+	+	−	−	+	−	−	+	−	+	+	+	+	−	−	−	−	−	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Hepatocellular carcinoma						X			X					X		X									X
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+
Gallbladder & common bile duct	N	N	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	−	−	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma, NOS											X														
Small intestine	−	−	−	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Malig. lymphoma, lymphocytic type																							X		
Large intestine	+	−	−	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenocarcinoma																									
Urinary bladder	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	−	+	+	+	+	+	+	+	−	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																								X	
Pheochromocytoma																									
Thyroid	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	−	−	+	−	−	−	−	−	−	−	−	+	+	−	−	−	−	+	−	−	+	−	+	+	−
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malig. lymphoma, undiffer type													X												
Malig. lymphoma, lymphocytic type																									
Malignant lymphoma, mixed type									X																
Granulocytic leukemia								X																	

+: Tissue examined microscopically
−: Required tissue not examined microscopically
X: Tumor incidence
N: Necropsy, no autolysis, no microscopic examination
S: Animal missexed
: No tissue information submitted
C: Necropsy, no histology due to protocol
A: Autolysis
M: Animal missing
B: No necropsy performed

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

ANIMAL NUMBER	017	018	020	021	022	023	024	027	029	030	031	033	034	037	038	039	040	041	042	044	046	047	048	049	050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS																										1
Fibroma																										1
Fibrosarcoma																										1
Hemangiosarcoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma							X					X					X									3
Alveolar/bronchiolar carcinoma																		X			X					2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Malignant lymphoma, mixed type																								X		1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+		37
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+		50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+		50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+		50
Hepatocellular adenoma	X			X	X									X		X					X	X				7
Hepatocellular carcinoma				X							X			X							X	X				10
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Gallbladder & common bile duct	+	+	+	N	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	N	+	+	+		*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		46
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Papilloma, NOS																										1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		45
Malig. lymphoma, lymphocytic type																										1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		46
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Tubular cell adenocarcinoma									X																	1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
ENDOCRINE SYSTEM																										
Pituitary	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+		44
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Adenoma, NOS																								X		2
Pheochromocytoma		X																			X					2
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Parathyroid	–	+	+	–	–	–	–	–	–	+	+	+	–	–	+	–	+	+	+	–	–	–	+	+		18
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+		48
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		*50
Malig. lymphoma, undiffer type															X			X								3
Malig. lymphoma, lymphocytic type																				X						1
Malignant lymphoma, mixed type																						X				2
Granulocytic leukemia																										1

* Animals necropsied

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL: LOW DOSE

ANIMAL NUMBER	042	043	055	077	081	095	149	141	311	334	347	323	355	020	039	396	488	022	033	044	066	088	099	101	111
WEEKS ON STUDY	069	075	076	080	082	083	083	091	092	092	095	096	097	099	100	103	103	105	105	105	105	105	105	105	105
INTEGUMENTARY SYSTEM																									
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Undifferentiated carcinoma																									
Papilloma, NOS																									
Subcutaneous tissue	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS				X										X		X									
Fibroma																									
Fibrosarcoma						X																			
RESPIRATORY SYSTEM																									
Lungs and bronchi	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic														X											
Alveolar/bronchiolar adenoma																			X						
Alveolar/bronchiolar carcinoma			X																						
Sarcoma, NOS, metastatic																X									
Trachea	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	−	+	+	+	+	+	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																			X						
Spleen	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+
Lymph nodes	−	+	+	+	−	−	+	+	−	−	+	+	+	−	+	+	+	+	+	+	+	+	−	−	+
Malig. lymphoma, histiocytic type																									
Thymus	−	+	−	−	−	−	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	−
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma								X			X						X		X						
Hepatocellular carcinoma	X				X			X							X			X	X						
Sarcoma, NOS, metastatic																X									
Hemangiosarcoma												X							X						
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	+	+	N	+	+	+	+	+	+	+	+	+	+	N	+	+	N	+	+	+	+	+	+
Pancreas	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	−	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	−	−	+	+	−	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Large intestine	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS											X														
Thyroid	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	−	−	−	−	−	+	+	+	+	+	−	−	+	−	−	+	+	−	+	+	+	−	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malig. lymphoma, lymphocytic type																									
Malig. lymphoma, histiocytic type									X																

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

ANIMAL NUMBER	012	015	016	017	018	019	021	022	023	024	025	026	027	028	029	030	033	037	038	040	041	043	044	046	050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Undifferentiated carcinoma								X																		1
Papilloma, NOS																				X						1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS																			X							4
Fibroma							X																			1
Fibrosarcoma											X							X								3
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular carcinoma, metastatic																										1
Alveolar/bronchiolar adenoma			X				X													X						4
Alveolar/bronchiolar carcinoma																										1
Sarcoma, NOS, metastatic																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	47
Hemangioma																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	49
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	44
Malig. lymphoma, histiocytic type																		X								1
Thymus	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	−	−	+	−	38
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	•	−	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma									X	X																6
Hepatocellular carcinoma				X				X										X						X		10
Sarcoma, NOS, metastatic																										1
Hemangiosarcoma					X														X							4
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	N	+	+	N	N	+	+	+	N	N	+	N	+	+	+	+	+	+	+	+	+	N	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Adenocarcinoma, NOS																								X		1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	47
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	48
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma, NOS																										1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Parathyroid	+	−	−	+	−	−	+	−	−	+	−	−	+	+	−	−	+	−	−	+	+	+	−	+	−	25
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Prostate	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	47
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Astrocytoma							X																			1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malig. lymphoma, lymphocytic type	X																									1
Malig. lymphoma, histiocytic type																										1

* Animals necropsied

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL: HIGH DOSE

ANIMAL NUMBER	00 01	00 02	01 18	02 27	00 09	00 07	03 36	05 00	01 13	02 23	02 29	03 30	04 21	04 47	02 25	02 28	03 34	03 33	00 05	01 10	02 26	02 22	00 03	00 04	00 06
WEEKS ON STUDY	00 01	03 11	04 11	08 80	08 83	08 84	08 85	08 85	08 86	08 86	08 86	08 86	08 88	09 91	09 95	09 98	09 98	10 00	10 03	10 03	10 03	10 04	10 05	10 05	10 05
INTEGUMENTARY SYSTEM																									
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS														X											
Hemangioma								X																	
Mast cell tumor																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	X	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic																									
Alveolar/bronchiolar adenoma																						X			
Alveolar/bronchiolar carcinoma				X																					
Trachea	−	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	−	−	−	−	−	−	−	−	+	+	−	+	−	−	−	−	+	+	+	+	+	+	+	+
Thymus	−	+	−	−	−	+	+	+	−	+	−	−	−	+	−	+	+	+	−	−	−	+	−	−	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	-	-	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma						X	X							X			X			X	X				
Hepatocellular carcinoma						X			X									X	X			X			
Hemangiosarcoma				X											X										X
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	+	+	N	+	+	N	+	+	+	+	+	N	N	+	+	+	+	+	+	N	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	−	+	+	+	+	+
Adenoma, NOS																									
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma																X				X		X			
Thyroid	−	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	−	−	−	−	+	−	+	+	+	+	+	−	−	−	−	+	+	+	−	−	−	−	−	−	−
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malig. lymphoma, histiocytic type																						X			

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

ANIMAL NUMBER	00 08	01 11	01 12	01 14	01 15	01 16	01 17	01 19	02 00	02 21	02 24	03 01	03 32	03 35	03 37	03 38	03 39	04 00	04 01	04 03	04 44	04 45	04 46	04 48	04 49	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Squamous cell carcinoma										X																1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS																										1
Hemangioma																										1
Mast cell tumor					X																					1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular carcinoma, metastatic																										1
Alveolar/bronchiolar adenoma																			X							2
Alveolar/bronchiolar carcinoma																				X						2
Trachea	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	49
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	36
Thymus	+	+	+	+	+	+	–	+	+	+	–	–	+	+	–	+	+	+	+	–	+	+	+	–	–	31
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma													X					X	X				X			10
Hepatocellular carcinoma			X			X																		X		8
Hemangiosarcoma																										3
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	46
Adenoma, NOS																								X		1
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma																										3
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Parathyroid	–	–	+	+	+	+	+	+	–	–	–	–	+	–	–	–	+	+	+	–	+	–	+	–	+	22
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malig. lymphoma, histiocytic type																										1

* Animals necropsied

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL: VEHICLE CONTROL

ANIMAL NUMBER	035	040	023	046	021	038	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019
WEEKS ON STUDY	003	003	088	095	097	104	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
INTEGUMENTARY SYSTEM																									
Skin paint site	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue	M	M	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma															X										
RESPIRATORY SYSTEM																									
Lungs and bronchi	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic																									
Alveolar/bronchiolar carcinoma														X											
Trachea	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	M	M	+	–	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	M	M	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Hepatocellular carcinoma																									
Hemangiosarcoma			X																						
Bile duct	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+
Pancreas	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma, NOS																									
Small intestine	M	M	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS																									
Large intestine	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	M	M	+	–	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	M	M	+	+	+	+	+	+	+	+	+	+	–	+	+	+	–	+	+	+	+	+	+	+	+
Adenoma, NOS						X	X														X				
Adrenal	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Thyroid	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma						X		X																	
Parathyroid	M	M	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	–
Pancreatic islets	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma									X																
REPRODUCTIVE SYSTEM																									
Mammary gland	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrial stromal polyp																					X				
Ovary	M	M	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papillary adenoma																									
Luteoma																									
Teratoma, NOS																									
NERVOUS SYSTEM																									
Brain	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	M	M	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, NOS			X																						
Malig. lymphoma, undiffer. type																									
Malig. lymphoma, lymphocytic type						X																			
Malig. lymphoma, histiocytic type					X																				
Malignant lymphoma, mixed type							X																		

+: Tissue examined microscopically
–: Required tissue not examined microscopically
X: Tumor incidence
N: Necropsy, no autolysis, no microscopic examination
S: Animal missexed
: No tissue information submitted
C: Necropsy, no histology due to protocol
A: Autolysis
M: Animal missing
B: No necropsy performed

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

ANIMAL NUMBER	020	022	024	025	026	027	028	029	030	031	032	033	034	036	037	039	041	042	043	044	045	047	048	049	050	TOTAL:
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*48
Hemangiosarcoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Hepatocellular carcinoma, metastatic																							X			1
Alveolar/bronchiolar carcinoma									X		X															3
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph nodes	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Thymus	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Hepatocellular adenoma						X							X													2
Hepatocellular carcinoma																							X			1
Hemangiosarcoma																										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	*48
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Papilloma, NOS									X																	1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Adenomatous polyp, NOS														X												1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Urinary bladder	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Adenoma, NOS		X	X																						X	6
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma, NOS														X												1
Thyroid	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Follicular cell adenoma																										2
Parathyroid	+	+	+	−	−	−	−	−	−	−	−	+	−	+	+	+	+	+	+	−	+	−	−	−		30
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Islet cell adenoma																										1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	*48
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Endometrial stromal polyp					X									X												3
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Papillary adenoma																X										1
Luteoma					X																					1
Teratoma, NOS			X																							1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*48
Malignant lymphoma, NOS																										1
Malig. lymphoma, undiffer. type																								X		1
Malig. lymphoma, lymphocytic type		X																								2
Malig. lymphoma, histiocytic type																				X						2
Malignant lymphoma, mixed type																										1

* Animals necropsied

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL: LOW DOSE

ANIMAL NUMBER	02 04	03 05	00 02	00 03	00 05	02 01	02 05	03 07	04 04	04 05	04 06	01 00	04 01	03 01	03 06	03 03	02 02	00 01	00 04	00 06	00 07	00 08	00 09	01 11	01 12
WEEKS ON STUDY	00 04	04 43	05 58	08 85	08 85	08 87	09 91	09 92	09 92	09 92	09 92	09 97	09 97	09 99	10 02	10 03	10 04	10 05	10 05	10 05	10 05	10 05	10 05	10 05	10 05
INTEGUMENTARY SYSTEM																									
Skin paint site	M	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
Lungs and bronchi	M	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																									X
Trachea	M	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	–	+	+	+	+
Spleen	M	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	M	–	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, metastatic										X															
Thymus	M	–	+	–	+	+	+	+	+	+	–	+	–	+	+	–	+	+	+	+	+	+	–	+	+
CIRCULATORY SYSTEM																									
Heart	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	–
Liver	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Hepatocellular carcinoma														X	X		X								
Hemangiosarcoma						X																			X
Bile duct	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	M	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	M	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma, NOS																				X					
Small intestine	M	–	–	+	+	+	+	+	+	+	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+
Large intestine	M	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																									
Malig. lymphoma, lymphocytic type																									
Urinary bladder	M	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	M	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	–	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS															X	X			X					X	
Adrenal	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									X
Cortical adenoma																									
Pheochromocytoma																									
Thyroid	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Parathyroid	M	–	–	+	–	+	+	+	+	–	+	+	+	+	–	+	+	–	+	–	+	–	–	–	–
Pancreatic islets	M	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	M	N	+	+	+	+	N	N	N	+	+	+	N	N	+	+	N	+	+	+	+	N	+	+	+
Adenocarcinoma, NOS															X										
Uterus	M	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma																									
Endometrial stromal polyp																								X	
Endometrial stromal sarcoma																									
Ovary	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor				X																					
NERVOUS SYSTEM																									
Brain	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
SPECIAL SENSE ORGANS																									
Harderian gland	M	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	M	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Hepatocellular carcinoma, metastatic														X											
Malig. lymphoma, undiffer. type																									
Malig. lymphoma, lymphocytic type					X		X		X			X								X			X		
Malig. lymphoma, histiocytic type													X												
Malignant lymphoma, mixed type				X							X													X	

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

ANIMAL NUMBER	013	014	015	016	017	018	019	020	023	026	027	028	029	030	032	034	038	039	040	042	043	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Alveolar/bronchiolar carcinoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	−	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	45
Carcinoma, NOS, metastatic																										1
Thymus	+	+	+	−	−	+	+	−	+	+	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	38
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	45
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular adenoma				X					X			X								X						4
Hepatocellular carcinoma																										3
Hemangiosarcoma																										2
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*49
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Papilloma, NOS																										1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tubular cell adenoma																X										1
Malig lymphoma, lymphocytic type														X												1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	46
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	−	+	+	−	+	+	+	+	−	+	+	+	+	−	+	+	+	42
Carcinoma, NOS																							X			1
Adenoma, NOS													X			X										6
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma, NOS																										1
Cortical adenoma										X															X	2
Pheochromocytoma												X														1
Thyroid	+	+	+	+	+	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+	−	+	+	+	46
Follicular cell adenoma							X																			1
Parathyroid	+	+	+	−	−	−	−	−	−	−	−	−	−	+	+	+	+	+	+	−	+	−	−	−	−	23
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Islet cell adenoma																								X		1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	N	+	+	+	N	N	N	N	+	N	+	+	+	+	N	N	+	+	+	+	N	+	+	+	*49
Adenocarcinoma, NOS																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Leiomyosarcoma																		X								1
Endometrial stromal polyp																										1
Endometrial stromal sarcoma			X																							1
Ovary	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Granulosa cell tumor																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, NOS, invasive																							X			1
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Adenoma, NOS										X																1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Hepatocellular carcinoma, metastatic																										1
Malig lymphoma, undiffer type			X													X										3
Malig lymphoma, lymphocytic type		X								X					X											6
Malig lymphoma, histiocytic type																				X		X				6
Malignant lymphoma, mixed type																										3

* Animals necropsied

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF *JP-5* NAVY FUEL: HIGH DOSE

ANIMAL NUMBER	0036	0038	0039	0043	0009	0010	0050	0016	0024	0011	0019	0040	0026	0027	0028	0032	0042	0006	0025	0030	0031	0035	0034	0045	0005
WEEKS ON STUDY	001	001	001	014	028	039	058	060	081	083	088	074	076	076	076	076	076	079	079	079	079	079	081	082	083
INTEGUMENTARY SYSTEM																									
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, invasive																		X							
Sarcoma, NOS										X															
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																		X							
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	−	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Malig. lymphoma, undiffer. type																									
Lymph nodes	−	−	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenosquamous carcinoma, metastatic																									
Thymus	+	+	−	−	+	−	+	−	+	−	+	−	−	−	−	+	+	−	+	+	+	+	+	−	−
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma									X																
Hepatocellular carcinoma																									
Hemangiosarcoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	+	N	N	N	+	N	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma, NOS																									
Small intestine	−	−	−	+	+	−	+	+	−	−	+	+	−	+	−	+	−	+	+	+	+	+	+	+	+
Large intestine	+	+	−	+	+	+	+	+	−	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	−	+	+	+	+	+	+	−	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	−	+	+	−	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Thyroid	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Parathyroid	−	+	−	−	+	+	−	+	+	−	+	+	+	−	+	−	−	+	+	−	−	+	−	−	−
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	N	+	+	+	+	+	+	+	+	+	N	+	N	N	+	+	+	N	+	N	+	+
Adenosquamous carcinoma																									
Uterus	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS, unc prim or metastatic																	X								
Endometrial stromal sarcoma																									
Ovary	+	+	+	+	+	+	+	+	−	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+
Teratoma, NOS				X																					
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, NOS																									
Malig. lymphoma, lymphocytic type																	X								
Malignant lymphoma, mixed type																							X		

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

ANIMAL NUMBER	0212	0222	0411	0117	0444	0449	0220	0448	0001	0002	0003	0004	0007	0008	0012	0113	0114	0115	0118	0223	0229	0333	0337	0446	0447	TOTAL:
WEEKS ON STUDY	0883	0883	0883	0885	0885	0885	0888	0889	0900	0900	0900	0900	0900	0900	0900	0900	0900	0900	0900	0900	0900	0900	0900	0900	0900	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, invasive																										1
Sarcoma, NOS																										1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Squamous cell carcinoma																										1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS												X														1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	−	+	+	+	+	47
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Malig. lymphoma, undiffer. type									X																	1
Lymph nodes	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Adenosquamous carcinoma, metastatic								X																		1
Thymus	+	+	+	+	+	−	+	−	+	+	+	−	+	+	+	−	+	+	−	+	+	+	−	+	+	32
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma															X											2
Hepatocellular carcinoma			X														X									2
Hemangiosarcoma		X																								1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	N	+	+	+	+	+	N	N	+	+	N	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	47
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Papilloma, NOS														X												1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	44
ENDOCRINE SYSTEM																										
Pituitary	−	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	43
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thyroid	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	−	+	−	+	+	+	+	46
Follicular cell adenoma									X			X													X	3
Parathyroid	−	−	−	−	−	−	−	−	−	+	+	+	+	−	−	−	+	~	−	−	−	+	−	−	−	18
REPRODUCTIVE SYSTEM																										
Mammary gland	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenosquamous carcinoma								X																		1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Neoplasm, NOS, unc prim or metastatic																										1
Endometrial stromal sarcoma									X																	1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Teratoma, NOS																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malignant lymphoma, NOS																								X		1
Malig. lymphoma, lymphocytic type			X																							1
Malignant lymphoma, mixed type																										2

* Animals necropsied

APPENDIX C

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	50
INTEGUMENTARY SYSTEM			
#Skin paint site	(49)	(49)	(49)
Mineralization	1 (2%)		
Ulcer, NOS	1 (2%)	25 (51%)	36 (73%)
Inflammation, chronic	6 (12%)	42 (86%)	46 (94%)
Fibrosis		1 (2%)	1 (2%)
Exfoliative dermatitis	3 (6%)	5 (10%)	5 (10%)
Melanin	1 (2%)	3 (6%)	7 (14%)
Hyperplasia, focal		1 (2%)	4 (8%)
Hyperkeratosis	1 (2%)		1 (2%)
Acanthosis	5 (10%)	41 (84%)	45 (92%)
*Skin	(50)	(49)	(50)
Epidermal inclusion cyst		1 (2%)	
Hemorrhage		1 (2%)	
Ulcer, NOS		6 (12%)	7 (14%)
Inflammation, suppurative		1 (2%)	1 (2%)
Inflammation, chronic	2 (4%)	14 (29%)	†20 (40%)
Exfoliative dermatitis	1 (2%)		2 (4%)
Acanthosis	1 (2%)	13 (27%)	21 (42%)
*Subcutaneous tissue	(50)	(49)	(50)
Abscess, NOS			1 (2%)
Inflammation, chronic	1 (2%)		
RESPIRATORY SYSTEM			
*Nasal cavity	(50)	(49)	(50)
Hemorrhage	8 (16%)	10 (20%)	10 (20%)
Inflammation, suppurative			2 (4%)
#Trachea	(50)	(46)	(47)
Hemorrhage	1 (2%)	1 (2%)	1 (2%)
#Lung	(50)	(49)	(49)
Congestion, NOS		1 (2%)	
Hemorrhage	2 (4%)	6 (12%)	6 (12%)
Inflammation, interstitial	2 (4%)	1 (2%)	1 (2%)
Inflammation, granulomatous focal			1 (2%)
Epithelialization	1 (2%)		
#Lung/alveoli	(50)	(49)	(49)
Histiocytosis		1 (2%)	
HEMATOPOIETIC SYSTEM			
#Spleen	(50)	(48)	(49)
Amyloidosis		1 (2%)	
Hematopoiesis	9 (18%)	14 (29%)	40 (82%)
#Lymph node	(42)	(42)	(40)
Plasmacytosis		1 (2%)	2 (5%)
#Mandibular lymph node	(42)	(42)	(40)
Plasmacytosis			1 (3%)
#Mediastinal lymph node	(42)	(42)	(40)
Hemorrhage		1 (2%)	
#Hepatic lymph node	(42)	(42)	(40)
Hyperplasia, lymphoid	2 (5%)		
#Lumbar lymph node	(42)	(42)	(40)
Hyperplasia, lymphoid	1 (2%)		

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM (Continued)			
#Mesenteric lymph node	(42)	(42)	(40)
Hemorrhage	19 (45%)	22 (52%)	17 (43%)
Inflammation, granulomatous	1 (2%)		
Hyperplasia, lymphoid	1 (2%)	1 (2%)	
Hematopoiesis		1 (2%)	
#Renal lymph node	(42)	(42)	(40)
Plasmacytosis		1 (2%)	
#Axillary lymph node	(42)	(42)	(40)
Plasmacytosis		1 (2%)	18 (45%)
Hyperplasia, lymphoid			1 (3%)
#Inguinal lymph node	(42)	(42)	(40)
Degeneration, cystic			1 (3%)
Plasmacytosis			3 (8%)
#Lung	(50)	(49)	(49)
Leukocytosis, neutrophilic		1 (2%)	
#Liver	(50)	(48)	(49)
Leukemoid reaction		1 (2%)	
Hematopoiesis		3 (6%)	1 (2%)
#Ileum	(43)	(44)	(49)
Hyperplasia, lymphoid	1 (2%)		
#Thymus	(41)	(35)	(40)
Cyst, NOS	1 (2%)	2 (6%)	2 (5%)
Depletion, lymphoid		1 (3%)	
CIRCULATORY SYSTEM			
*Multiple organs	(50)	(49)	(50)
Embolus, septic		3 (6%)	1 (2%)
#Mesenteric lymph node	(42)	(42)	(40)
Thrombosis, NOS	1 (2%)		
#Heart/atrium	(50)	(49)	(49)
Infection, bacterial		1 (2%)	
#Myocardium	(50)	(49)	(49)
Mineralization	6 (12%)		
Inflammation, chronic		1 (2%)	
#Cardiac valve	(50)	(49)	(49)
Inflammation, suppurative			1 (2%)
Infection, bacterial		2 (4%)	1 (2%)
*Aorta	(50)	(49)	(50)
Inflammation, chronic			1 (2%)
*Superior mesentric vein	(50)	(49)	(50)
Thrombosis, NOS		1 (2%)	
#Thyroid	(47)	(46)	(44)
Polyangiitis			1 (2%)
DIGESTIVE SYSTEM			
#Salivary gland	(50)	(49)	(49)
Lymphocytic inflammatory infiltrate	8 (16%)	3 (6%)	4 (8%)
#Liver	(50)	(48)	(49)
Mineralization			1 (2%)
Necrosis, coagulative	4 (8%)	3 (6%)	3 (6%)
Amyloidosis		1 (2%)	1 (2%)
Ground glass cyto change	1 (2%)		
Focal cellular change		1 (2%)	
#Liver/caudate lobe	(50)	(48)	(49)
Torsion		1 (2%)	3 (6%)
#Liver/centrilobular	(50)	(48)	(49)
Necrosis, NOS		1 (2%)	
#Pancreatic acinus	(50)	(48)	(49)
Atrophy, NOS	1 (2%)		

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#Gastric fundus	(48)	(46)	(49)
Mineralization		1 (2%)	
Cyst, NOS		1 (2%)	
Erosion			2 (4%)
*Rectum	(50)	(49)	(50)
Prolapse	1 (2%)		
URINARY SYSTEM			
#Kidney	(50)	(48)	(49)
Hydronephrosis	1 (2%)		
Cyst, NOS		1 (2%)	
Hemorrhage			1 (2%)
Glomerulonephritis, NOS	1 (2%)	1 (2%)	1 (2%)
Pyelonephritis, NOS	4 (8%)	4 (8%)	2 (4%)
Lymphocytic inflammatory infiltrate	14 (28%)	8 (17%)	15 (31%)
Inflammation, interstitial	2 (4%)	8 (17%)	2 (4%)
Abscess, NOS			2 (4%)
Pyelonephritis, chronic			1 (2%)
Fibrosis, diffuse		1 (2%)	
Infarct, NOS		1 (2%)	
Amyloidosis	1 (2%)	1 (2%)	
Metaplasia, osseous		1 (2%)	
#Renal papilla	(50)	(48)	(49)
Necrosis, NOS		1 (2%)	
#Kidney/glomerulus	(50)	(48)	(49)
Dilatation, NOS			1 (2%)
#Kidney/tubule	(50)	(48)	(49)
Calculus, microscopic examination	1 (2%)		
Mineralization	1 (2%)		
Dilatation, NOS	1 (2%)		
#Urinary bladder	(49)	(46)	(49)
Calculus, gross observation only	1 (2%)	1 (2%)	2 (4%)
Calculus, microscopic examination	1 (2%)		1 (2%)
Dilatation, NOS		1 (2%)	
Hemorrhage		1 (2%)	
Lymphocytic inflammatory infiltrate	7 (14%)	6 (13%)	18 (37%)
Inflammation, chronic	6 (12%)	2 (4%)	2 (4%)
*Urethra	(50)	(49)	(50)
Inflammation, chronic	1 (2%)		
ENDOCRINE SYSTEM			
#Anterior pituitary	(48)	(45)	(45)
Cyst, NOS		1 (2%)	1 (2%)
#Adrenal	(49)	(48)	(49)
Inflammation, suppurative		1 (2%)	
Infarct, NOS			1 (2%)
#Adrenal/capsule	(49)	(48)	(49)
Hyperplasia, NOS	1 (2%)		
#Adrenal cortex	(49)	(48)	(49)
Hyperplasia, focal		1 (2%)	
#Adrenal medulla	(49)	(48)	(49)
Hyperplasia, focal	1 (2%)		1 (2%)
#Thyroid	(47)	(46)	(44)
Cystic follicles		1 (2%)	
Hyperplasia, follicular cell		1 (2%)	
#Thyroid follicle	(47)	(46)	(44)
Atrophy, NOS			2 (5%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*Mammary gland	(50)	(49)	(50)
Inflammation, granulomatous		1 (2%)	
*Penis	(50)	(49)	(50)
Ulcer, NOS	1 (2%)		
Inflammation, necrotizing	1 (2%)		
Acanthosis	1 (2%)		
*Prepuce	(50)	(49)	(50)
Retention of content	1 (2%)		
Inflammation, chronic	1 (2%)		
Foreign material, NOS	1 (2%)		
*Preputial gland	(50)	(49)	(50)
Dilatation/ducts	4 (8%)	2 (4%)	3 (6%)
Cyst, NOS			1 (2%)
Inflammation, suppurative	1 (2%)		
Abscess, NOS	8 (16%)	3 (6%)	1 (2%)
Inflammation, chronic	1 (2%)	1 (2%)	
#Prostate	(50)	(48)	(49)
Ectopia		1 (2%)	
Lymphocytic inflammatory infiltrate	3 (6%)	2 (4%)	2 (4%)
Inflammation, suppurative	4 (8%)		
Inflammation, chronic	1 (2%)	1 (2%)	2 (4%)
*Seminal vesicle	(50)	(49)	(50)
Retention of content	1 (2%)		
#Testis	(50)	(49)	(49)
Mineralization	16 (32%)	16 (33%)	7 (14%)
Granuloma, spermatic		3 (6%)	
Hypospermatogenesis	1 (2%)	1 (2%)	
Hyperplasia, interstitial cell	1 (2%)		
*Epididymis	(50)	(49)	(50)
Inflammation, chronic			1 (2%)
*Vas deferens	(50)	(49)	(50)
Inflammation, suppurative		1 (2%)	
NERVOUS SYSTEM			
#Brain	(50)	(49)	(49)
Congestion, NOS			1 (2%)
Hemorrhage			3 (6%)
#Brain/thalamus	(50)	(49)	(49)
Calculus, microscopic examination	21 (42%)	21 (43%)	19 (39%)
SPECIAL SENSE ORGANS			
*Eye	(50)	(49)	(50)
Phthisis bulbi	1 (2%)		
*Eye/cornea	(50)	(49)	(50)
Inflammation, suppurative	1 (2%)		
*Eye/iris	(50)	(49)	(50)
Pigmentation, NOS			1 (2%)
MUSCULOSKELETAL SYSTEM			
*Cartilage, NOS	(50)	(49)	(50)
Necrosis, NOS	8 (16%)	9 (18%)	3 (6%)
BODY CAVITIES			
*Abdominal cavity	(50)	(49)	(50)
Necrosis, fat	1 (2%)		

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
*Multiple organs	(50)	(49)	(50)
Lymphocytic inflammatory infiltrate	17 (34%)	20 (41%)	7 (14%)
Amyloidosis		6 (12%)	1 (2%)
Tail			
Inflammation, chronic			1
SPECIAL MORPHOLOGY SUMMARY			
No lesion reported			1
Animal missexed/no necropsy		1	

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

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
#Skin paint site	(50)	(50)	(48)
Mineralization		1 (2%)	
Epidermal inclusion cyst			3 (6%)
Ulcer, NOS		27 (54%)	39 (81%)
Inflammation, acute		1 (2%)	
Inflammation, chronic		33 (66%)	46 (96%)
Exfoliative dermatitis		3 (6%)	3 (6%)
Degeneration, ballooning		1 (2%)	
Melanin	1 (2%)	7 (14%)	4 (8%)
Hyperplasia, focal		1 (2%)	2 (4%)
Hyperkeratosis		2 (4%)	1 (2%)
Acanthosis		30 (60%)	39 (81%)
*Skin	(50)	(50)	(50)
Epidermal inclusion cyst		1 (2%)	1 (2%)
Ulcer, NOS		8 (16%)	†5 (10%)
Inflammation, chronic	1 (2%)	†17 (34%)	†17 (34%)
Acanthosis		7 (14%)	†12 (24%)
*Subcutaneous tissue	(50)	(50)	(50)
Abscess, NOS		2 (4%)	†5 (10%)
RESPIRATORY SYSTEM			
*Nasal cavity	(50)	(50)	(50)
Hemorrhage	10 (20%)	4 (8%)	9 (18%)
Inflammation, suppurative		1 (2%)	1 (2%)
#Trachea	(47)	(49)	(49)
Hemorrhage	1 (2%)	1 (2%)	
#Lung	(50)	(50)	(50)
Congestion, NOS		6 (12%)	1 (2%)
Edema, NOS		1 (2%)	1 (2%)
Hemorrhage	3 (6%)	1 (2%)	6 (12%)
Inflammation, suppurative		1 (2%)	
Abscess, NOS			2 (4%)
#Lung/alveoli	(50)	(50)	(50)
Histiocytosis	1 (2%)	1 (2%)	
HEMATOPOIETIC SYSTEM			
*Multiple organs	(50)	(50)	(50)
Leukemoid reaction		1 (2%)	
#Skin paint site	(50)	(50)	(48)
Mastocytosis			1 (2%)
#Bone marrow	(48)	(47)	(50)
Hyperplasia, hematopoietic	1 (2%)		
#Spleen	(50)	(49)	(50)
Necrosis, NOS		1 (2%)	1 (2%)
Amyloidosis	1 (2%)	2 (4%)	1 (2%)
Hematopoiesis	5 (10%)	24 (49%)	34 (68%)
#Lymph node	(50)	(43)	(44)
Plasmacytosis			2 (5%)
#Mandibular lymph node	(50)	(43)	(44)
Hemorrhage		1 (2%)	
Degeneration, cystic	1 (2%)		
Necrosis, NOS		1 (2%)	
Leukocytosis, neutrophilic		1 (2%)	
Plasmacytosis		2 (5%)	3 (7%)
Hematopoiesis		1 (2%)	

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM (Continued)			
#Lumbar lymph node	(50)	(43)	(44)
Degeneration, cystic	1 (2%)		
Leukocytosis, neutrophilic	1 (2%)		
Plasmacytosis	1 (2%)		
#Mesenteric lymph node	(50)	(43)	(44)
Hemorrhage	2 (4%)	7 (16%)	4 (9%)
#Axillary lymph node	(50)	(43)	(44)
Histiocytosis		1 (2%)	
Plasmacytosis	1 (2%)	6 (14%)	24 (55%)
Hyperplasia, lymphoid			1 (2%)
#Inguinal lymph node	(50)	(43)	(44)
Plasmacytosis		3 (7%)	6 (14%)
Hyperplasia, lymphoid		1 (2%)	1 (2%)
*Skull	(50)	(50)	(50)
Myelofibrosis	22 (44%)	6 (12%)	1 (2%)
*Sternum	(50)	(50)	(50)
Myelofibrosis	43 (86%)	11 (22%)	1 (2%)
#Lung	(50)	(50)	(50)
Leukocytosis, neutrophilic		1 (2%)	
#Liver	(50)	(50)	(50)
Leukemoid reaction		2 (4%)	
Hematopoiesis	1 (2%)	5 (10%)	9 (18%)
#Adrenal	(50)	(49)	(50)
Hematopoiesis		2 (4%)	
#Thymus	(46)	(32)	(44)
Cyst, NOS			1 (2%)
Necrosis, NOS			3 (7%)
Depletion, lymphoid	1 (2%)	1 (3%)	1 (2%)
Lymphocytosis			1 (2%)
CIRCULATORY SYSTEM			
*Multiple organs	(50)	(50)	(50)
Embolus, septic		7 (14%)	1 (2%)
#Heart/atrium	(50)	(50)	(50)
Inflammation, acute			1 (2%)
#Left ventricle	(50)	(50)	(50)
Dilatation, NOS	1 (2%)		
#Myocardium	(50)	(50)	(50)
Inflammation, suppurative		1 (2%)	
Inflammation, acute	1 (2%)	1 (2%)	
Inflammation, chronic		1 (2%)	
Degeneration, NOS	1 (2%)		
#Cardiac valve	(50)	(50)	(50)
Thrombosis, NOS		1 (2%)	
Inflammation, suppurative		3 (6%)	1 (2%)
Infection, bacterial		7 (14%)	1 (2%)
#Kidney	(50)	(50)	(50)
Embolus, septic		1 (2%)	
DIGESTIVE SYSTEM			
*Hard palate	(50)	(50)	(50)
Abscess, NOS		1 (2%)	
*Lip	(50)	(50)	(50)
Abscess, NOS			1 (2%)
#Salivary gland	(49)	(49)	(47)
Lymphocytic inflammatory infiltrate		2 (4%)	1 (2%)
Abscess, NOS			1 (2%)

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#Liver	(50)	(50)	(50)
Lymphocytic inflammatory infiltrate		1 (2%)	1 (2%)
Inflammation, multifocal	1 (2%)	1 (2%)	
Necrosis, coagulative		2 (4%)	1 (2%)
Amyloidosis	1 (2%)	4 (8%)	2 (4%)
Metamorphosis, fatty	2 (4%)		
Ground glass cyto change	2 (4%)		2 (4%)
Eosinophilic cyto change	1 (2%)		
#Liver/caudate lobe	(50)	(50)	(50)
Torsion	1 (2%)	1 (2%)	1 (2%)
#Pancreas	(50)	(48)	(50)
Dilatation/ducts			1 (2%)
Lymphocytic inflammatory infiltrate	1 (2%)		
Inflammation, chronic	1 (2%)		
Focal cellular change			1 (2%)
#Gastric fundus	(49)	(46)	(50)
Mineralization		2 (4%)	1 (2%)
Cyst, NOS			1 (2%)
Ulcer, NOS			1 (2%)
Erosion			1 (2%)
#Ileum	(47)	(37)	(46)
Infarct, NOS	1 (2%)		
URINARY SYSTEM			
#Kidney	(50)	(50)	(50)
Polycystic kidney		1 (2%)	
Glomerulonephritis, NOS	1 (2%)		
Pyelonephritis, NOS		3 (6%)	
Lymphocytic inflammatory infiltrate	9 (18%)	11 (22%)	15 (30%)
Inflammation, interstitial	3 (6%)	1 (2%)	2 (4%)
Inflammation, suppurative		3 (6%)	
Abscess, NOS		1 (2%)	
Fibrosis, diffuse	2 (4%)	1 (2%)	
Amyloidosis	2 (4%)		1 (2%)
Metaplasia, osseous	1 (2%)		
#Renal papilla	(50)	(50)	(50)
Necrosis, NOS		2 (4%)	1 (2%)
#Kidney/tubule	(50)	(50)	(50)
Dilatation, NOS			1 (2%)
Cytologic alteration, NOS		1 (2%)	
#Urinary bladder	(50)	(43)	(49)
Lymphocytic inflammatory infiltrate	4 (8%)	15 (35%)	15 (31%)
ENDOCRINE SYSTEM			
#Anterior pituitary	(49)	(48)	(46)
Cyst, NOS	2 (4%)		
Hemorrhage	1 (2%)		
Focal cellular change		1 (2%)	
#Adrenal	(50)	(49)	(50)
Necrosis, NOS		1 (2%)	
#Adrenal/capsule	(50)	(49)	(50)
Hyperplasia, NOS	1 (2%)		
#Adrenal cortex	(50)	(49)	(50)
Cyst, NOS		2 (4%)	
Lipoidosis			1 (2%)
Hyperplasia, focal	1 (2%)	1 (2%)	

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM (Continued)			
#Thyroid	(47)	(44)	(48)
Cystic follicles		1 (2%)	
Hyperplasia, follicular cell	2 (4%)	1 (2%)	1 (2%)
#Thyroid follicle	(47)	(44)	(48)
Atrophy, NOS		1 (2%)	3 (6%)
REPRODUCTIVE SYSTEM			
*Mammary gland	(50)	(50)	(50)
Dilatation/ducts		1 (2%)	1 (2%)
*Vagina	(50)	(50)	(50)
Inflammation, suppurative		1 (2%)	
#Uterus	(50)	(50)	(50)
Hemorrhage	1 (2%)		
Abscess, NOS		1 (2%)	
#Uterus/endometrium	(50)	(50)	(50)
Hyperplasia, cystic	41 (82%)	20 (40%)	22 (44%)
#Ovary	(50)	(47)	(49)
Mineralization	1 (2%)		1 (2%)
Cyst, NOS			1 (2%)
Follicular cyst, NOS	2 (4%)	2 (4%)	1 (2%)
Parovarian cyst	11 (22%)	3 (6%)	1 (2%)
Hemorrhagic cyst	2 (4%)		1 (2%)
Angiectasis	1 (2%)		
NERVOUS SYSTEM			
#Brain	(50)	(50)	(50)
Congestion, NOS			2 (4%)
Hemorrhage			3 (6%)
Demyelinization		1 (2%)	
#Brain/Thalamus	(50)	(50)	(50)
Calculus, microscopic examination	21 (42%)	15 (30%)	20 (40%)
SPECIAL SENSE ORGANS			
*Eye/Cornea	(50)	(50)	(50)
Inflammation, suppurative	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*Mandible	(50)	(50)	(50)
Inflammation, chronic			1 (2%)
*Cartilage, NOS	(50)	(50)	(50)
Necrosis, NOS	3 (6%)	2 (4%)	2 (4%)
BODY CAVITIES			
*Mediastinum	(50)	(50)	(50)
Inflammation, chronic	1 (2%)		
*Abdominal cavity	(50)	(50)	(50)
Mineralization		1 (2%)	
Necrosis, fat	3 (6%)	1 (2%)	
*Mesentery	(50)	(50)	(50)
Inflammation, chronic		1 (2%)	

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
*Multiple organs	(50)	(50)	(50)
Lymphocytic inflammatory infiltrate	34 (68%)	11 (22%)	10 (20%)
Bacterial septicemia		1 (2%)	
Amyloidosis	1 (2%)	23 (46%)	23 (46%)
Tail			
Inflammation, chronic		1	
Foot			
Inflammation, chronic			1
SPECIAL MORPHOLOGY SUMMARY			
No lesion reported		1	

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

APPENDIX D

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE IN THE TWO-YEAR DERMAL STUDIES OF JP-5 NAVY FUEL

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
#Skin paint site	(48)	(50)	(50)
Ulcer, NOS	2 (4%)	11 (22%)	27 (54%)
Inflammation, acute/chronic	1 (2%)	8 (16%)	28 (56%)
Inflammation, chronic	9 (19%)	9 (18%)	11 (22%)
Inflammation, chronic focal	3 (6%)		
Exfoliative dermatitis	1 (2%)	4 (8%)	6 (12%)
Necrosis, focal			1 (2%)
Melanin	1 (2%)		
Hyperplasia, epithelial	4 (8%)	11 (22%)	21 (42%)
Hyperkeratosis	1 (2%)	1 (2%)	
*Skin	(50)	(50)	(50)
Ulcer, NOS	2 (4%)	5 (10%)	13 (26%)
Inflammation, acute/chronic		5 (10%)	10 (20%)
Inflammation, chronic	1 (2%)	6 (12%)	7 (14%)
Fibrosis	1 (2%)		
Exfoliative dermatitis		4 (8%)	5 (10%)
Hyperplasia, epithelial		3 (6%)	4 (8%)
Hyperkeratosis	1 (2%)		
*Subcutaneous tissue	(50)	(50)	(50)
Lymphocytic inflammatory infiltrate		1 (2%)	
Lipogranuloma	1 (2%)		
RESPIRATORY SYSTEM			
*Nasal cavity	(50)	(50)	(50)
Inflammation, acute/chronic	1 (2%)	1 (2%)	
*Nasal gland	(50)	(50)	(50)
Necrosis, focal	1 (2%)		
*Nasal turbinate	(50)	(50)	(50)
Inflammation, suppurative	1 (2%)		
#Trachea	(48)	(48)	(47)
Inflammation, chronic focal	1 (2%)		
#Lung/bronchus	(50)	(49)	(49)
Hyperplasia, epithelial	1 (2%)		
#Lung	(50)	(49)	(49)
Atelectasis	3 (6%)	1 (2%)	1 (2%)
Congestion, NOS	4 (8%)	2 (4%)	1 (2%)
Hemorrhage	2 (4%)	1 (2%)	3 (6%)
Lymphocytic inflammatory infiltrate	17 (34%)	24 (49%)	18 (37%)
Inflammation, interstitial			1 (2%)
Hyperplasia, adenomatous	2 (4%)		
#Lung/alveoli	(50)	(49)	(49)
Histiocytosis	3 (6%)		1 (2%)
HEMATOPOIETIC SYSTEM			
#Bone marrow	(47)	(47)	(49)
Atrophy, focal	1 (2%)		
Hyperplasia, NOS	1 (2%)		
Hyperplasia, granulocytic	1 (2%)		8 (16%)
#Spleen	(49)	(49)	(49)
Amyloid, NOS	2 (4%)	2 (4%)	8 (16%)
Angiectasis		1 (2%)	
Hyperplasia, lymphoid	2 (4%)	1 (2%)	
Hematopoiesis	2 (4%)	6 (12%)	1 (2%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM (Continued)			
#Lymph node	(43)	(44)	(36)
Hemorrhage		1 (2%)	
Plasmacytosis		1 (2%)	
#Mesenteric lymph node	(43)	(44)	(36)
Congestion, NOS	3 (7%)	1 (2%)	2 (6%)
Hemorrhage		1 (2%)	
Angiectasis	1 (2%)		
Hyperplasia, lymphoid	3 (7%)	1 (2%)	
Hematopoiesis	1 (2%)	3 (7%)	1 (3%)
#Inguinal lymph node	(43)	(44)	(36)
Hyperplasia, lymphoid	1 (2%)		
#Lung	(50)	(49)	(49)
Leukocytosis, NOS	2 (4%)	2 (4%)	1 (2%)
#Heart	(50)	(50)	(49)
Leukocytosis, NOS		1 (2%)	
#Ileum	(45)	(45)	(48)
Hyperplasia, lymphoid	1 (2%)		
#Cecum	(46)	(49)	(50)
Hyperplasia, lymphoid	1 (2%)	1 (2%)	
#Thymus	(37)	(38)	(31)
Hemorrhage	1 (3%)		
Inflammation, acute	1 (3%)		
CIRCULATORY SYSTEM			
#Heart	(50)	(50)	(49)
Lymphocytic inflammatory infiltrate			1 (2%)
Calcification, NOS	1 (2%)		
#Myocardium	(50)	(50)	(49)
Inflammation, chronic focal	2 (4%)	1 (2%)	
Degeneration, NOS	3 (6%)	2 (4%)	
Necrosis, focal		1 (2%)	2 (4%)
#Cardiac valve	(50)	(50)	(49)
Thrombosis, NOS	1 (2%)		
*Artery	(50)	(50)	(50)
Periarteritis	1 (2%)		
#Pancreas	(46)	(49)	(50)
Periarteritis	1 (2%)		1 (2%)
DIGESTIVE SYSTEM			
*Tooth	(50)	(50)	(50)
Abscess, NOS		1 (2%)	
#Salivary gland	(50)	(49)	(49)
Calculus, microscopic examination	1 (2%)		
Lymphocytic inflammatory infiltrate	1 (2%)		
#Liver	(50)	(50)	(50)
Lymphocytic inflammatory infiltrate	1 (2%)	2 (4%)	
Inflammation, chronic	1 (2%)		
Inflammation, chronic focal	2 (4%)	1 (2%)	
Degeneration, lipoid	1 (2%)		
Necrosis, NOS		1 (2%)	
Necrosis, focal	1 (2%)	1 (2%)	1 (2%)
Infarct, NOS	2 (4%)	2 (4%)	3 (6%)
Amyloid, NOS	2 (4%)	2 (4%)	22 (44%)
Basophilic cyto change		2 (4%)	
Ground glass cyto change	5 (10%)	2 (4%)	1 (2%)
#Liver/centrilobular	(50)	(50)	(50)
Necrosis, NOS	1 (2%)		
Hepatocytomegaly	2 (4%)		

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
*Gallbladder	(50)	(50)	(50)
Hyperplasia, epithelial			1 (2%)
#Bile duct	(50)	(50)	(50)
Cyst, NOS		1 (2%)	1 (2%)
Hyperplasia, NOS			1 (2%)
#Pancreatic acinus	(46)	(49)	(50)
Atrophy, focal		1 (2%)	
#Glandular stomach	(48)	(49)	(49)
Cyst, NOS		1 (2%)	
Inflammation, suppurative	1 (2%)		
#Forestomach	(48)	(49)	(49)
Abscess, NOS			1 (2%)
Hyperplasia, epithelial	1 (2%)		1 (2%)
#Duodenum	(45)	(45)	(48)
Polyp, NOS			1 (2%)
*Rectum	(50)	(50)	(50)
Prolapse		2 (4%)	
Inflammation, suppurative		1 (2%)	
URINARY SYSTEM			
#Kidney	(50)	(49)	(50)
Hydronephrosis			1 (2%)
Pyelonephritis, NOS		1 (2%)	
Lymphocytic inflammatory infiltrate	26 (52%)	34 (69%)	24 (48%)
Inflammation, suppurative	2 (4%)		
Pyelonephritis, acute	1 (2%)		
Abscess, NOS	3 (6%)		
Inflammation, chronic	1 (2%)		
Nephropathy	2 (4%)		1 (2%)
Infection, bacterial	1 (2%)		
Amyloid, NOS	3 (6%)	2 (4%)	22 (44%)
Calcification, NOS	1 (2%)		
Calcification, focal	1 (2%)		1 (2%)
Atrophy, NOS	1 (2%)		
#Kidney/cortex	(50)	(49)	(50)
Amyloid, NOS			1 (2%)
Atrophy, NOS			2 (4%)
Atrophy, focal		1 (2%)	2 (4%)
#Renal papilla	(50)	(49)	(50)
Necrosis, NOS			5 (10%)
#Kidney/tubule	(50)	(49)	(50)
Dilatation, NOS	1 (2%)		
Calcification, NOS	1 (2%)		
#Kidney/pelvis	(50)	(49)	(50)
Calculus, gross observation only		1 (2%)	
Dilatation, NOS	2 (4%)	3 (6%)	
#Urinary bladder	(48)	(47)	(48)
Retention of content		1 (2%)	
Lymphocytic inflammatory infiltrate	16 (33%)	13 (28%)	20 (42%)
Inflammation, acute/chronic	2 (4%)		
Inflammation, chronic	3 (6%)	1 (2%)	
Hyperplasia, epithelial	3 (6%)	1 (2%)	

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#Anterior pituitary	(44)	(48)	(46)
Cyst, NOS	2 (5%)	1 (2%)	
Hyperplasia, focal	1 (2%)	2 (4%)	1 (2%)
#Adrenal/capsule	(50)	(49)	(50)
Hyperplasia, NOS	41 (82%)	46 (94%)	42 (84%)
#Adrenal cortex	(50)	(49)	(50)
Degeneration, NOS	1 (2%)		
Degeneration, lipoid	1 (2%)		
Amyloid, NOS			5 (10%)
Hypertrophy, focal	7 (14%)	4 (8%)	1 (2%)
Hyperplasia, focal	2 (4%)	4 (8%)	1 (2%)
#Adrenal medulla	(50)	(49)	(50)
Fibrosis		1 (2%)	
Fibrosis, focal	1 (2%)		
Amyloid, NOS	1 (2%)		
Hyperplasia, focal	6 (12%)	3 (6%)	2 (4%)
#Thyroid	(48)	(49)	(48)
Follicular cyst, NOS	2 (4%)		
Necrosis, focal	1 (2%)		
Amyloid, NOS			3 (6%)
Hyperplasia, C-cell			1 (2%)
Hyperplasia, follicular cell	3 (6%)		
#Parathyroid	(18)	(25)	(22)
Cyst, NOS	1 (6%)		
Lymphocytic inflammatory infiltrate	1 (6%)		
#Pancreatic islets	(46)	(49)	(50)
Hyperplasia, focal			1 (2%)
REPRODUCTIVE SYSTEM			
*Prepuce	(50)	(50)	(50)
Retention of content		1 (2%)	
Inflammation, suppurative	1 (2%)		
*Preputial gland	(50)	(50)	(50)
Dilatation/ducts	2 (4%)	2 (4%)	
Retention of content		1 (2%)	
Cystic ducts		1 (2%)	
Abscess, NOS	2 (4%)	8 (16%)	2 (4%)
Hyperplasia, epithelial		1 (2%)	
#Prostate	(48)	(47)	(50)
Lymphocytic inflammatory infiltrate	4 (8%)	2 (4%)	
Inflammation, suppurative	2 (4%)	1 (2%)	1 (2%)
Inflammation, acute/chronic	1 (2%)	1 (2%)	
Inflammation, chronic	1 (2%)		
*Seminal vesicle	(50)	(50)	(50)
Abscess, NOS	1 (2%)		
#Testis	(50)	(49)	(50)
Calcification, focal	17 (34%)	22 (45%)	11 (22%)
Hyperplasia, interstitial cell	1 (2%)		
*Epididymis	(50)	(50)	(50)
Calcification, focal	1 (2%)		
NERVOUS SYSTEM			
#Brain/meninges	(50)	(50)	(49)
Lymphocytic inflammatory infiltrate	1 (2%)	2 (4%)	
Inflammation, chronic	1 (2%)		
#Brain	(50)	(50)	(49)
Calcification, NOS			1 (2%)
Calcification, focal	33 (66%)	20 (40%)	24 (49%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
SPECIAL SENSE ORGANS			
*Nasolacrimal duct	(50)	(50)	(50)
Hemorrhage	1 (2%)		
Inflammation, chronic	1 (2%)		
Hyperplasia, epithelial	2 (4%)		
MUSCULOSKELETAL SYSTEM			
*Maxilla	(50)	(50)	(50)
Abscess, NOS	1 (2%)	1 (2%)	1 (2%)
Inflammation, acute/chronic		1 (2%)	
*Mandible	(50)	(50)	(50)
Granuloma, NOS		1 (2%)	
BODY CAVITIES			
*Mediastinum	(50)	(50)	(50)
Inflammation, chronic		1 (2%)	
Infarct, NOS		1 (2%)	
*Abdominal cavity	(50)	(50)	(50)
Inflammation, suppurative		1 (2%)	
*Pleura	(50)	(50)	(50)
Inflammation, granulomatous focal	1 (2%)		
ALL OTHER SYSTEMS			
*Multiple organs	(50)	(50)	(50)
Lymphocytic inflammatory infiltrate	9 (18%)		
Inflammation, acute/chronic			1 (2%)
Amyloid, NOS			9 (18%)
SPECIAL MORPHOLOGY SUMMARY			
No lesion reported	1		

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

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS MISSING	2	1	
ANIMALS NECROPSIED	48	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	48	49	50
INTEGUMENTARY SYSTEM			
#Skin paint site	(48)	(48)	(50)
Ulcer, NOS		14 (29%)	27 (54%)
Inflammation, acute			1 (2%)
Inflammation, acute/chronic		14 (29%)	26 (52%)
Inflammation, chronic		8 (17%)	9 (18%)
Exfoliative dermatitis		2 (4%)	1 (2%)
Hyperplasia, epithelial		4 (8%)	19 (38%)
Hyperkeratosis			1 (2%)
*Skin	(48)	(49)	(50)
Epidermal inclusion cyst			2 (4%)
Ulcer, NOS		3 (6%)	14 (28%)
Abscess, NOS			1 (2%)
Inflammation, acute/chronic		3 (6%)	13 (26%)
Inflammation, chronic		2 (4%)	6 (12%)
Exfoliative dermatitis		2 (4%)	1 (2%)
Hyperplasia, epithelial		2 (4%)	9 (18%)
*Subcutaneous tissue	(48)	(49)	(50)
Epidermal inclusion cyst			1 (2%)
RESPIRATORY SYSTEM			
*Nasal cavity	(48)	(49)	(50)
Abscess, NOS			1 (2%)
#Lung	(48)	(48)	(50)
Emphysema, NOS			1 (2%)
Atelectasis			3 (6%)
Congestion, NOS	1 (2%)	3 (6%)	4 (8%)
Hemorrhage			1 (2%)
Bronchopneumonia, NOS			1 (2%)
Lymphocytic inflammatory infiltrate	16 (33%)	26 (54%)	15 (30%)
Pneumonia, interstitial chronic		1 (2%)	
Inflammation, chronic focal	1 (2%)		
#Lung/alveoli	(48)	(48)	(50)
Histiocytosis	1 (2%)	2 (4%)	
HEMATOPOIETIC SYSTEM			
#Skin paint site	(48)	(48)	(50)
Mastocytosis			1 (2%)
#Bone marrow	(48)	(44)	(46)
Hyperplasia, NOS	1 (2%)		1 (2%)
Myelofibrosis	41 (85%)	19 (43%)	3 (7%)
Hyperplasia, granulocytic		1 (2%)	14 (30%)
#Spleen	(48)	(47)	(50)
Fibrosis, focal		1 (2%)	
Amyloid, NOS		1 (2%)	6 (12%)
Angiectasis	1 (2%)		
Hyperplasia, lymphoid	2 (4%)	1 (2%)	
Hematopoiesis	1 (2%)	6 (13%)	5 (10%)
#Splenic follicles	(48)	(47)	(50)
Necrosis, NOS			1 (2%)

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM (Continued)			
#Lymph node	(47)	(45)	(45)
Inflammation, acute			1 (2%)
Hyperplasia, NOS			3 (7%)
Plasmacytosis			1 (2%)
Hyperplasia, lymphoid		1 (2%)	
#Mandibular lymph node	(47)	(45)	(45)
Cyst, NOS			1 (2%)
Hyperplasia, NOS		1 (2%)	3 (7%)
Angiectasis			1 (2%)
Plasmacytosis		1 (2%)	4 (9%)
#Tracheal lymph node	(47)	(45)	(45)
Hyperplasia, lymphoid	1 (2%)		
#Mesenteric lymph node	(47)	(45)	(45)
Hyperplasia, lymphoid	1 (2%)		
#Axillary lymph node	(47)	(45)	(45)
Inflammation, suppurative			1 (2%)
Hyperplasia, NOS			7 (16%)
Plasmacytosis			2 (4%)
Hyperplasia, lymphoid		1 (2%)	1 (2%)
#Inguinal lymph node	(47)	(45)	(45)
Inflammation, suppurative			1 (2%)
*Maxilla	(48)	(49)	(50)
Myelofibrosis	1 (2%)		
#Lung	(48)	(48)	(50)
Leukocytosis, NOS			1 (2%)
#Liver	(48)	(49)	(50)
Hyperplasia, granulocytic			1 (2%)
Hematopoiesis		1 (2%)	
#Jejunum	(46)	(45)	(41)
Hyperplasia, lymphoid	1 (2%)		
#Kidney	(48)	(49)	(50)
Hyperplasia, lymphoid			1 (2%)
#Adrenal	(48)	(49)	(49)
Hematopoiesis		1 (2%)	
#Adrenal cortex	(48)	(49)	(49)
Hematopoiesis			2 (4%)
#Thymic lymphocytes	(44)	(38)	(32)
Necrosis, NOS			1 (3%)
CIRCULATORY SYSTEM			
#Mandibular lymph node	(47)	(45)	(45)
Lymphangiectasis			1 (2%)
#Lung	(48)	(48)	(50)
Thrombosis, NOS			1 (2%)
#Heart	(48)	(49)	(50)
Periarteritis		1 (2%)	
#Myocardium	(48)	(49)	(50)
Inflammation, acute/chronic			1 (2%)
Inflammation, chronic focal	1 (2%)		
Fibrosis, focal		1 (2%)	
Degeneration, NOS	1 (2%)	1 (2%)	
Calcification, focal	1 (2%)		
*Aorta	(48)	(49)	(50)
Embolism, NOS			1 (2%)
#Stomach	(48)	(49)	(50)
Periarteritis		1 (2%)	
#Kidney	(48)	(49)	(50)
Periarteritis		1 (2%)	

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM			
*Oral cavity	(48)	(49)	(50)
Abscess, NOS		1 (2%)	
#Salivary gland	(47)	(45)	(50)
Inflammation, chronic		1 (2%)	
#Liver	(48)	(49)	(50)
Lymphocytic inflammatory infiltrate	6 (13%)	3 (6%)	1 (2%)
Necrosis, NOS	1 (2%)	1 (2%)	
Necrosis, focal	4 (8%)	1 (2%)	2 (4%)
Necrosis, coagulative			1 (2%)
Amyloid, NOS		1 (2%)	11 (22%)
Metamorphosis, fatty			1 (2%)
Cytoplasmic vacuolization	1 (2%)		
Basophilic cyto change	2 (4%)		1 (2%)
Ground glass cyto change	2 (4%)	3 (6%)	
Hypertrophy, focal	1 (2%)		
Hyperplasia, focal	1 (2%)		
Angiectasis		1 (2%)	
#Liver/centrilobular	(48)	(49)	(50)
Necrosis, NOS		1 (2%)	
#Pancreas	(48)	(47)	(50)
Inflammation, chronic		2 (4%)	
Inflammation, granulomatous focal	1 (2%)		
Necrosis, NOS			1 (2%)
Atrophy, NOS		1 (2%)	
#Pancreatic acinus	(48)	(47)	(50)
Degeneration, NOS	1 (2%)		
Atrophy, NOS		1 (2%)	
#Stomach	(48)	(49)	(50)
Ulcer, acute			1 (2%)
#Glandular stomach	(48)	(49)	(50)
Atrophy, NOS			1 (2%)
#Forestomach	(48)	(49)	(50)
Ulcer, NOS	1 (2%)		
#Gastric fundus	(48)	(49)	(50)
Hyperplasia, epithelial			1 (2%)
#Small intestine	(46)	(45)	(41)
Amyloid, NOS		1 (2%)	
URINARY SYSTEM			
#Kidney	(48)	(49)	(50)
Hydronephrosis			1 (2%)
Lymphocytic inflammatory infiltrate	28 (58%)	20 (41%)	13 (26%)
Inflammation, suppurative			1 (2%)
Pyelonephritis, acute			2 (4%)
Inflammation, chronic			2 (4%)
Granuloma, pyogenic			3 (6%)
Nephropathy			1 (2%)
Amyloid, NOS		1 (2%)	12 (24%)
Atrophy, NOS			1 (2%)
Atrophy, focal	1 (2%)		
#Kidney/cortex	(48)	(49)	(50)
Atrophy, NOS		1 (2%)	1 (2%)
Atrophy, focal	2 (4%)	2 (4%)	
#Renal papilla	(48)	(49)	(50)
Necrosis, NOS			2 (4%)
#Perirenal tissue	(48)	(49)	(50)
Hemorrhagic cyst		1 (2%)	

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
URINARY SYSTEM (Continued)			
#Kidney/tubule	(48)	(49)	(50)
Dilatation, NOS		1 (2%)	1 (2%)
Pigmentation, NOS			1 (2%)
#Kidney/pelvis	(48)	(49)	(50)
Dilatation, NOS		2 (4%)	1 (2%)
#Urinary bladder	(45)	(46)	(44)
Lymphocytic inflammatory infiltrate	22 (49%)	24 (52%)	17 (39%)
Inflammation, suppurative			1 (2%)
Hyperplasia, epithelial			1 (2%)
ENDOCRINE SYSTEM			
#Anterior pituitary	(46)	(42)	(43)
Hyperplasia, focal	16 (35%)	8 (19%)	3 (7%)
Angiectasis	3 (7%)	1 (2%)	
#Adrenal	(48)	(49)	(49)
Congestion, NOS			2 (4%)
#Adrenal/capsule	(48)	(49)	(49)
Hyperplasia, NOS	46 (96%)	49 (100%)	44 (90%)
#Adrenal cortex	(48)	(49)	(49)
Degeneration, lipoid	2 (4%)	2 (4%)	
Necrosis, focal			1 (2%)
Amyloid, NOS			2 (4%)
Hypertrophy, focal	1 (2%)		1 (2%)
#Adrenal medulla	(48)	(49)	(49)
Fibrosis, focal	1 (2%)		
Hyperplasia, focal	1 (2%)		
Angiectasis			1 (2%)
#Thyroid	(47)	(46)	(46)
Amyloid, NOS			1 (2%)
Hyperplasia, C-cell	1 (2%)		
Hyperplasia, follicular cell	4 (9%)	3 (7%)	
#Parathyroid	(30)	(23)	(18)
Cyst, NOS	2 (7%)		
REPRODUCTIVE SYSTEM			
*Mammary gland	(48)	(49)	(50)
Galactocele		1 (2%)	1 (2%)
Hyperplasia, cystic			3 (6%)
Lactation		3 (6%)	6 (12%)
*Mammary lobule	(48)	(49)	(50)
Hyperplasia, NOS	1 (2%)	1 (2%)	
#Uterus	(48)	(48)	(49)
Hemorrhagic cyst		1 (2%)	
Inflammation, suppurative	1 (2%)		
#Uterus/endometrium	(48)	(48)	(49)
Hyperplasia, cystic	45 (94%)	41 (85%)	23 (47%)
Hyperplasia, stromal			2 (4%)
#Ovary	(47)	(48)	(47)
Cyst, NOS	13 (28%)	7 (15%)	4 (9%)
Hemorrhagic cyst	3 (6%)	3 (6%)	3 (6%)
Atrophy, NOS	30 (64%)	19 (40%)	7 (15%)
NERVOUS SYSTEM			
#Brain/meninges	(48)	(49)	(50)
Lymphocytic inflammatory infiltrate	1 (2%)	1 (2%)	
Perivascular cuffing		1 (2%)	
#Cerebral ventricle	(48)	(49)	(50)
Dilatation, NOS			1 (2%)

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM (Continued)			
#Lateral ventricle	(48)	(49)	(50)
Dilatation, NOS			1 (2%)
#Brain	(48)	(49)	(50)
Hydrocephalus, NOS		1 (2%)	
Congestion, NOS			1 (2%)
Malacia		1 (2%)	
Calcification, focal	9 (19%)	15 (31%)	18 (36%)
#Brain stem	(48)	(49)	(50)
Demyelinization		1 (2%)	
SPECIAL SENSE ORGANS			
*Nasolacrimal duct	(48)	(49)	(50)
Inflammation, chronic		1 (2%)	
MUSCULOSKELETAL SYSTEM			
*Maxilla	(48)	(49)	(50)
Abscess, NOS			2 (4%)
*Sternum	(48)	(49)	(50)
Necrosis, NOS		1 (2%)	
*Skeletal muscle	(48)	(49)	(50)
Inflammation, suppurative			1 (2%)
BODY CAVITIES			
*Abdominal cavity	(48)	(49)	(50)
Inflammation, acute/chronic			1 (2%)
Granuloma, NOS	1 (2%)		
Necrosis, fat	2 (4%)		
*Epicardium	(48)	(49)	(50)
Lymphocytic inflammatory infiltrate		1 (2%)	
ALL OTHER SYSTEMS			
*Multiple organs	(48)	(49)	(50)
Lymphocytic inflammatory infiltrate	8 (17%)	6 (12%)	1 (2%)
Amyloid, NOS			17 (34%)
SPECIAL MORPHOLOGY SUMMARY			
Animal missing/no necropsy	2	1	

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

APPENDIX E

ANALYSES OF PRIMARY TUMORS IN MICE IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL AND JP-5 NAVY FUEL

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL

	Vehicle Control	250 mg/kg	500 mg/kg
Skin, Application Site: Squamous Cell Papilloma or Carcinoma			
Overall Rates (a)	0/49 (0%)	0/49 (0%)	3/49 (6%)
Adjusted Rates (b)	0.0%	0.0%	11.5%
Terminal Rates (c)	0/30 (0%)	0/19 (0%)	3/26 (12%)
Week of First Observation			84
Life Table Tests (d)	P=0.019	(e)	P=0.073
Incidental Tumor Tests (d)	P=0.019	(e)	P=0.073
Cochran-Armitage Trend Test (d)	P=0.037		
Fisher Exact Test (d)		(e)	P=0.121
Integumentary System: Squamous Cell Papilloma or Carcinoma			
Overall Rates (a)	1/50 (2%)	2/49 (4%)	3/50 (6%)
Adjusted Rates (b)	2.8%	5.3%	11.5%
Terminal Rates (c)	1/30 (3%)	1/19 (5%)	3/26 (12%)
Week of First Observation	105	101	84
Life Table Tests (d)	P=0.130	P=0.519	P=0.196
Incidental Tumor Tests (d)	P=0.130	P=0.519	P=0.196
Cochran-Armitage Trend Test (d)	P=0.223		
Fisher Exact Test (d)		P=0.492	P=0.309
Subcutaneous Tissue: Fibroma			
Overall Rates (a)	3/50 (6%)	0/49 (0%)	0/50 (0%)
Adjusted Rates (b)	8.3%	0.0%	0.0%
Terminal Rates (c)	3/30 (10%)	0/19 (0%)	0/26 (0%)
Week of First Observation	105		
Life Table Tests (d)	P=0.050N	P=0.111N	P=0.184N
Incidental Tumor Tests (d)	P=0.050N	P=0.111N	P=0.184N
Cochran-Armitage Trend Test (d)	P=0.038N		
Fisher Exact Test (d)		P=0.125N	P=0.121N
Integumentary System: Fibrosarcoma			
Overall Rates (a)	11/50 (22%)	4/49 (8%)	3/50 (6%)
Adjusted Rates (b)	28.9%	10.5%	7.0%
Terminal Rates (c)	4/30 (13%)	1/19 (5%)	0/26 (0%)
Week of First Observation	74	92	55
Life Table Tests (d)	P=0.028N	P=0.036N	P=0.064N
Incidental Tumor Tests (d)	P=0.005N	P=0.034N	P=0.007N
Cochran-Armitage Trend Test (d)	P=0.011N		
Fisher Exact Test (d)		P=0.049N	P=0.020N
Integumentary System: Fibroma or Fibrosarcoma			
Overall Rates (a)	13/50 (26%)	4/49 (8%)	3/50 (6%)
Adjusted Rates (b)	34.2%	10.5%	7.0%
Terminal Rates (c)	6/30 (20%)	1/19 (5%)	0/26 (0%)
Week of First Observation	74	92	55
Life Table Tests (d)	P=0.009N	P=0.012N	P=0.029N
Incidental Tumor Tests (d)	P=0.001N	P=0.011N	P=0.003N
Cochran-Armitage Trend Test (d)	P=0.003N		
Fisher Exact Test (d)		P=0.017N	P=0.006N
Integumentary System: Sarcoma or Fibrosarcoma			
Overall Rates (a)	11/50 (22%)	5/49 (10%)	3/50 (6%)
Adjusted Rates (b)	28.9%	13.2%	7.0%
Terminal Rates (c)	4/30 (13%)	1/19 (5%)	0/26 (0%)
Week of First Observation	74	92	55
Life Table Tests (d)	P=0.032N	P=0.068N	P=0.064N
Incidental Tumor Tests (d)	P=0.006N	P=0.066N	P=0.007N
Cochran-Armitage Trend Test (d)	P=0.012N		
Fisher Exact Test (d)		P=0.093N	P=0.020N

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	Vehicle Control	250 mg/kg	500 mg/kg
Integumentary System: Fibroma, Sarcoma, or Fibrosarcoma			
Overall Rates (a)	13/50 (26%)	5/49 (10%)	3/50 (6%)
Adjusted Rates (b)	34.2%	13.2%	7.0%
Terminal Rates (c)	6/30 (20%)	1/19 (5%)	0/26 (0%)
Week of First Observation	74	92	55
Life Table Tests (d)	P=0.011N	P=0.025N	P=0.029N
Incidental Tumor Tests (d)	P=0.002N	P=0.024N	P=0.003N
Cochran-Armitage Trend Test (d)	P=0.003N		
Fisher Exact Test (d)		P=0.037N	P=0.006N
Lung: Alveolar/Bronchiolar Adenoma			
Overall Rates (a)	4/50 (8%)	5/49 (10%)	2/49 (4%)
Adjusted Rates (b)	10.7%	12.6%	7.7%
Terminal Rates (c)	3/30 (10%)	3/19 (16%)	2/26 (8%)
Week of First Observation	76	77	84
Life Table Tests (d)	P=0.426N	P=0.545	P=0.487N
Incidental Tumor Tests (d)	P=0.291N	P=0.545	P=0.382N
Cochran-Armitage Trend Test (d)	P=0.292N		
Fisher Exact Test (d)		P=0.487	P=0.349N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates (a)	4/50 (8%)	7/49 (14%)	2/49 (4%)
Adjusted Rates (b)	10.7%	17.7%	7.7%
Terminal Rates (c)	3/30 (10%)	3/19 (16%)	2/26 (8%)
Week of First Observation	76	77	84
Life Table Tests (d)	P=0.461N	P=0.304	P=0.487N
Incidental Tumor Tests (d)	P=0.331N	P=0.303	P=0.382N
Cochran-Armitage Trend Test (d)	P=0.308N		
Fisher Exact Test (d)		P=0.251	P=0.349N
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (a)	5/50 (10%)	5/49 (10%)	1/50 (2%)
Adjusted Rates (b)	13.9%	13.2%	3.8%
Terminal Rates (c)	5/30 (17%)	0/19 (0%)	1/26 (4%)
Week of First Observation	105	89	84
Life Table Tests (d)	P=0.164N	P=0.597N	P=0.190N
Incidental Tumor Tests (d)	P=0.164N	P=0.597N	P=0.190N
Cochran-Armitage Trend Test (d)	P=0.090N		
Fisher Exact Test (d)		P=0.617	P=0.102N
Circulatory System: Hemangioma or Hemangiosarcoma			
Overall Rates (a)	4/50 (8%)	2/49 (4%)	2/50 (4%)
Adjusted Rates (b)	11.1%	5.3%	6.6%
Terminal Rates (c)	3/30 (10%)	1/19 (5%)	1/26 (4%)
Week of First Observation	98	87	71
Life Table Tests (d)	P=0.361N	P=0.311N	P=0.476N
Incidental Tumor Tests (d)	P=0.290N	P=0.311N	P=0.382N
Cochran-Armitage Trend Test (d)	P=0.253N		
Fisher Exact Test (d)		P=0.349N	P=0.339N
Liver: Hepatocellular Adenoma			
Overall Rates (a)	5/50 (10%)	10/48 (21%)	10/49 (20%)
Adjusted Rates (b)	13.5%	26.1%	32.0%
Terminal Rates (c)	3/30 (10%)	5/19 (26%)	7/26 (27%)
Week of First Observation	76	77	61
Life Table Tests (d)	P=0.034	P=0.152	P=0.052
Incidental Tumor Tests (d)	P=0.100	P=0.150	P=0.134
Cochran-Armitage Trend Test (d)	P=0.106		
Fisher Exact Test (d)		P=0.113	P=0.122

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	Vehicle Control	250 mg/kg	500 mg/kg
Liver: Hepatocellular Carcinoma			
Overall Rates (a)	5/50 (10%)	9/48 (19%)	5/49 (10%)
Adjusted Rates (b)	13.3%	22.2%	19.2%
Terminal Rates (c)	2/30 (7%)	4/19 (21%)	5/26 (19%)
Week of First Observation	66	67	84
Life Table Tests (d)	P=0.357	P=0.228	P=0.439
Incidental Tumor Tests (d)	P=0.557N	P=0.226	P=0.507
Cochran-Armitage Trend Test (d)	P=0.544		
Fisher Exact Test (d)		P=0.172	P=0.617
Liver: Hepatocellular Adenoma or Carcinoma			
Overall Rates (a)	9/50 (18%)	17/48 (35%)	14/49 (29%)
Adjusted Rates (b)	23.5%	41.1%	46.3%
Terminal Rates (c)	5/30 (17%)	8/19 (42%)	11/26 (42%)
Week of First Observation	66	67	61
Life Table Tests (d)	P=0.035	P=0.080	P=0.048
Incidental Tumor Tests (d)	P=0.162	P=0.071	P=0.134
Cochran-Armitage Trend Test (d)	P=0.141		
Fisher Exact Test (d)		P=0.042	P=0.157
Adrenal Gland: Pheochromocytoma			
Overall Rates (a)	3/49 (6%)	0/48 (0%)	0/49 (0%)
Adjusted Rates (b)	8.0%	0.0%	0.0%
Terminal Rates (c)	2/30 (7%)	0/19 (0%)	0/26 (0%)
Week of First Observation	76		
Life Table Tests (d)	P=0.050N	P=0.113N	P=0.180N
Incidental Tumor Tests (d)	P=0.024N	P=0.112N	P=0.091N
Cochran-Armitage Trend Test (d)	P=0.038N		
Fisher Exact Test (d)		P=0.125N	P=0.121N
Harderian Gland: Adenoma			
Overall Rates (a)	3/50 (6%)	1/49 (2%)	0/50 (0%)
Adjusted Rates (b)	8.3%	2.6%	0.0%
Terminal Rates (c)	3/30 (10%)	1/19 (5%)	0/26 (0%)
Week of First Observation	105	105	
Life Table Tests (d)	P=0.086N	P=0.286N	P=0.184N
Incidental Tumor Tests (d)	P=0.086N	P=0.286N	P=0.184N
Cochran-Armitage Trend Test (d)	P=0.061N		
Fisher Exact Test (d)		P=0.316N	P=0.121N

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence at week 105 for the vehicle control and 250 mg/kg groups and week 84 for the 500 mg/kg group
(d) Beneath the vehicle control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the vehicle controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).
(e) No P value is reported because no tumors were observed in the 250 mg/kg and vehicle control groups.

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL

	Vehicle Control	250 mg/kg	500 mg/kg
Application Site: Squamous Cell Carcinoma			
Overall Rates (a)	0/50 (0%)	1/45 (2%)	2/48 (4%)
Adjusted Rates (b)	0.0%	4.3%	6.1%
Terminal Rates (c)	2/40 (0%)	1/12 (8%)	1/29 (3%)
Week of First Observation		84	74
Life Table Tests (d)	P=0.090	P=0.353	P=0.160
Incidental Tumor Tests (d)	P=0.122	P=0.353	P=0.359
Cochran-Armitage Trend Test (d)	P=0.139		
Fisher Exact Test (d)		P=0.474	P=0.237
Integumentary System: Sarcoma, Fibrosarcoma, or Neurofibrosarcoma			
Overall Rates (a)	3/50 (6%)	1/45 (2%)	1/50 (2%)
Adjusted Rates (b)	6.3%	3.7%	3.4%
Terminal Rates (c)	2/40 (5%)	0/12 (0%)	1/29 (3%)
Week of First Observation	101	81	84
Life Table Tests (d)	P=0.382N	P=0.572N	P=0.497N
Incidental Tumor Tests (d)	P=0.267N	P=0.305N	P=0.497N
Cochran-Armitage Trend Test (d)	P=0.206N		
Fisher Exact Test (d)		P=0.349N	P=0.309N
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (a)	14/50 (28%)	4/45 (9%)	5/50 (10%)
Adjusted Rates (b)	29.2%	16.3%	14.9%
Terminal Rates (c)	12/40 (30%)	0/12 (0%)	3/29 (10%)
Week of First Observation	97	81	32
Life Table Tests (d)	P=0.121N	P=0.219N	P=0.172N
Incidental Tumor Tests (d)	P=0.047N	P=0.126N	P=0.068N
Cochran-Armitage Trend Test (d)	P=0.010N		
Fisher Exact Test (d)		P=0.016N	P=0.020N
Circulatory System: Hemangiosarcoma			
Overall Rates (a)	3/50 (6%)	0/45 (0%)	0/50 (0%)
Adjusted Rates (b)	6.3%	0.0%	0.0%
Terminal Rates (c)	3/40 (8%)	0/12 (0%)	0/29 (0%)
Week of First Observation	105		
Life Table Tests (d)	P=0.094N	P=0.277N	P=0.223N
Incidental Tumor Tests (d)	P=0.094N	P=0.277N	P=0.223N
Cochran-Armitage Trend Test (d)	P=0.040N		
Fisher Exact Test (d)		P=0.142N	P=0.121N
Liver: Hepatocellular Adenoma			
Overall Rates (a)	4/50 (8%)	2/45 (4%)	2/50 (4%)
Adjusted Rates (b)	8.3%	8.7%	5.9%
Terminal Rates (c)	4/40 (10%)	2/12 (17%)	0/29 (0%)
Week of First Observation	105	105	76
Life Table Tests (d)	P=0.483N	P=0.656	P=0.558N
Incidental Tumor Tests (d)	P=0.309N	P=0.656	P=0.197N
Cochran-Armitage Trend Test (d)	P=0.256N		
Fisher Exact Test (d)		P=0.390N	P=0.339N
Liver: Hepatocellular Carcinoma			
Overall Rates (a)	0/50 (0%)	2/45 (4%)	3/50 (6%)
Adjusted Rates (b)	0.0%	8.7%	10.3%
Terminal Rates (c)	0/40 (0%)	0/12 (0%)	3/29 (10%)
Week of First Observation		90	84
Life Table Tests (d)	P=0.033	P=0.097	P=0.049
Incidental Tumor Tests (d)	P=0.033	P=0.097	P=0.049
Cochran-Armitage Trend Test (d)	P=0.085		
Fisher Exact Test (d)		P=0.222	P=0.121

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF MARINE DIESEL FUEL (Continued)

	Vehicle Control	250 mg/kg	500 mg/kg
Liver: Hepatocellular Adenoma or Carcinoma			
Overall Rates (a)	4/50 (8%)	4/45 (9%)	5/50 (10%)
Adjusted Rates (b)	8.3%	17.4%	15.6%
Terminal Rates (c)	4/40 (10%)	2/12 (17%)	3/29 (10%)
Week of First Observation	105	90	76
Life Table Tests (d)	P=0.167	P=0.235	P=0.230
Incidental Tumor Tests (d)	P=0.253	P=0.235	P=0.498
Cochran-Armitage Trend Test (d)	P=0.431		
Fisher Exact Test (d)		P=0.582	P=0.500
Pituitary Gland: Adenoma			
Overall Rates (a)	5/49 (10%)	2/44 (5%)	1/46 (2%)
Adjusted Rates (b)	10.6%	9.1%	3.6%
Terminal Rates (c)	4/39 (10%)	2/11 (18%)	1/28 (4%)
Week of First Observation	94	105	84
Life Table Tests (d)	P=0.204N	P=0.590N	P=0.259N
Incidental Tumor Tests (d)	P=0.204N	P=0.590N	P=0.259N
Cochran-Armitage Trend Test (d)	P=0.071N		
Fisher Exact Test (d)		P=0.264N	P=0.117N
Uterus: Endometrial Stromal Polyp			
Overall Rates (a)	3/50 (6%)	0/45 (0%)	0/50 (0%)
Adjusted Rates (b)	6.3%	0.0%	0.0%
Terminal Rates (c)	2/40 (5%)	0/12 (0%)	0/29 (0%)
Week of First Observation	102		
Life Table Tests (d)	P=0.094N	P=0.277N	P=0.223N
Incidental Tumor Tests (d)	P=0.094N	P=0.277N	P=0.223N
Cochran-Armitage Trend Test (d)	P=0.040N		
Fisher Exact Test (d)		P=0.142N	P=0.121N

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence at week 105 for the vehicle control and 250 mg/kg groups and week 84 for the 500 mg/kg group
(d) Beneath the vehicle control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the vehicle controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL

	Vehicle Control	250 mg/kg	500 mg/kg
Subcutaneous Tissue: Sarcoma			
Overall Rates (a)	1/50 (2%)	4/50 (8%)	1/49 (2%)
Adjusted Rates (b)	2.3%	10.3%	2.7%
Terminal Rates (c)	0/36 (0%)	1/33 (3%)	0/28 (0%)
Week of First Observation	84	80	91
Life Table Tests (d)	P=0.552	P=0.171	P=0.746
Incidental Tumor Tests (d)	P=0.314N	P=0.322	P=0.347N
Cochran-Armitage Trend Test (d)	P=0.593		
Fisher Exact Test (d)		P=0.181	P=0.747
Subcutaneous Tissue: Fibrosarcoma			
Overall Rates (a)	1/50 (2%)	3/50 (6%)	0/49 (0%)
Adjusted Rates (b)	2.8%	8.1%	0.0%
Terminal Rates (c)	1/36 (3%)	2/33 (6%)	0/28 (0%)
Week of First Observation	105	83	
Life Table Tests (d)	P=0.436N	P=0.284	P=0.550N
Incidental Tumor Tests (d)	P=0.324N	P=0.381	P=0.550N
Cochran-Armitage Trend Test (d)	P=0.384N		
Fisher Exact Test (d)		P=0.309	P=0.505N
Subcutaneous Tissue: Fibroma or Fibrosarcoma			
Overall Rates (a)	2/50 (4%)	4/50 (8%)	0/49 (0%)
Adjusted Rates (b)	5.6%	11.1%	0.0%
Terminal Rates (c)	2/36 (6%)	3/33 (9%)	0/28 (0%)
Week of First Observation	105	83	
Life Table Tests (d)	P=0.287N	P=0.305	P=0.295N
Incidental Tumor Tests (d)	P=0.208N	P=0.388	P=0.295N
Cochran-Armitage Trend Test (d)	P=0.228N		
Fisher Exact Test (d)		P=0.339	P=0.253N
Subcutaneous Tissue: Fibroma, Sarcoma, or Fibrosarcoma			
Overall Rates (a)	3/50 (6%)	8/50 (16%)	1/49 (2%)
Adjusted Rates (b)	7.7%	20.5%	2.7%
Terminal Rates (c)	2/36 (6%)	4/33 (12%)	0/28 (0%)
Week of First Observation	84	80	91
Life Table Tests (d)	P=0.379N	P=0.091	P=0.365N
Incidental Tumor Tests (d)	P=0.128N	P=0.193	P=0.105N
Cochran-Armitage Trend Test (d)	P=0.300N		
Fisher Exact Test (d)		P=0.100	P=0.316N
Lung: Alveolar/Bronchiolar Adenoma			
Overall Rates (a)	3/50 (6%)	4/49 (8%)	2/48 (4%)
Adjusted Rates (b)	8.3%	12.1%	7.1%
Terminal Rates (c)	3/36 (8%)	4/33 (12%)	2/28 (7%)
Week of First Observation	105	105	105
Life Table Tests (d)	P=0.542N	P=0.452	P=0.615N
Incidental Tumor Tests (d)	P=0.542N	P=0.452	P=0.615N
Cochran-Armitage Trend Test (d)	P=0.437N		
Fisher Exact Test (d)		P=0.489	P=0.520N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates (a)	5/50 (10%)	5/49 (10%)	4/48 (8%)
Adjusted Rates (b)	13.9%	14.0%	12.6%
Terminal Rates (c)	5/36 (14%)	4/33 (12%)	3/28 (11%)
Week of First Observation	105	76	80
Life Table Tests (d)	P=0.564N	P=0.585	P=0.635N
Incidental Tumor Tests (d)	P=0.562	P=0.581	P=0.548N
Cochran-Armitage Trend Test (d)	P=0.458N		
Fisher Exact Test (d)		P=0.617	P=0.526N

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	Vehicle Control	250 mg/kg	500 mg/kg
Hematopoietic System: Malignant Lymphoma, Undifferentiated Type			
Overall Rates (a)	3/50 (6%)	0/50 (0%)	0/49 (0%)
Adjusted Rates (b)	8.0%	0.0%	0.0%
Terminal Rates (c)	2/36 (6%)	0/33 (0%)	0/28 (0%)
Week of First Observation	103		
Life Table Tests (d)	P=0.052N	P=0.138N	P=0.165N
Incidental Tumor Tests (d)	P=0.045N	P=0.133N	P=0.144N
Cochran-Armitage Trend Test (d)	P=0.038N		
Fisher Exact Test (d)		P=0.121N	P=0.125N
Hematopoietic System: Malignant Lymphoma, Mixed Type			
Overall Rates (a)	3/50 (6%)	0/50 (0%)	0/49 (0%)
Adjusted Rates (b)	7.8%	0.0%	0.0%
Terminal Rates (c)	2/36 (6%)	0/33 (0%)	0/28 (0%)
Week of First Observation	94		
Life Table Tests (d)	P=0.052N	P=0.138N	P=0.166N
Incidental Tumor Tests (d)	P=0.045N	P=0.133N	P=0.144N
Cochran-Armitage Trend Test (d)	P=0.038N		
Fisher Exact Test (d)		P=0.121N	P=0.125N
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (a)	8/50 (16%)	3/50 (6%)	1/49 (2%)
Adjusted Rates (b)	20.7%	8.3%	3.4%
Terminal Rates (c)	6/36 (17%)	2/33 (6%)	0/28 (0%)
Week of First Observation	94	92	104
Life Table Tests (d)	P=0.020N	P=0.132N	P=0.043N
Incidental Tumor Tests (d)	P=0.008N	P=0.088N	P=0.027N
Cochran-Armitage Trend Test (d)	P=0.009N		
Fisher Exact Test (d)		P=0.100N	P=0.017N
Hematopoietic System: Lymphoma or Leukemia			
Overall Rates (a)	9/50 (18%)	3/50 (6%)	1/49 (2%)
Adjusted Rates (b)	22.6%	8.3%	3.4%
Terminal Rates (c)	6/36 (17%)	2/33 (6%)	0/28 (0%)
Week of First Observation	94	92	104
Life Table Tests (d)	P=0.011N	P=0.087N	P=0.027N
Incidental Tumor Tests (d)	P=0.003N	P=0.053N	P=0.013N
Cochran-Armitage Trend Test (d)	P=0.004N		
Fisher Exact Test (d)		P=0.061N	P=0.009N
Circulatory System: Hemangiosarcoma			
Overall Rates (a)	1/50 (2%)	4/50 (8%)	3/49 (6%)
Adjusted Rates (b)	2.5%	11.4%	8.2%
Terminal Rates (c)	0/36 (0%)	3/33 (9%)	1/28 (4%)
Week of First Observation	102	96	80
Life Table Tests (d)	P=0.191	P=0.158	P=0.260
Incidental Tumor Tests (d)	P=0.286	P=0.164	P=0.435
Cochran-Armitage Trend Test (d)	P=0.244		
Fisher Exact Test (d)		P=0.181	P=0.301
Circulatory System: Hemangioma or Hemangiosarcoma			
Overall Rates (a)	1/50 (2%)	4/50 (8%)	4/49 (8%)
Adjusted Rates (b)	2.5%	11.4%	10.3%
Terminal Rates (c)	0/36 (0%)	3/33 (9%)	1/28 (4%)
Week of First Observation	102	96	80
Life Table Tests (d)	P=0.109	P=0.158	P=0.154
Incidental Tumor Tests (d)	P=0.216	P=0.164	P=0.378
Cochran-Armitage Trend Test (d)	P=0.140		
Fisher Exact Test (d)		P=0.181	P=0.175

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	Vehicle Control	250 mg/kg	500 mg/kg
Liver: Hepatocellular Adenoma			
Overall Rates (a)	7/50 (14%)	6/50 (12%)	10/49 (20%)
Adjusted Rates (b)	19.4%	15.9%	27.4%
Terminal Rates (c)	7/36 (19%)	3/33 (9%)	4/28 (14%)
Week of First Observation	105	91	84
Life Table Tests (d)	P=0.141	P=0.557N	P=0.172
Incidental Tumor Tests (d)	P=0.320	P=0.486N	P=0.380
Cochran-Armitage Trend Test (d)	P=0.230		
Fisher Exact Test (d)		P=0.500N	P=0.282
Liver: Hepatocellular Carcinoma			
Overall Rates (a)	10/50 (20%)	10/50 (20%)	8/49 (16%)
Adjusted Rates (b)	25.1%	25.5%	22.7%
Terminal Rates (c)	7/36 (19%)	6/33 (18%)	3/28 (11%)
Week of First Observation	83	69	84
Life Table Tests (d)	P=0.523N	P=0.533	P=0.570N
Incidental Tumor Tests (d)	P=0.269N	P=0.470N	P=0.277N
Cochran-Armitage Trend Test (d)	P=0.368N		
Fisher Exact Test (d)		P=0.598	P=0.416N
Liver: Hepatocellular Adenoma or Carcinoma			
Overall Rates (a)	13/50 (26%)	14/50 (28%)	17/49 (35%)
Adjusted Rates (b)	32.8%	34.7%	43.9%
Terminal Rates (c)	10/36 (28%)	8/33 (24%)	7/28 (25%)
Week of First Observation	83	69	84
Life Table Tests (d)	P=0.103	P=0.423	P=0.120
Incidental Tumor Tests (d)	P=0.296	P=0.582N	P=0.396
Cochran-Armitage Trend Test (d)	P=0.202		
Fisher Exact Test (d)		P=0.500	P=0.235
Adrenal: Pheochromocytoma			
Overall Rates (a)	2/50 (4%)	0/49 (0%)	3/49 (6%)
Adjusted Rates (b)	5.6%	0.0%	9.3%
Terminal Rates (c)	2/36 (6%)	0/33 (0%)	1/28 (4%)
Week of First Observation	105		98
Life Table Tests (d)	P=0.317	P=0.258N	P=0.403
Incidental Tumor Tests (d)	P=0.357	P=0.258N	P=0.456
Cochran-Armitage Trend Test (d)	P=0.383		
Fisher Exact Test (d)		P=0.253N	P=0.490

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

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL

	Vehicle Control	250 mg/kg	500 mg/kg
Lung: Alveolar/Bronchiolar Carcinoma			
Overall Rates (a)	3/48 (6%)	1/48 (2%)	0/47 (0%)
Adjusted Rates (b)	6.4%	2.3%	0.0%
Terminal Rates (c)	3/44 (7%)	1/33 (3%)	0/17 (0%)
Week of First Observation	105	105	
Life Table Tests (d)	P=0.166N	P=0.338N	P=0.347N
Incidental Tumor Tests (d)	P=0.166N	P=0.338N	P=0.347N
Cochran-Armitage Trend Test (d)	P=0.062N		
Fisher Exact Test (d)		P=0.308N	P=0.125N
Hematopoietic System: Malignant Lymphoma, Undifferentiated Type			
Overall Rates (a)	1/48 (2%)	3/49 (6%)	1/47 (2%)
Adjusted Rates (b)	2.1%	6.8%	5.9%
Terminal Rates (c)	1/44 (2%)	3/33 (9%)	1/17 (6%)
Week of First Observation	105	105	90
Life Table Tests (d)	P=0.286	P=0.282	P=0.520
Incidental Tumor Tests (d)	P=0.286	P=0.282	P=0.520
Cochran-Armitage Trend Test (d)	P=0.603		
Fisher Exact Test (d)		P=0.316	P=0.747
Hematopoietic System: Malignant Lymphoma, Lymphocytic Type			
Overall Rates (a)	2/48 (4%)	7/49 (14%)	1/47 (2%)
Adjusted Rates (b)	4.3%	15.9%	3.8%
Terminal Rates (c)	1/44 (2%)	6/33 (18%)	0/17 (0%)
Week of First Observation	104	97	83
Life Table Tests (d)	P=0.296	P=0.067	P=0.688
Incidental Tumor Tests (d)	P=0.465	P=0.067	P=0.503N
Cochran-Armitage Trend Test (d)	P=0.431N		
Fisher Exact Test (d)		P=0.084	P=0.508N
Hematopoietic System: Malignant Lymphoma, Histiocytic Type			
Overall Rates (a)	2/48 (4%)	6/49 (12%)	0/47 (0%)
Adjusted Rates (b)	4.3%	13.2%	0.0%
Terminal Rates (c)	1/44 (2%)	2/33 (6%)	0/17 (0%)
Week of First Observation	97	85	
Life Table Tests (d)	P=0.567	P=0.119	P=0.480N
Incidental Tumor Tests (d)	P=0.423N	P=0.163	P=0.480N
Cochran-Armitage Trend Test (d)	P=0.259N		
Fisher Exact Test (d)		P=0.141	P=0.253N
Hematopoietic System: Malignant Lymphoma, Mixed Type			
Overall Rates (a)	1/48 (2%)	3/49 (6%)	2/47 (4%)
Adjusted Rates (b)	2.1%	6.6%	6.1%
Terminal Rates (c)	1/44 (2%)	1/33 (3%)	0/17 (0%)
Week of First Observation	105	85	76
Life Table Tests (d)	P=0.162	P=0.288	P=0.303
Incidental Tumor Tests (d)	P=0.471N	P=0.396	P=0.725N
Cochran-Armitage Trend Test (d)	P=0.390		
Fisher Exact Test (d)		P=0.316	P=0.492
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (a)	7/48 (15%)	19/49 (39%)	5/47 (11%)
Adjusted Rates (b)	14.6%	41.2%	20.3%
Terminal Rates (c)	4/44 (9%)	12/33 (36%)	2/17 (12%)
Week of First Observation	88	85	76
Life Table Tests (d)	P=0.064	P=0.004	P=0.270
Incidental Tumor Tests (d)	P=0.551	P=0.010	P=0.347N
Cochran-Armitage Trend Test (d)	P=0.374N		
Fisher Exact Test (d)		P=0.006	P=0.395N

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF JP-5 NAVY FUEL (Continued)

	Vehicle Control	250 mg/kg	500 mg/kg
Liver: Hepatocellular Adenoma			
Overall Rates (a)	2/48 (4%)	4/49 (8%)	2/47 (4%)
Adjusted Rates (b)	4.3%	9.1%	8.1%
Terminal Rates (c)	2/44 (5%)	4/33 (12%)	1/17 (6%)
Week of First Observation	105	105	61
Life Table Tests (d)	P=0.230	P=0.307	P=0.397
Incidental Tumor Tests (d)	P=0.370	P=0.307	P=0.632
Cochran-Armitage Trend Test (d)	P=0.579		
Fisher Exact Test (d)		P=0.349	P=0.684
Liver: Hepatocellular Carcinoma			
Overall Rates (a)	1/48 (2%)	3/49 (6%)	2/47 (4%)
Adjusted Rates (b)	2.1%	6.8%	9.5%
Terminal Rates (c)	1/44 (2%)	0/33 (0%)	1/17 (6%)
Week of First Observation	105	99	83
Life Table Tests (d)	P=0.118	P=0.282	P=0.215
Incidental Tumor Tests (d)	P=0.256	P=0.282	P=0.497
Cochran-Armitage Trend Test (d)	P=0.390		
Fisher Exact Test (d)		P=0.316	P=0.492
Liver: Hepatocellular Adenoma or Carcinoma			
Overall Rates (a)	3/48 (6%)	7/49 (14%)	4/47 (9%)
Adjusted Rates (b)	6.4%	15.9%	17.2%
Terminal Rates (c)	3/44 (7%)	4/33 (12%)	2/17 (12%)
Week of First Observation	105	99	61
Life Table Tests (d)	P=0.060	P=0.133	P=0.125
Incidental Tumor Tests (d)	P=0.183	P=0.133	P=0.403
Cochran-Armitage Trend Test (d)	P=0.418		
Fisher Exact Test (d)		P=0.167	P=0.488
Pituitary Gland: Adenoma			
Overall Rates (a)	6/46 (13%)	6/42 (14%)	0/41 (0%)
Adjusted Rates (b)	13.3%	15.8%	0.0%
Terminal Rates (c)	5/42 (12%)	4/28 (14%)	0/16 (0%)
Week of First Observation	104	102	
Life Table Tests (d)	P=0.202N	P=0.499	P=0.149N
Incidental Tumor Tests (d)	P=0.202N	P=0.499	P=0.149N
Cochran-Armitage Trend Test (d)	P=0.031N		
Fisher Exact Test (d)		P=0.554	P=0.019N
Pituitary Gland: Adenoma or Carcinoma			
Overall Rates (a)	6/46 (13%)	7/42 (17%)	0/41 (0%)
Adjusted Rates (b)	13.3%	18.4%	0.0%
Terminal Rates (c)	5/42 (12%)	5/28 (18%)	0/16 (0%)
Week of First Observation	104	89	
Life Table Tests (d)	P=0.246N	P=0.371	P=0.149N
Incidental Tumor Tests (d)	P=0.246N	P=0.371	P=0.149N
Cochran-Armitage Trend Test (d)	P=0.037N		
Fisher Exact Test (d)		P=0.429	P=0.019N
Adrenal Gland: Adenoma or Cortical Adenoma			
Overall Rates (a)	1/48 (2%)	3/49 (6%)	0/46 (0%)
Adjusted Rates (b)	2.1%	6.8%	0.0%
Terminal Rates (c)	1/44 (2%)	3/33 (9%)	0/17 (0%)
Week of First Observation	105	105	
Life Table Tests (d)	P=0.608	P=0.282	P=0.702N
Incidental Tumor Tests (d)	P=0.608	P=0.282	P=0.702N
Cochran-Armitage Trend Test (d)	P=0.391N		
Fisher Exact Test (d)		P=0.316	P=0.511N

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF *JP-5* NAVY FUEL (*Continued*)

	Vehicle Control	250 mg/kg	500 mg/kg
Thyroid Gland: Follicular Cell Adenoma			
Overall Rates (a)	2/47 (4%)	1/46 (2%)	3/43 (7%)
Adjusted Rates (b)	4.3%	2.4%	20.0%
Terminal Rates (c)	1/43 (2%)	1/30 (3%)	3/15 (20%)
Week of First Observation	104	105	90
Life Table Tests (d)	P=0.086	P=0.540N	P=0.086
Incidental Tumor Tests (d)	P=0.086	P=0.540N	P=0.086
Cochran-Armitage Trend Test (d)	P=0.364		
Fisher Exact Test (d)		P=0.508N	P=0.457
Uterus: Endometrial Stromal Polyp			
Overall Rates (a)	3/48 (6%)	1/48 (2%)	0/46 (0%)
Adjusted Rates (b)	6.4%	2.3%	0.0%
Terminal Rates (c)	3/44 (7%)	1/33 (3%)	0/17 (0%)
Week of First Observation	105	105	
Life Table Tests (d)	P=0.166N	P=0.338N	P=0.347N
Incidental Tumor Tests (d)	P=0.166N	P=0.338N	P=0.347N
Cochran-Armitage Trend Test (d)	P=0.064N		
Fisher Exact Test (d)		P=0.308N	P=0.129N
Uterus: Endometrial Stromal Polyp or Sarcoma			
Overall Rates (a)	3/48 (6%)	2/48 (4%)	1/46 (2%)
Adjusted Rates (b)	6.4%	4.7%	5.9%
Terminal Rates (c)	3/44 (7%)	2/33 (6%)	1/17 (6%)
Week of First Observation	105	105	90
Life Table Tests (d)	P=0.542N	P=0.541N	P=0.694N
Incidental Tumor Tests (d)	P=0.542N	P=0.541N	P=0.694N
Cochran-Armitage Trend Test (d)	P=0.234N		
Fisher Exact Test (d)		P=0.500N	P=0.325N

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence at week 105 for the vehicle control and 250 mg/kg groups and week 90 for the 500 mg/kg group
(d) Beneath the vehicle control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the vehicle controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).

APPENDIX F

HISTORICAL INCIDENCES OF TUMORS IN B6C3F$_1$ MICE RECEIVING NO TREATMENT

TABLE F1. HISTORICAL INCIDENCE OF INTEGUMENTARY SYSTEM SQUAMOUS CELL TUMORS IN B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

Study	Incidence in Controls	
	Male	Female
Historical Incidence at Litton Bionetics, Inc.		
Caprolactam	0/50	0/50
Bisphenol A	0/49	0/50
11-Aminoundecanoic acid	0/50	(b) 1/50
2,6-Dichloro-*p*-phenylenediamine	0/50	0/50
Melamine	0/49	0/47
TOTAL	0/248 (0.0%)	1/247 (0.4%)
SD (c)	0.00%	0.89%
Range (d)		
High	0/50	1/50
Low	0/50	0/50
Overall Historical Incidence		
TOTAL	(e) 6/1,791 (0.3%)	(f) 8/1,791 (0.4%)
SD (c)	0.89%	0.99%
Range (d)		
High	2/50	2/48
Low	0/50	0/50

(a) Data as of August 3, 1984, for studies of at least 104 weeks
(b) Papilloma, NOS
(c) Standard deviation
(d) Range and SD are presented for groups of 35 or more animals.
(e) Includes one squamous cell papilloma and five squamous cell carcinomas
(f) Includes one papilloma, NOS, two squamous cell papillomas, and five squamous cell carcinomas

TABLE F2. HISTORICAL INCIDENCE OF HEPATOCELLULAR TUMORS IN MALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at Litton Bionetics, Inc.			
Caprolactam	3/50	5/50	8/50
Bisphenol A	5/49	11/49	16/49
11-Aminoundecanoic acid	1/50	16/50	17/50
2,6-Dichloro-*p*-phenylenediamine	4/50	12/50	16/50
Melamine	2/45	10/45	12/45
TOTAL	15/244 (6.1%)	54/244 (22.1%)	69/244 (28.3%)
SD (b)	3.16%	7.88%	7.40%
Range (c)			
High	5/49	16/50	17/50
Low	1/50	5/50	8/50
Overall Historical Incidence			
TOTAL	179/1,784 (10.0%)	377/1,784 (21.1%)	540/1,784 (30.3%)
SD (b)	7.36%	6.54%	8.04%
Range (c)			
High	(d) 22/50	16/50	(e) 29/50
Low	0/49	4/50	7/50

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

TABLE F3. HISTORICAL INCIDENCE OF HEMATOPOIETIC SYSTEM TUMORS IN MALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

Study	Incidence in Controls		
	Leukemia	Lymphoma	Leukemia or Lymphoma
Historical Incidence at Litton Bionetics, Inc.			
Caprolactam	0/50	9/50	9/50
Bisphenol A	0/49	2/49	2/49
11-Aminoundecanoic acid	0/50	2/50	2/50
2,6-Dichloro-*p*-phenylenediamine	0/50	5/50	5/50
Melamine	0/49	1/49	1/49
TOTAL	0/248 (0.0%)	19/248 (7.7%)	19/248 (7.7%)
SD (b)	0.00%	6.52%	6.52%
Range (c)			
High	0/50	9/50	9/50
Low	0/50	1/49	1/49
Overall Historical Incidence			
TOTAL	(d) 6/1,791 (0.3%)	217/1,791 (12.1%)	223/1,791 (12.5%)
SD (b)	0.76%	7.35%	7.55%
Range (c)			
High	1/49	16/50	16/50
Low	0/50	1/50	1/50

(a) Data as of August 3, 1984, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.
(d) One mast cell leukemia was also observed. The inclusion of this tumor would not affect the reported ranges.

TABLE F4. HISTORICAL INCIDENCE OF HEMATOPOIETIC SYSTEM TUMORS IN FEMALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

Study	Incidence in Controls		
	Leukemia	Lymphoma	Leukemia or Lymphoma
Historical Incidence at Litton Bionetics, Inc.			
Caprolactam	4/50	17/50	21/50
Bisphenol A	2/50	11/50	13/50
11-Aminoundecanoic acid	0/50	9/50	9/50
2,6-Dichloro-*p*-phenylenediamine	1/50	17/50	18/50
Melamine	0/47	15/47	15/47
TOTAL	7/247 (2.8%)	69/247 (27.9%)	76/247 (30.8%)
SD (b)	3.35%	7.47%	9.23%
Range (c)			
High	4/50	17/50	21/50
Low	0/50	9/50	9/50
Overall Historical Incidence			
TOTAL	25/1,791 (1.4%)	481/1,791 (26.9%)	506/1,791 (28.3%)
SD (b)	2.48%	10.20%	9.76%
Range (c)			
High	5/50	(d) 31/50	(d) 31/50
Low	0/50	5/50	6/50

(a) Data as of August 3, 1984, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.
(d) Second high: 23/50

APPENDIX G

MUTAGENICITY OF MARINE DIESEL FUEL IN SALMONELLA

TABLE G1. MUTAGENICITY OF MARINE DIESEL FUEL IN *SALMONELLA TYPHIMURIUM*

Strain	Dose (µg/plate)	Revertants/plate (a) −S9	+S9 (rat)	+S9 (hamster)
TA100	0	142 ± 18.9	121 ± 12.1	128 ± 2.4
	3	119 ± 19.0	--	--
	10	115 ± 6.1	--	--
	33	134 ± 0.9	132 ± 13.2	127 ± 7.5
	100	107 ± 6.1	141 ± 7.2	137 ± 4.5
	333	95 ± 6.9	146 ± 6.5	152 ± 11.5
	1,000	--	139 ± 7.4	156 ± 4.0
	3,333	--	96 ± 6.0	107 ± 12.0
TA1535	0	25 ± 4.7	12 ± 2.3	12 ± 0.9
	3	30 ± 1.5	--	--
	10	31 ± 3.7	--	--
	33	24 ± 0.6	12 ± 1.7	11 ± 1.8
	100	20 ± 1.9	16 ± 1.5	12 ± 1.9
	333	17 ± 6.5	12 ± 0.6	12 ± 1.2
	1,000	--	16 ± 2.2	10 ± 1.9
	3,333	--	10 ± 0.9	7 ± 1.5
TA1537	0	6 ± 2.3	12 ± 2.6	6 ± 2.3
	3	7 ± 1.8	--	--
	10	7 ± 1.2	--	--
	33	5 ± 1.0	7 ± 1.8	5 ± 1.3
	100	6 ± 1.5	10 ± 2.2	8 ± 3.3
	333	5 ± 1.0	7 ± 2.7	6 ± 1.0
	1,000	--	11 ± 0.7	7 ± 1.2
	3,333	--	8 ± 2.0	8 ± 1.5
TA98	0	17 ± 1.7	29 ± 4.1	26 ± 2.3
	3	18 ± 1.8	--	--
	10	18 ± 2.9	--	--
	33	14 ± 2.6	25 ± 2.1	25 ± 1.5
	100	19 ± 0.3	24 ± 2.2	25 ± 2.5
	333	11 ± 1.5	26 ± 5.5	33 ± 0.3
	1,000	--	27 ± 1.5	37 ± 1.9
	3,333	--	29 ± 2.5	34 ± 4.6

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

APPENDIX H

MUTAGENICITY OF JP-5 NAVY FUEL IN SALMONELLA

TABLE H1. MUTAGENICITY OF JP-5 NAVY FUEL IN *SALMONELLA TYPHIMURIUM*

Strain	Dose (µg/plate)	Revertants/plate (a) −S9	+S9 (rat)	+S9 (hamster)
TA100	0	101 ± 6.0	130 ± 11.8	125 ± 2.1
	100	84 ± 3.2	140 ± 7.3	137 ± 6.9
	333	91 ± 7.8	166 ± 2.6	138 ± 9.9
	1,000	92 ± 2.1	176 ± 4.6	138 ± 9.2
	3,333	57 ± 6.7	161 ± 4.3	151 ± 6.5
	10,000	59 ± 10.0	169 ± 11.3	131 ± 17.1
TA1535	0	15 ± 1.2	16 ± 1.2	16 ± 1.5
	100	17 ± 3.0	18 ± 5.4	18 ± 1.2
	333	13 ± 3.8	18 ± 0.9	12 ± 2.4
	1,000	9 ± 1.5	15 ± 1.2	14 ± 0.7
	3,333	8 ± 2.6	13 ± 2.9	19 ± 3.2
	10,000	9 ± 1.5	15 ± 0.7	19 ± 1.5
TA97	0	6 ± 0.7	7 ± 0.9	3 ± 0.3
	10	6 ± 0.9	8 ± 2.6	9 ± 3.5
	33	3 ± 2.3	6 ± 1.0	6 ± 1.8
	100	5 ± 2.3	7 ± 0.6	7 ± 5.0
	333	4 ± 2.1	7 ± 1.0	7 ± 2.3
	10,000	4 ± 0.6	11 ± 1.7	9 ± 2.2
TA98	0	18 ± 1.8	41 ± 5.9	26 ± 3.1
	100	13 ± 0.7	32 ± 3.2	34 ± 3.1
	333	15 ± 1.5	42 ± 2.6	31 ± 4.2
	1,000	18 ± 4.3	41 ± 1.2	32 ± 3.8
	3,333	17 ± 1.8	37 ± 6.6	29 ± 3.7
	10,000	21 ± 2.7	34 ± 3.5	27 ± 3.8

(a) The S9 fractions were prepared from the livers of Aroclor 1254-induced male Sprague-Dawley rats and male Syrian hamsters. Cells and test compound or solvent (95% ethanol) were incubated for 20 min at 37° C in the presence of either S9 or buffer. After the addition of soft agar, the contents of each tube were poured onto minimal medium, and the plates were incubated at 37° C for 48 h (Haworth et al., 1983). The experiment was performed twice, each in triplicate; because the results were similar, data from only one experiment are shown.

APPENDIX I

CHEMICAL CHARACTERIZATION OF MARINE DIESEL FUEL

APPENDIX I. CHEMICAL CHARACTERIZATION

I. Identity and Purity Determinations of Marine Diesel Fuel Lot No. 9110L Performed by the Analytical Chemistry Laboratory

A. Physical properties	Determined	Literature Values
1. Boiling point:	201°-253° C (visual, capillary	180°-370° C (typical)
2. Density:	d_{25}^{27}: 0.83651 ± 0.00026(δ)	d: 0.8-0.9
3. Appearance:	Clear amber liquid	

B. Spectral data

1. Infrared

Instrument:	Beckman IR-12	
Cell:	Thin film between silver chloride plates	
Results:	See Figure 5	No literature reference found. Spectrum consistent with a mixture of aliphatic and aromatic hydrocarbons.

2. Ultraviolet/visible

Instrument:	Cary 118	
Solvent:	Hexane	

Results:

λmax (nm)	Absorbance/ Concentration (mg/ml)	
254	7.77 ± 0.53(δ)	No literature reference was found. Spectrum consistent with structure.
276 (shoulder)	6.00 ± 0.29(δ)	
325 (shoulder)	0.42 ± 0.04(δ)	
358 (shoulder)	0.0328 ± 0.0004(δ)	
378	0.02383 ± 0.00002(δ)	

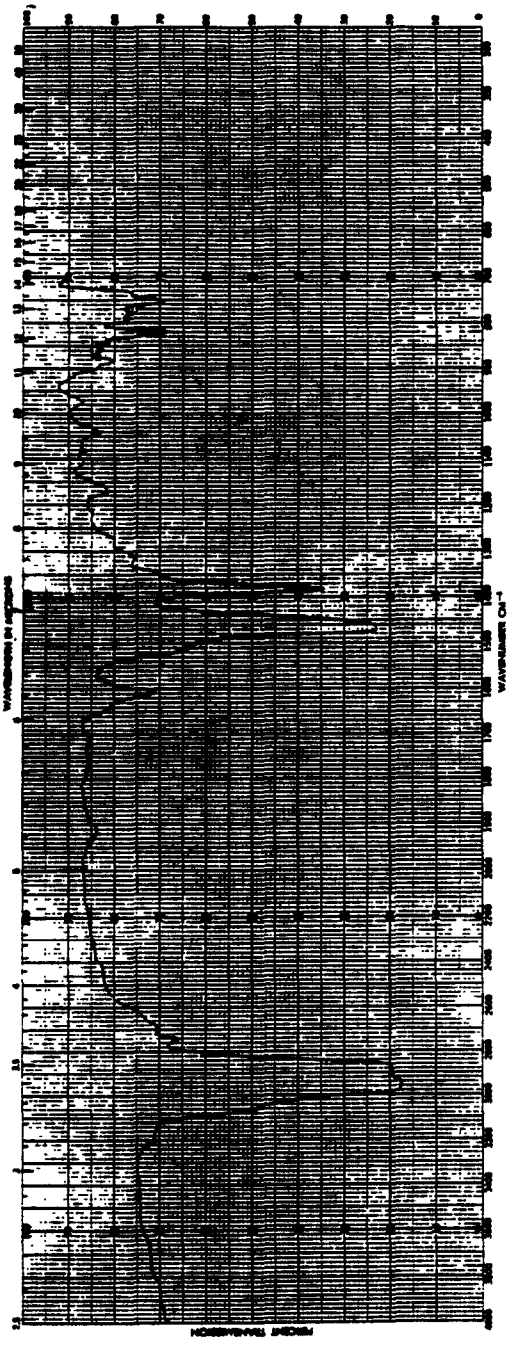

FIGURE 5. INFRARED ABSORPTION SPECTRUM OF MARINE DIESEL FUEL (LOT NO. 9110L)

	Determined	Literature Values
3. Nuclear magnetic resonance		
Instrument:	Varian EM-360-A	
Solvent:	Deuterated benzene with internal tetramethyl silane	
Assignments:	See Figure 6	No literature reference found. Spectrum consistent with the structure of mixture of hydrocarbons with aromatic and aliphatic protons present. The majority of the absorbance is in the aliphatic region (94.9%) with much less in the aromatic region (5.1%).
Chemical shift (δ):	a 0.54-2.90 ppm (aliphatic protons) b 6.68-7.70 ppm (aromatic protons)	
Integration (percent of total):	a 94.9 (aliphatic region) b 5.1 (aromatic region)	

C. **Water analysis (Karl Fischer):** 0.04% ± 0.02(δ)%

D. **Elemental analysis:** Based on manufacturer's specifications of 12.7% $C_{15}H_{32}$ (paraffins), 43.7% $C_{10}H_8$ (naphthalenes), and 43.6% C_6H_6 (aromatics).

Element	C	H
Theory	91.94	8.06
Determined	86.88 86.80	12.86 12.00

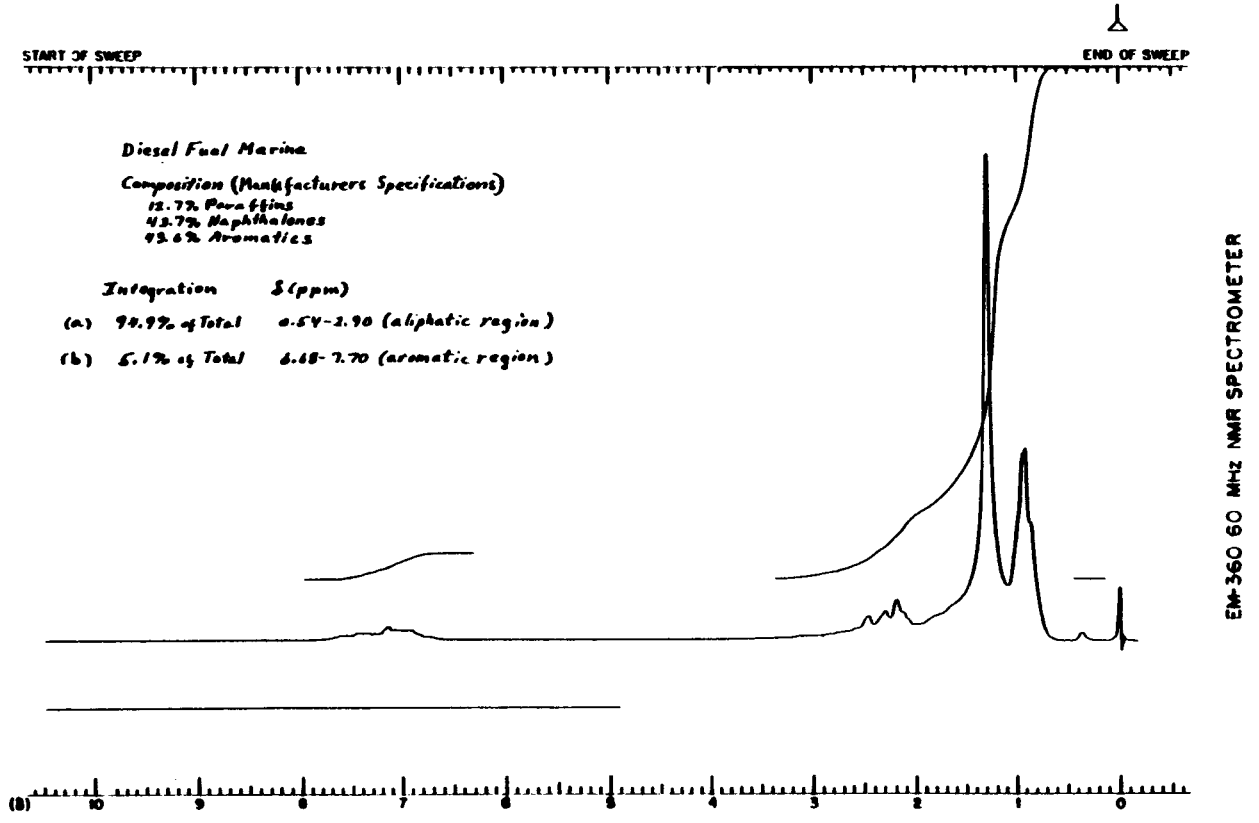

FIGURE 6. NUCLEAR MAGNETIC RESONANCE SPECTRUM OF MARINE DIESEL FUEL (LOT NO. 9110L)

E. Chromatographic analysis

1. Capillary gas chromatography

Instrument: Varian 3700
Detector: Flame ionization
Column: SP2100, Grade A, 30 m × 0.25 mm ID, capillary
Inlet temperature: 200° C
Detector temperature: 250° C
Carrier gas: Prepurified nitrogen
Carrier flow rate: 1.0 ml/min plus 30 ml/min makeup
Oven temperature program: 50°-250° C at 2° C/min
Sample injected: Neat liquid 0.1 µl, split 1 to 100

Results: There was no single major peak. More than 200 peaks resolved (Figure 7). Evaluation of the data was done by quantitating the 12 largest peaks and expressing the areas as a percent of the largest peak (peak no. 5) and percent of total area of all 12 peaks.

Peak No.	Retention Time (min)	Retention Time Relative to Peak No. 5	Area (percent of peak no. 5)	Area (percent of total 12 peak area)
1	10.64	0.28	11.5	1.7
2	16.45	0.44	22.3	3.3
3	23.25	0.62	43.6	6.4
4	30.34	0.81	85.5	12.3
5	37.43	1.00	100	14.7
6	44.32	1.18	88.6	13.0
7	50.83	1.36	86.2	12.7
8	57.03	1.52	89.4	13.2
9	62.84	1.68	71.0	10.4
10	68.46	1.83	43.1	6.3
11	74.07	1.98	25.4	3.7
12	79.00	2.11	15.4	2.3

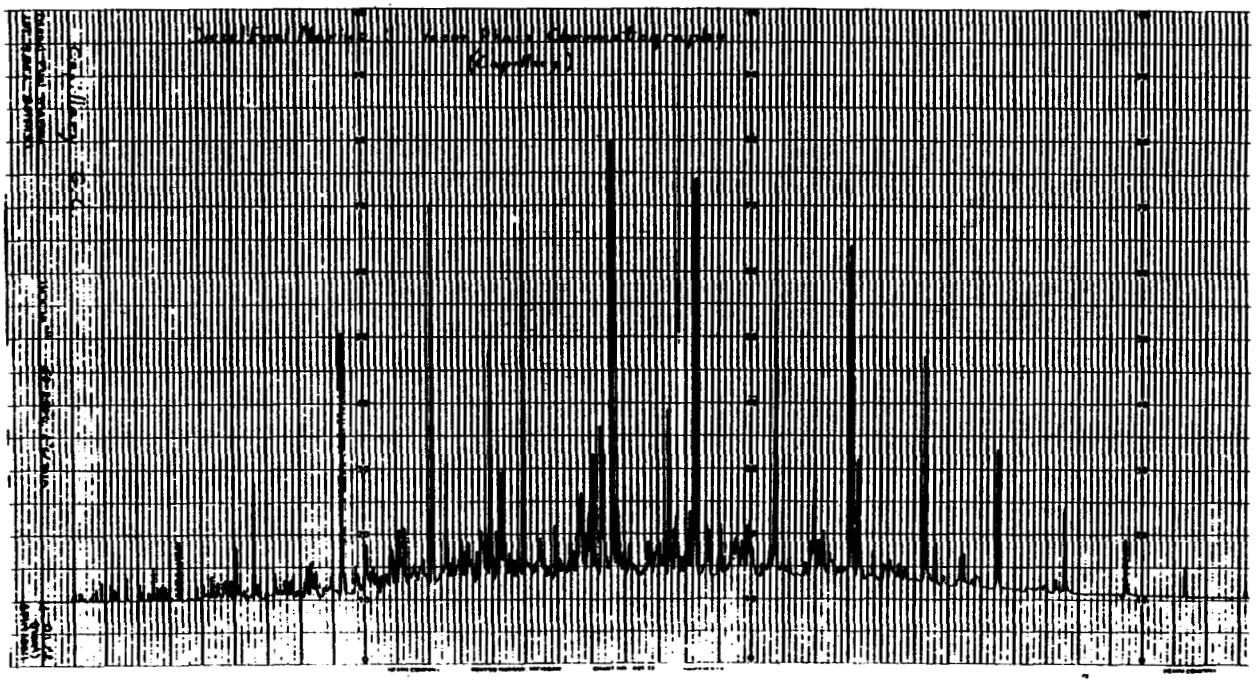

FIGURE 7. GAS (CAPILLARY) CHROMATOGRAPHY OF MARINE DIESEL FUEL (LOT NO. 9110L)

2. **Thin-layer chromatography**

Plates: Silica Gel 60 F-254
Reference standard: Pyrene, 10 µg (10 µg/µl in acetone)
Amount spotted: 1 and 3 µl as neat liquid
Visualization: Ultraviolet, 254 and 366 nm and iodine vapor

System 1: Hexane:diethyl ether (85:15)

Spot Intensity	R_f	R_{st}
Major	0.92	1.24
Major	0.86	1.17
Minor	0.81	1.09
Slight trace	0.29	0.38
Trace	0.24	0.32
Trace	0.10	0.14
Trace	origin	origin

System 2: Carbon tetrachloride (100%)

Spot Intensity	R_f	R_{st}
Major	0.86	1.03
Minor	0.80	0.96
Trace	0.62	0.74
Slight trace	0.56	0.67
Trace	0.46	0.56
Trace	origin	origin

F. **Conclusions:** The results of the elemental analyses for carbon and hydrogen were 86.46% and 12.43%, respectively. Theoretical values could not be determined because the sample consists of a mixture of many hydrocarbons of varying structures and molecular weights. Thin-layer chromatography by one system indicated two major spots, one minor spot, three traces, and one slight trace. A second thin-layer system indicated one major spot, one minor spot, three traces, and one slight trace. Karl Fischer analysis indicated 0.04% ± 0.02% water. Capillary gas chromatography resolved over 200 separate components. The data for gas chromatography could not be expressed in a conventional manner. Therefore, the 12 largest peaks were listed with retention times and areas relative to the largest peak and areas relative to the 12-peak total area. The infrared and nuclear magnetic resonance spectra were consistent with the structures of mixed aliphatic and aromatic hydrocarbons. Nuclear magnetic resonance indicates 94.9% of the total absorbance in the aliphatic region and 5.1% of the total absorbance in the aromatic region. The ultraviolet/visible spectrum indicated absorbances in the ultraviolet region characteristic of aromatic compounds. Maxima were expressed as absorbance divided by concentration in milligrams per milliliter.

II. Chemical Stability Study of Lot No. 9110L Performed by the Analytical Chemistry Laboratory

A. **Sample storage:** Samples of marine diesel fuel were stored for 2 weeks at −20°, 5°, 25°, or 60° C in glass tubes with Teflon®-lined lids.

B. **Analytical method:** Gas chromatography

Instrument: Varian 3700
Detector: Flame ionization
Column: SP2100, Grade A, 30 m × 0.25 mm ID, capillary
Inlet temperature: 200° C
Detector temperature: 250° C
Carrier gas: Prepurified nitrogen
Carrier flow rate: 1.0 ml/min plus 30 ml/min makeup
Oven temperature program: 50°-250° C at 2° C/min
Sample injected: Neat liquid, 0.1 µl, split 1 to 100

C. **Results:** Comparisons of the peak areas of the 12 largest peaks were made, expressed as a percent of the total area of the 12 largest peaks.

Storage Temperature

Peak No.	−20° C	5° C	25° C	60° C
1	1.7	1.7	1.6	1.7
2	3.3	3.3	3.2	3.3
3	6.4	6.6	6.5	6.7
4	12.3	12.1	12.4	12.9
5	14.7	14.9	14.8	15.7
5	13.0	13.6	13.6	12.9
7	12.7	12.8	13.0	12.4
8	13.2	12.8	13.1	13.2
9	10.4	10.5	10.5	10.0
10	6.3	6.2	6.2	6.1
11	3.7	3.5	3.4	3.4
12	2.3	2.0	1.7	1.9

D. **Conclusion:** Marine diesel fuel is stable as the neat liquid when stored for 2 weeks at temperatures up to 60° C.

III. Chemical Stability Study of Lot No. 9110L Performed by the Study Laboratory

A. Storage conditions: Bulk chemical--at or below −20° C until December 1979, then at 4° C
Reference--at or below −20° C

B. Analytical methods

1. **Gas chromatography**

Analyses performed on 2/22/79 and 6/19/79

Instrument: Hewlett-Packard 5840A with a 7672 automatic liquid sampler
Detector: Flame ionization
Column: 10% UCW-98 on 80/100 mesh Chromosorb W, 1.8 m × 2 mm ID, glass, silanized
Detector temperature: 350° C
Inlet temperature: 250° C
Oven temperature program: 40° C for 4 min, then to 220° C at 5° C/min, held at 220° C for 10 min
Carrier gas: Nitrogen, 20 ml/min
Sample injected: 2 or 3 µl of neat liquid

Analysis performed on 11/27/79

Instrument: Shimadzu GC-Mini 2 with TP-M2 temperature programmer and C-RIA recording data processor
Detector: Flame ionization
Column: 3.8% UCW-98 on 80/100 mesh Supelcoport, 1.8 m × 2 mm ID, glass, silanized
Detector temperature: 250° C
Inlet temperature: 250° C
Oven temperature program: 40° C for 5 min, then to 250° C at 0.5° C/min, held at 250° C for 30 min
Carrier gas: Nitrogen, 200 ml/min
Sample injected: 1 µl of neat liquid

Analyses performed from 12/21/79 to 1/20/83

Instrument: Hewlett Packard 5880A with Model 7672A liquid autosampler
Detector: Flame ionization
Column: 3.8% UCW-98 on 80/100 mesh Supelcoport, 1.8 m × 2 mm ID, glass
Detector temperature: 350° C
Inlet temperature: 270° or 275° C
Oven temperature program: 35° C for 5 min, then to 250° C at 5° C/min, held at 250° C for 2 min
Carrier gas: Nitrogen, 40 ml/min
Sample injected: 1 µl of neat liquid

2. **Infrared spectroscopy**

   Instrument: Perkin-Elmer Model 457 (2/1/79 and 6/18/79)
   Perkin-Elmer Model 598 (11/16/79)
   Perkin-Elmer Model 398 (4/8/80-1/20/83)

   Cell: Neat liquid between potassium bromide plates

C. **Results**

1. **Gas chromatography:** Peak areas of low-, medium-, and high-boiling components were grouped, by visual inspection, into sets using major valleys found in the chromatograms. Peak-group areas were compared as a percent of all peak groups for bulk chemical and reference samples.

   No change in relative areas was detected between bulk chemical and reference samples within the limits of instrumental and column variability.

2. **Infrared spectroscopy:** Results are comparable to those obtained by the analytical chemistry laboratory.

D. **Conclusion:** No notable change in composition of marine diesel fuel occurred throughout the studies.

APPENDIX J

CHEMICAL CHARACTERIZATION OF JP-5 NAVY FUEL

APPENDIX J. CHEMICAL CHARACTERIZATION

I. Identity and Purity Determinations of JP-5 Navy Fuel Lot No. WP8477 Performed by the Analytical Chemistry Laboratory

A. Physical properties	Determined	Literature Values
1. Boiling point:	176°-260° C (visual capillary boiling point)	170°-300° C
2. Density:	d_{25}^{24}: 0.8056 ± 0.0007(δ)	d: 0.81
3. Appearance:	Clear, pale yellow, viscous liquid	

B. Spectral data

1. Infrared

Instrument:	Beckman IR-12	
Cell:	Thin film between silver chloride plates	
Results:	See Figure 8	No literature reference found. Spectrum consistent with structure of mixture of aliphatic and aromatic hydrocarbons.

2. Ultraviolet/visible

Instrument:	Cary 118	
Solvent:	Hexane	
Results:	No absorbance was seen between 800 and 350 nm at a concentration of 4 mg/ml in hexane. Four maxima were observed between 350 and 228 nm.	No literature reference found. Spectrum consistent with structure.

λ_{max} (nm)	Absorbance/ Concentration (mg/ml)
319 (shoulder)	0.04686 ± 0.00003(δ)
273	1.265 ± 0.009(δ)
268	1.24 ± 0.01(δ)
220	21.91 ± 1.36(δ)

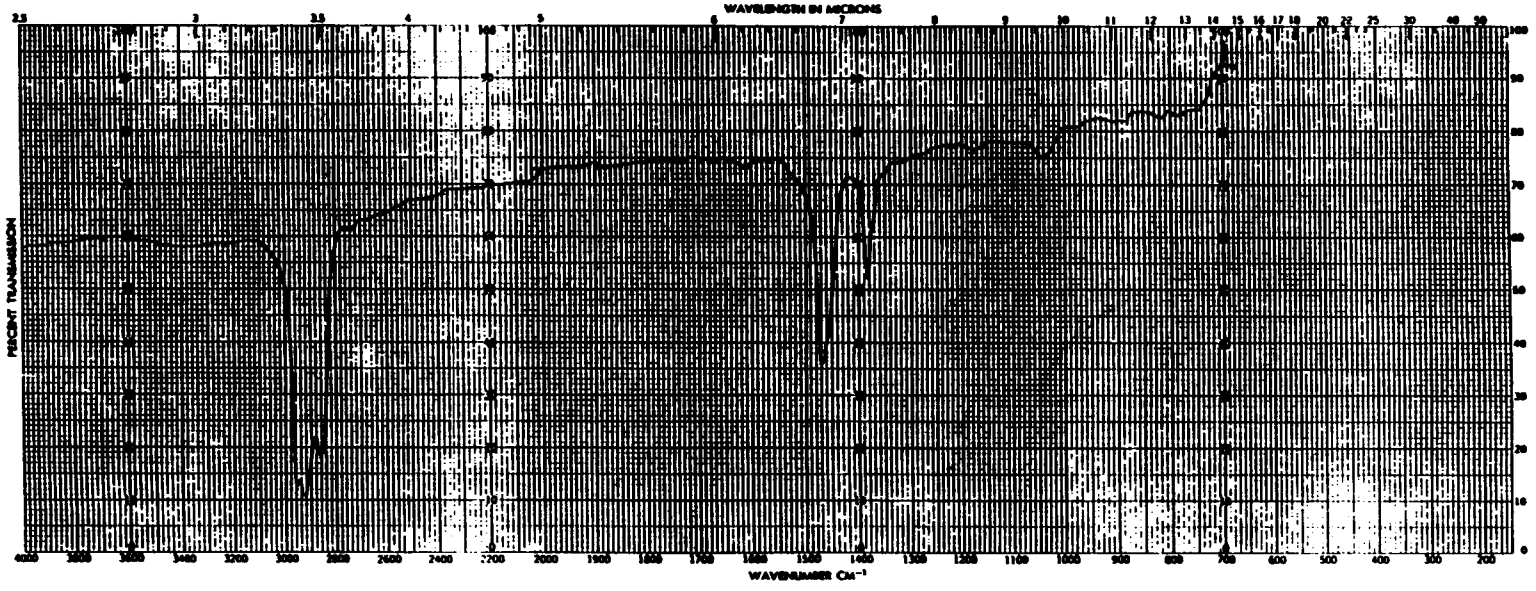

FIGURE 8. INFRARED ABSORPTION SPECTRUM OF JP-5 NAVY FUEL (LOT NO. WP8477)

3. **Nuclear magnetic resonance**

	Determined	Literature Values
Instrument:	Varian EM-360-A	
Solvent:	Deuterated benzene with internal tetramethylsilane	
Assignments:	See Figure 9	No literature reference found. Spectrum consistent with structure of mixture of hydrocarbons with aromatic and aliphatic protons present. The majority of the absorbance is in the aliphatic region (approximately 97%) with much less in the aromatic region (approximately 3%).
Chemical shift (δ):	a 0.60-2.60 ppm b 6.56-7.25 ppm	
Integration ratios (approximate percent of total):	a 97 (aliphatic region) b 3 (aromatic region)	

C. **Water analysis (Karl Fischer):** 0.010% ± 0.005(δ)%

D. **Elemental analysis:** Based on 15.9% C_nH_n (aromatics), 0.5% C_nH_{2n} (olefins), 30.8% C_nH_{2n+2} (paraffins), and 52.8%C_nH_{2n} (cycloparaffins). The n value was taken as 10 to approximate the range given as C_5-C_{16}.

Element	C	H
Theory (T)	86.31	13.69
Determined (D)	86.07 85.97	13.85 14.00
Percent D/T	99.6	101.7

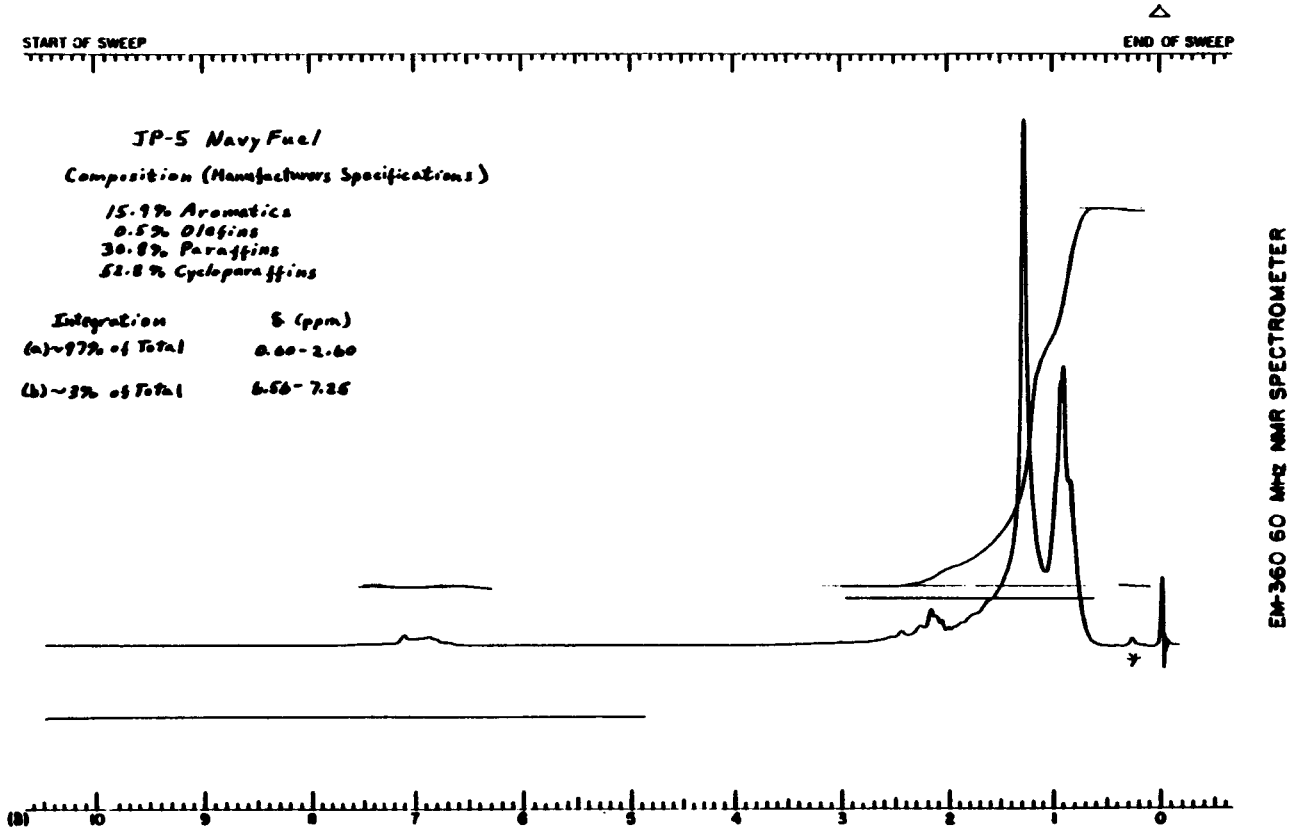

FIGURE 9. NUCLEAR MAGNETIC RESONANCE SPECTRUM OF JP-5 NAVY FUEL (LOT NO. WP8477)

E. Chromatographic analysis

1. Capillary gas chromatography

Instrument: Varian 3700
Detector: Flame ionization
Inlet temperature: 200° C
Detector temperature: 250° C
Carrier gas: Prepurified nitrogen, 1.0 ml/min plus 30 ml/min makeup
Oven temperature program: 50°-200° C at 2° C/minute
Sample injected: Neat liquid 0.1 µl, split 1 to 100

Results: There was no single major peak; more than 150 peaks were resolved (Figure 10). Evaluation of the data was done by quantitating eight of the largest peaks and expressing the areas as a percent of the largest peak (peak no. 3) and percent of total area of all eight peaks.

Peak No.	Retention Time (min)	Retention Time Relative to Peak No. 3	Area (percent of peak no. 3)	Area (percent of total 8 peak area)
1	10.69	0.46	13.4	3.4
2	16.41	0.70	46.3	11.7
3	23.25	1.00	100	25.3
4	30.39	1.31	84.5	21.4
5	37.43	1.61	64.6	16.3
6	44.28	1.90	53.2	13.4
7	50.78	2.18	27.3	6.9
8	56.93	2.45	6.1	1.6

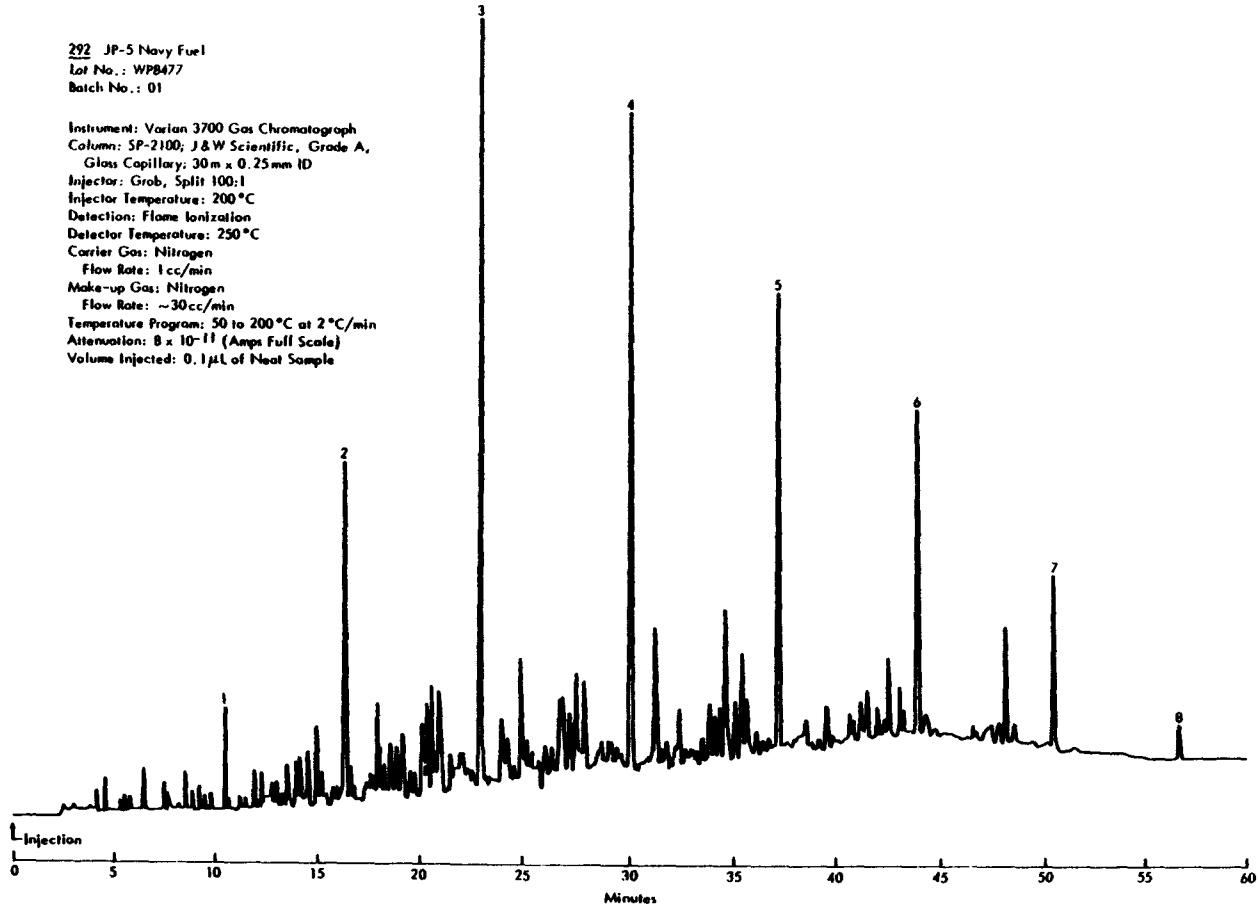

FIGURE 10. GAS (CAPILLARY) CHROMATOGRAPHY OF JP-5 NAVY FUEL (LOT NO. WP8477)

2. **Thin-layer chromatography**

Plates: Silica Gel 60 F-254, 0.25 mm layer
Reference standard: Naphthalene, 10 µg (10 µg/µl in acetone)
Amount spotted: 2 and 6 µl as neat liquid
Visualization: Ultraviolet, 254 nm, iodine vapor
Solvent: Hexanes (100%)

Spot Intensity	R_f	R_{st}
Major	0.892	1.395
Trace	0.716	1.118
Trace	0.606	1.949
Trace	0.509	0.796
Trace	0.308	0.481
Trace	origin	origin

F. **Conclusion:** The results of the elemental analyses for carbon and hydrogen averaged 86.02% and 13.93%. The theoretical values cannot be precisely stated because the compound is a mixture of acyclic and cyclic compounds, both aromatic and aliphatic with chain lengths ranging from C_5 to C_{16}. Thin-layer chromatography indicated one major and five trace spots. Karl Fischer analysis indicated 0.010% ± 0.005(δ)% water. Capillary gas chromatography resolved over 150 separate components. The data for gas chromatography could not be expressed in a conventional manner. Therefore, eight of the largest peaks were listed with retention times and areas relative to the largest peak and areas relative to the eight-peak total area. The infrared and nuclear magnetic resonance spectra were consistent for mixtures of aliphatic and aromatic hydrocarbons. Nuclear magnetic resonance indicated approximately 97% of total absorbance in the aliphatic region and approximately 3% of the total absorbance in the aromatic region. The ultraviolet/visible spectrum indicated absorbance in the ultraviolet region characteristic of aromatic compounds. Maxima were expressed as absorbance divided by concentration in milligrams per milliliter.

II. Special Bulk Chemical Reanalysis of JP-5 Navy Fuel Lot No. WP8477 Performed by the Analytical Chemistry Laboratory

A. Purpose: Comparison of gas (packed and capillary columns) chromatographic profiles obtained for a sample returned from the testing laboratory with that obtained for a reference sample which had been stored in a freezer at the analytical chemistry laboratory.

B. Analytical method

1. **Packed-column gas chromatography**

Instrument: Varian 3700
Detector: Flame ionization
Column: 3% SP2100 on 100/120 Supelcoport; 1.8 m × 2 mm ID, glass
Inlet temperature: 200° C
Detector temperature: 250° C
Carrier gas: Nitrogen, 30 ml/min
Oven temperature program: 70° C for 4 min, then 70°-200° C at 5°/min
Sample injected: Solution (3.5 ml) of 1.5% JP-5 navy fuel in absolute ethanol

2. **Capillary gas chromatography**

Instrument: Varian 3700
Detector: Flame ionization
Column: SP2100, Grade AA, capillary, 30 m × 0.25 mm ID
Inlet temperature: 200° C
Detector temperature: 250° C
Carrier gas: Nitrogen, 20 cm/second
Makeup flow rate: 30 ml/min
Splitter flow rate: 100 ml/min
Oven temperature program: 50°-175° C at 2° C/min
Sample injected: Neat liquid (0.1 ml)

C. Results

1. **Packed-column gas chromatography:** Thirty-eight peaks and shoulders were observed for both the sample returned from the study laboratory and for the reference sample. Visual inspection of the profiles indicated that the two samples were identical.

2. **Capillary gas chromatography:** There was no single major peak. More than 150 peaks resolved for both the sample returned from the study laboratory and for the reference sample. Visual inspection of the profiles indicated that the two samples were identical. In addition, eight of the largest peaks were quantitated and their heights expressed as a percent of the largest peak (peak no. 3) and a percent of all eight peaks. By this method, the correlation between the two samples was very good, and differences were within the range of experimental error.

Peak No.	Retention Time (min)	Retention Time (relative to peak 3)	Height (percent of peak no. 3) Test Sample	Height (percent of peak no. 3) Reference Sample	Height (percent of eight-peak total height) Test Sample	Height (percent of eight-peak total height) Reference Sample
1	10.8	0.47	14.8	15.2	3.9	4.0
2	16.5	0.71	45.6	45.7	12.1	11.9
3	23.1	1.00	100	100	26.5	26.0
4	30.2	1.31	78.8	79.5	20.9	20.7
5	37.1	1.61	64.1	66.4	17.0	17.3
6	43.8	1.90	46.4	48.9	12.3	12.7
7	50.3	2.18	22.5	23.2	6.0	6.0
8	56.4	2.44	5.1	5.6	1.4	1.4

D. **Conclusion:** The gas chromatographic profiles obtained on a 3% SP2100 packed column indicated 38 peaks and shoulders that were visually identical for the sample returned from the study laboratory and the reference sample. The gas chromatographic profiles obtained with an SP2100 capillary column indicated over 150 peaks. These profiles were also observed to be identical for both samples.

III. Chemical Stability Study of JP-5 Navy Fuel Lot No. WP8477 Performed by the Analytical Chemistry Laboratory

A. Sample storage: Samples of JP-5 navy fuel were stored in glass vials with Teflon®-lined screw caps at temperatures of – 20°, 5°, 25°, or 60° C for 2 weeks.

B. Analytical method: Gas chromatography

Instrument: Varian 3700
Detector: Flame ionization
Column: SP2100, Grade A, capillary, 30 m × 0.25 mm ID
Inlet temperature: 200° C
Detector temperature: 250° C
Carrier gas: Prepurified nitrogen
Carrier flow rate: 1.0 ml/min plus 30 ml/min makeup
Oven temperature program: 50°-200° C at 2° C/min

C. Results: Evaluation of the data was done by quantitating eight of the largest peaks in each temperature sample and expressing the areas as a percent of the total area of all eight peaks. The recoveries of JP-5 navy fuel for each sample were compared with the recovery for the – 20° C sample.

Storage Temperature

Peak No.	– 20° C	5° C	25° C	60° C
1	3.4	3.4	3.6	3.4
2	11.7	11.2	11.8	11.3
3	25.3	24.1	25.4	24.6
4	21.4	21.1	20.8	20.9
5	16.3	17.1	16.8	16.8
6	13.4	14.5	13.3	14.2
7	6.9	7.3	6.7	7.2
8	1.6	1.5	1.6	1.7

D. Conclusion: JP-5 navy fuel is stable as the bulk chemical stored for 2 weeks at temperatures up to 60° C.

IV. Chemical Stability Study of JP-5 Navy Fuel Lot No. WP8477 Performed by the Study Laboratory

A. Storage conditions: Bulk chemical--before 4/80 less than 20° C, then 4° C
Reference--before 11/79 less than 20° C, then −20° C or less

B. Analytical methods

1. Gas chromatography

Analyses performed on 2/25/79 and 6/12/79

Instrument: Hewlett-Packard 5840A with a 7672 automatic liquid sampler
Detector: Flame ionization
Column: 10% UCW-98 on 80/100 mesh Chromosorb W 1.8 m × 2 mm ID, glass, silanized
Detector temperature: 350° C
Inlet temperature: 250° C
Oven temperature program: 40° C for 4.00 min, then to 220° C at 5° C/min, held for 10 min
Carrier gas: Nitrogen, 30 ml/min
Sample size: Approximately 3 µl (2/25/79) or 37 µg (6/12/79) neat JP-5

Analyses performed from 12/12/79 to 12/20/82

Instrument: Hewlett-Packard 5880 with a 7672A automatic liquid sampler
Detector: Flame ionization
Column: 3.8% UCW-98 on 80/100 mesh Supelcoport, 1.8 m × 2 mm ID, glass, silanized
Detector temperature: 350° C
Inlet temperature: 275° C
Oven temperature program: 35° C for 5 min, then to 250° C at 5° C/min, held at 250° C for 2 min
Carrier gas: Nitrogen, 40 ml/min
Sample size: 1 µl, neat JP-5

2. Infrared spectroscopy

Instrument: Perkin-Elmer, 598
Cell: Neat liquid between potassium bromide plates

C. Results

1. **Gas chromatography:** Results were interpreted by peak grouping between major valleys in the chromatograms. Chromatograms were comparable for the reference and bulk chemical samples.

2. **Infrared spectroscopy:** No differences were observed between bulk chemical and reference samples. Spectra were consistent with that obtained by the analytical chemistry laboratory.

D. Conclusion: No significant change in composition of the bulk chemical was observed over the course of the studies

APPENDIX K

PREPARATION AND CHARACTERIZATION OF DOSE MIXTURES OF MARINE DIESEL FUEL

APPENDIX K. PREPARATION AND CHARACTERIZATION

I. Seven-Day Room Temperature Stability Studies Conducted at the Analytical Chemistry Laboratory

A. Sample preparation and storage: A stock solution (50.0% ± 0.08%, v/v; 418 mg/ml) of marine diesel fuel was prepared by pipetting 25 ml of compound into a 50-ml volumetric flask and diluting to the mark with absolute ethanol. This solution was subdivided by placing 10 aliquots (approximately 4 ml) into individual 8.5-ml septum vials. A pair of these samples were analyzed immediately and duplicate pairs were stored at room temperature (25° C) for 1, 4, 6, or 7 days.

B. Analysis: On the days of analysis, 3 ml of each stored sample was pipetted into a 200-ml volumetric flask and was diluted to the mark with absolute ethanol. This diluted solution was analyzed directly with the gas chromatographic system outlined below.

Instrument: Varian 3700 with CDS 111 Microprocessor
Detection: Flame ionization
Column: 3% SP2100 on 100/120 mesh Supelcoport 1.8 m × 2 mm ID, glass, silanized
Inlet temperature: 200° C
Oven temperature program: 70° C for 4 min, then 70°-200° C at 5° C/min
Detector temperature: 300° C
Carrier gas: Nitrogen, 30 ml/min

C. Quality control: The samples were analyzed in duplicate. A fresh standard solution was prepared on each day of analysis by dissolving marine diesel fuel in ethanol (6.8 mg/ml) to verify that the elution pattern was unchanged. It was also used daily to monitor the absolute areas of the major peaks compared with those in the sample, since a quantitative loss in all peaks would not be reflected by the ratio comparison.

D. Results

	Day 0	Day 1	Day 4	Day 6	Day 7
Area of major peak from sample (a)	6,947 ± 180	6,713 ± 196	7,298 ± 30	7,229 ± 26	6,486 ± 570
Area of standard peak (a)	7,144 ± 13	7,144 ± 13	7,696 ± 168	7,781 ± 45	6,546 ± 411
Ratio (b) of sample peak to standard peak	0.97 ± 0.03	0.94 ± 0.03	0.95 ± 0.02	0.93 ± 0.01	0.99 ± 0.11

(a) The figures are averages ($\times 10^{-2}$) of duplicate measurements for the standard and quadruplicate measurements for the sample determinations. The error values quoted are the actual deviations of the determinations from the average.
(b) Dimensionless; theoretical ratio: 0.92.

Ratio of Individual Peak Areas to the Sum of All Seven Peak Areas (a)

Peak No.	Retention Time (min)	Day 0	Day 1	Day 4	Day 6	Day 7
1	6.1	0.047	0.043	0.049	0.048	0.046
2	9.3	0.109	0.107	0.105	0.107	0.106
3	12.2	0.137	0.138	0.133	0.135	0.134
4 (major)	14.8	0.207	0.207	0.204	0.205	0.204
5	17.3	0.158	0.158	0.151	0.152	0.156
6	19.6	0.170	0.171	0.174	0.173	0.175
7	21.8	0.173	(b) 0.176	(b) 0.183	0.181	0.179

(a) Average of four values (in counts) for each entry; values reported are ± 0.006(δ) unless otherwise noted.
(b) ± 0.009(δ)

E. Discussion: Gas chromatographic analysis of marine diesel fuel yielded 40 peaks. Only seven of the largest peaks were monitored for this study, but all peaks were visually inspected on the chromatogram, and the chromatogram pattern remained unchanged.

The relative peak area of the seven monitored peaks did not show a significant change with time. The absolute peak area of the largest peak also remained constant from day to day throughout the 7-day study.

F. Conclusion: Marine diesel mixed with absolute ethanol at the 50% (v/v) concentration is stable when stored at room temperature (25° C) for 7 days.

II. Studies Conducted at the Study Laboratory

A. Sample preparation and storage: The dose mixtures were prepared by adding the proper amounts of marine diesel fuel to separate prelabeled clean and dry graduated cylinders. The final volume was reached by adding the desired amount of ACS-certified acetone. It was mixed by inversion until a uniform solution was obtained. The samples were stored at room temperature for 47 days. Duplicate volumes of each sample were transferred to separate autosampler vials with an SMI pipettor. Each vial was brought to a final volume of 1,000 µl with acetone. The volume of sample was chosen so that each vial contained marine diesel fuel in acetone within the concentration range of 20-100 mg/ml. Each vial was capped and shaken. Samples and standards were analyzed by the gas chromatographic conditions described below.

Instrument: Hewlett-Packard 5880
Column: 3% Dexsil 300 on 100/120 mesh Supelcoport; 1.8 m × 2 mm, silanized glass
Detection: Flame ionization
Inlet temperature: 385° C
Oven temperature program: 40° C for 2 min, then 40° C-350° C at 30° C/min, held at 350° C for 14.33 min
Detector temperature: 390° C
Carrier gas: Nitrogen, 40 ml/min

C. Results: The marine diesel fuel components were quantitated by peak summation of all of the peaks not present in the neat acetone chromatogram.

Storage Time (days)	Target Concentration (mg/ml)	Actual Concentration (mg/ml)	Percent of Target Concentration
7	50	48.5	97.1
	100	99.9	99.1
	200	200	100
47	50	51.8	104
	100	106	106
	200	208	104

D. Conclusion: Concentrations of marine diesel fuel in acetone ranging from 50 to 200 mg/ml were stable at room temperature for 47 days.

APPENDIX L

METHODS OF ANALYSIS OF DOSE MIXTURES OF MARINE DIESEL FUEL

APPENDIX L. METHODS OF ANALYSIS

I. Study Laboratory Procedure

Standard solutions and dose mixtures were diluted with acetone to obtain a target concentration range of 20-100 mg marine diesel fuel/ml. Marine diesel fuel content was determined by the following gas chromatographic system.

Instrument: Hewlett-Packard 5880
Column: 3% Dexsil 300 on 100/120 Supelcoport; 1.2 m × 2 mm, silanized glass
Detection: Flame ionization
Detector temperature: 390° C
Inlet temperature: 385° C
Oven temperature program: 40° C (1/81-7/81) or 45° C (7/81-11/82) for 2 min, then 30° C/min to 350° C, held at 350° C for 15 min (1/81-7/81) or 4 min (7/81-11/82)
Carrier gas: Nitrogen, 40 ml/min

The marine diesel fuel components were quantitated by peak summation of all the peaks not present in the neat acetone chromatogram.

II. Analytical Chemistry Laboratory Procedure

A. Preparation of standard spiked acetone: Two standard solutions of marine diesel fuel were prepared independently in the acetone submitted by the study laboratory. Both solutions were diluted with acetone to make four additional standards. The six standard solutions bracketed the specified target concentration range of the referee samples.

B. Analysis: Aliquots of the spiked acetone standards, referee samples (in triplicate), and undosed acetone were transferred to 100- or 250-ml volumetric flasks and diluted to volume with methanol. After being mixed, the marine diesel fuel content of the solutions was determined with the gas chromatographic system described below.

Instrument: Varian 3700 gas chromatograph with autosampler and Varian CDS 111-C integrator
Column: 10% SP2100 on 100/120 Supelcoport, 1.8 m × 2 mm ID, glass, silanized
Detection: Flame ionization
Detector temperature: 300° C
Inlet temperature: 200° C
Temperature program: 50° to 200° C at 5° C/min
Carrier gas: Nitrogen, 30 ml/min
Volume of solution injected: 3 or 3.5 µl

Under these test conditions the chromatograms exhibited 30-33 peaks. For the quantitative determination of marine diesel fuel in the samples, measurements were based on either the total area of all the peaks obtained for each sample (samples mixed on 1/13/81 and 9/21/82) or one of the well-resolved major peaks (samples mixed on 8/25/81 and 2/9/82).

The total amount of marine diesel fuel in the referee skin paint samples was determined from the linear regression equation computed from the standard data, relating peak area measurements of the selected peak of each spiked acetone standard to the amount of chemical in the respective spiked acetone standard.

C. Quality assurance measures: The referee sample was analyzed in triplicate, and the undosed acetone sample was analyzed once. Individually spiked portions of undosed acetone (six concentrations) prepared from two independently weighed standards were used to obtain standard data. Duplicate injections of each standard and sample were made into the gas chromatograph in a randomized order.

APPENDIX M

RESULTS OF ANALYSIS OF DOSE MIXTURES OF MARINE DIESEL FUEL

TABLE M1. RESULTS OF ANALYSIS OF DOSE MIXTURES IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL

Date Mixed	Target Concentration (mg/ml)	Actual Concentration (a) (mg/ml)	Percent of Target Concentration
01/13/81	57.3	58.2	102
	45.8	45.3	98.9
	112.5	116.4	103
	89.5	90.0	101
03/10/81	76.8	77.7	101
	60.0	60.4	101
	153.5	154.3	101
	118.0	117.8	99.8
05/05/81	82.8	82.1	99.2
	62.8	62.3	99.2
	161	161	100
	125	121	96.8
06/30/81	91.0	86.2	94.8
	71.8	65.1	90.7
	174.0	180	103
	139.0	135	97.2
08/25/81	93.5	93.2	99.7
	72.3	70.0	96.8
	177.5	178	100
	144.0	149	103
10/20/81	93.5	89.6	95.8
	73.5	71.1	96.7
	176.0	172	97.7
	146.0	144	98.6
12/15/81	93.5	93.9	100
	75.8	75.6	99.7
	174.0	176.0	101
	149.0	146.0	98.0
02/09/82	92.5	90.5	97.8
	76.3	76.1	99.7
	167.5	167	99.7
	149.5	147	98.3
04/06/82	91.8	82.2	(b) 89.5
	77.0	68.6	(b) 89.1
	165.5	150	90.6
	153.5	146	95.1
06/01/82	94.3	92.8	98.4
	81.5	79.8	97.9
	164.0	159	97.0
	156.5	155	99.0
07/27/82	92.8	93.7	101
	82.0	81.7	99.6
	159.3	163.1	102
	155.5	160.4	103
09/21/82	91.0	91.7	101
	79.1	77.6	98.1
11/16/82	86.7	85.2	98.3
	78.2	77.4	99.0
Mean of percent of target			98.5
Standard deviation			3.3
Coefficient of variation			3.4
Number of samples			48

(a) Results of duplicate analysis
(b) Out of specifications; not remixed.

TABLE M2. RESULTS OF REFEREE ANALYSIS OF DOSE MIXTURES IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL

Date Mixed	Target Concentration (mg/ml)	Determined Concentration (a)	
		Study Laboratory	Referee Laboratory
01/13/81	112.5	116.4	106.0
08/25/81	93.5	93.2	94.0
02/09/82	76.3	76.1	74.1
09/21/82	91.0	91.7	88.3

(a) Results of duplicate analysis

APPENDIX N

PREPARATION AND CHARACTERIZATION OF DOSE MIXTURES OF JP-5 NAVY FUEL

APPENDIX N. PREPARATION AND CHARACTERIZATION

I. Seven-Day Room Temperature Stability Studies Conducted at the Analytical Chemistry Laboratory

A. Sample preparation and storage: A stock solution (50.00% ± 0.08%, v/v) of JP-5 navy fuel was prepared by pipetting 25 ml of compound into a 50-ml volumetric flask and diluting to the mark with absolute ethanol. This solution was subdivided by placing 10 aliquots of approximately 4 ml each into individual 8.5-ml septum vials. A pair of these samples was analyzed immediately, and duplicate pairs were stored at room temperature (25 C°) for 1, 4, 6, or 7 days.

B. Analysis: On the days of analysis, 3 ml of each stored sample was pipetted into a 200-ml volumetric flask and was diluted to the mark with absolute ethanol. This diluted solution was analyzed directly by the gas chromatographic system outlined below.

Instrument: Varian 3700 with CDS 111 Microprocessor
Detection: Flame ionization
Column: 3% SP2100 on 100/120 mesh Supelcoport 1.8 m × 2 mm ID, glass, silanized
Inlet temperature: 200°
Oven temperature program: 70° C initial hold, 4 min; 70° C to 200° C at 5° C/min
Detector: 300°C
Carrier gas: Nitrogen, 30 ml/min

C. Quality control procedures: The samples were analyzed in duplicate. A fresh standard solution was prepared each day of analysis by dissolving the JP-5 navy fuel in ethanol (approximately 7.3 mg/ml). The standard was used for pattern comparison to verify that the elution pattern was unchanged. It was also used daily to monitor the absolute areas of the major peaks compared with those in the sample, since a quantitative loss in all peaks would not be reflected by ratio comparison measurements used to demonstrate the stability of the various components.

D. Results

	Day 0	Day 1	Day 4	Day 6	Day 7
Area of major peak from sample (a)	6,198 ± 61	6,230 ±17	6,563 ± 135	6,810 ± 135	6,038 ± 11
Area of standard peak	7,750 ± 20	7,635 ± 26	7,784 ± 172	8,392± 143	7,441 ± 38
Ratio (b) of sample peak to standard peak	0.80 ± 0.01	0.82 ± 0.01	0.84 ± 0.03	0.81 ± 0.02	0.81 ± 0.04
Theoretical ratio	0.80	0.83	0.84	0.81	0.85

(a) The figures are averages ($\times 10^{-2}$) of duplicate measurements for the standard and quadruplicate measurements for the sample determinations. The error values quoted are the actual deviations of the determinations from the average.
(b) Dimensionless

Ratio of Individual Peak Areas to the Sum of All Nine Peak Areas (a)

Peak No.	Retention Time (min)	Day 0	Day 1	Day 4	Day 6	Day 7
1	3.2	0.066	0.067	0.067	0.063	0.065	
2 (largest peak)	6.2	0.217	0.218	(b) 0.211	(b) 0.198	0.223
3	9.3	0.211	0.211	0.204	(b) 0.191	0.212
4	12.2	0.207	0.205	0.199	0.191	0.206
5	14.8	0.214	0.212	0.209	0.207	0.211
6	17.3	0.085	0.087	(b) 0.109	(b) 0.151	0.084

(a) Average of four values for each entry; values reported are ± 0.009 (δ) unless otherwise noted.
(b) ± 0.039(δ)

E. Discussion: Gas chromatographic analysis of the JP-5 navy fuel on the packed column yielded 35 peaks. Only six of the largest peaks were monitored for this study, but all the peaks in the chromatogram were visually inspected, and the relative pattern did not change.

The relative peak area of the six monitored peaks did not show a significant change with time. The absolute peak area of the largest peak also remained constant from day to day throughout the 7-day study.

F. Conclusion: JP-5 navy fuel mixed with absolute ethanol at the 50% (v/v) concentration level is stable when stored at room temperature (25° C) for 7 days.

II. Studies Conducted at the Study Laboratory

A. Sample preparation and storage: The dose mixtures were prepared by adding the proper amounts of JP-5 navy fuel to separate prelabeled clean and dry graduated cylinders. The final volume was reached by adding the desired amount of ACS-certified acetone. It was mixed by inversion until a uniform solution was obtained. The samples were stored at room temperature for 0, 6, 12, or 52 days.

B. Sample extraction and analysis: Duplicate volumes of each sample were transferred to separate autosampler vials with an SMI pipettor. Each vial was brought to a final volume of 1,000 µl with acetone. The volume of sample was chosen so that each vial contained JP-5 navy fuel in acetone within the concentration range of 20-100 mg/ml. Each vial was capped and shaken. Samples and standards were analyzed by the gas chromatographic conditions described below.

Instrument: Hewlett-Packard 5880
Column: 3% Dexsil 300 on 100/120 mesh Supelcoport; 1.8 m × 2 mm, silanized glass
Detection: Flame ionization
Inlet temperature: 385° C
Oven temperature program: 40° C for 2 min, then 40° C to 350° C at 30° C/min, held at 350° C for 14.33 min
Detector temperature: 390° C
Carrier gas: Nitrogen, 40 ml/min

C. Results: The JP-5 navy fuel components were quantitated by peak summation of all of the peaks not present in the neat acetone chromatogram.

Storage Time (days)	Target Concentration (mg/ml)	Actual Concentration (mg/ml)	Percent of Target Concentration
0	50	49.4	98.8
	100	101	101
	200	202	101
6	50	48.4	96.8
	100	99.3	99.3
	200	199	99.5
12	50	48.0	96.0
	100	99.4	99.4
	200	198	99.0
52	50	52.5	105
	100	108	108
	200	209	105

D. Conclusion: Concentrations of JP-5 navy fuel in acetone ranging from 50 to 200 mg/ml were stable at room temperature for 52 days.

APPENDIX O

METHODS OF ANALYSIS OF DOSE MIXTURES OF JP-5 NAVY FUEL

APPENDIX O. METHODS OF ANALYSIS

I. **Study Laboratory Procedure:** Standard solutions and dose mixtures were diluted with acetone to obtain a target concentration range of 20-100 mg JP-5 navy fuel/ml. The JP-5 navy fuel content was determined by the following gas chromatographic system.

Instrument: Hewlett-Packard 5880
Column: 3% Dexsil 300 on 100/120 mesh Supelcoport; 1.8 m × 2 mm, silanized glass
Detection: Flame ionization
Detector temperature: 390° C
Inlet temperature: 385° C
Oven temperature program: 40° C for 2 min, then 40° C to 350° C at 30° C/min , held at 350° C at 30° C for 14.33 min
Carrier gas: Nitrogen, 40 ml/min

II. **Analytical Chemistry Laboratory Procedure**

A. **Preparation of standard spiked acetone standards:** Two standard solutions of JP-5 navy fuel were prepared independently in methanol or reagent-grade acetone. These solutions were used to make six spiked acetone standards with concentrations bracketing the specified concentration range of the referee sample.

B. **Analysis:** Aliquots of the spiked acetone standards, referee samples (in triplicate), and undosed acetone were transferred to 100- or 250-ml volumetric flasks and diluted to volume with methanol. The JP-5 navy fuel content of the solutions was determined with the chromatographic system described below.

Instrument: Varian 3700 gas chromatograph with autosampler and Varian CDS 111-C integrator
Column: 10% SP2100 on 100/120 mesh Supelcoport, 1.8 m × 2 mm ID, glass, silanized
Detection: Flame ionization
Detector temperature: 300° C
Inlet temperature: 200° C
Oven temperature program: 70° C for 4 min, then 70° C to 200° C at 4° C/min
Carrier gas: Nitrogen, 30 ml/min
Volume of solution injected: 3 or 5 µl

Chromatograms under these conditions exhibited 29 or 30 peaks. For the quantitative determination of JP-5 navy fuel in the samples, one of the well-resolved major peaks was used for the measurements. The weight of JP-5 navy fuel in the referee acetone samples was determined from the linear regression equation obtained from the standard, relating peak area measurements of the selected peak of each spiked acetone standard to the milligrams of chemical in the respective spiked acetone standard.

C. **Quality assurance measures:** The referee samples were each analyzed in triplicate, and the undosed acetone was analyzed once. Six individually spiked portions of undosed acetone were prepared from two independently weighed standards and were used to obtain standard data. Duplicate injections of each standard and sample were made into the gas chromatograph in a randomized order.

APPENDIX P

RESULTS OF ANALYSIS OF DOSE MIXTURES OF JP-5 NAVY FUEL

TABLE P1. RESULTS OF ANALYSIS OF DOSE MIXTURES IN THE TWO-YEAR DERMAL STUDIES OF JP-5 NAVY FUEL (a)

Date Mixed	Target Concentration (mg/ml)	Actual Concentration (a) (mg/ml)	Percent of Target Concentration
12/10/80	58.0	63.1	109.0
	49.0	48.2	98.4
	114.5	102.0	(b) 89.0
	96.5	94.7	98.1
12/12/80	114.5	116.0	(c) 101.0
02/04/81	76.0	75.8	99.7
	60.3	60.9	101.0
	152.0	152.0	100.0
	123.0	110.0	(d) 89.4
04/01/81	85.8	86.7	101.0
	65.0	64.7	99.5
	167.5	170.7	102.0
	130.0	129.0	99.2
05/27/81	95.0	97.0	102.0
	73.5	74.7	102.0
	182.0	188.0	103.0
	140.5	144.0	102.0
07/22/81	--	--	(e)
07/29/81	98.5	97.9	99.4
	78.5	79.3	101.0
	181.5	185.0	102.0
	144.0	144.0	100.0
09/16/81	101.5	102.0	100.0
	84.5	87.0	103.0
	182.5	185.0	101.0
	144.5	149.0	103.0
11/11/81	100.3	98.6	98.3
	84.5	83.4	98.7
	178.0	175.0	98.3
	150.5	144.0	95.7
01/06/82	99.3	91.9	92.5
	83.5	77.5	92.8
	177.0	155.0	(b) 87.6
	151.5	131.0	(b) 86.5
01/11/82	177.0	170.0	(c) 96.0
	151.5	153.0	(c) 101.0
02/03/82	93.8	94.1	100.0
	85.3	84.1	98.6
	176.5	172.0	97.5
	149.5	147.0	98.3
03/03/82	95.3	95.5	100.0
	84.5	85.6	101.0
	171.0	172.0	101.0
	146.0	149.0	102.0

TABLE P1. RESULTS OF ANALYSIS OF DOSE MIXTURES IN THE TWO-YEAR DERMAL STUDIES OF JP-5 NAVY FUEL (a) (Continued)

Date Mixed	Target Concentration (mg/ml)	Actual Concentration (a) (mg/ml)	Percent of Target Concentration
04/28/82	98.0	99.5	102.0
	86.8	91.7	106.0
	173.0	188.0	109.0
	152.0	173.0	(b) 114.0
04/30/82	152.0	139.0	(c) 91.4
06/23/82	97.2	99.6	102.0
	88.3	91.0	103.0
	169.3	164.0	96.9
	149.0	146.0	98.0
08/18/82	95.6	97.6	102.0
	89.1	85.1	95.5
	161.2	161.5	100.0
	145.0	143.5	99.0
10/13/82	97.2	99.8	103.0
	94.0	99.0	105.0
	162.0	178.0	110.0
Mean of percent of target			100.0
Standard deviation			5.02
Coefficient of variation			5.02
Number of samples			55

(a) Results of duplicate analysis
(b) Out of specifications; not used in the study.
(c) Remix
(d) Out of specifications; not remixed.
(e) No reportable data

TABLE P2. RESULTS OF REFEREE ANALYSIS OF DOSE MIXTURES IN THE TWO-YEAR DERMAL STUDIES OF JP-5 NAVY FUEL

Date Mixed	Target Concentration (mg/ml)	Determined Concentration (a)	
		Study Laboratory	Referee Laboratory
07/22/81	144	(b)	149.9
01/06/82	83.5	77.5	83.3
08/18/82	161.2	161.5	165

(a) Results of duplicate analysis
(b) No reportable data

APPENDIX Q

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

Pelleted Diet: September 1980 to October 1982

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

TABLE Q1. INGREDIENTS OF NIH 07 RAT AND MOUSE RATION (a)

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

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

TABLE Q2. VITAMINS AND MINERALS IN NIH 07 RAT AND MOUSE RATION (a)

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

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

TABLE Q3. NUTRIENT COMPOSITION OF NIH 07 RAT AND MOUSE RATION (a)

Nutrient	Mean	Range	No. of Samples
Crude protein	24.04 ± 0.75	22.7-25.1	24
Crude fat (percent by weight)	4.84 ± 0.80	4.1-5.7	24
Crude fiber (percent by weight)	3.40 ± 0.29	2.9-4.3	24
Ash (percent by weight)	6.56 ± 0.50	5.7-7.43	24
Essential Amino Acids (percent of total diet)			
Arginine	1.260	1.21-1.31	2
Cystine	0.395	0.39-0.40	2
Glycine	1.175	1.15-1.20	2
Histidine	0.553	0.530-0.576	2
Isoleucine	0.908	0.881-0.934	2
Leucine	1.905	1.85-1.96	2
Lysine	1.250	1.20-1.30	2
Methionine	0.310	0.306-0.314	2
Phenylalanine	0.967	0.960-0.974	2
Threonine	0.834	0.827-0.840	2
Tryptophan	0.175	0.171-0.178	2
Tyrosine	0.587	0.566-0.607	2
Valine	1.085	1.05-1.12	2
Essential Fatty Acids (percent of total diet)			
Linoleic	2.37		1
Linolenic	0.308		1
Arachidonic	0.008		1
Vitamins			
Vitamin A (IU/kg)	10,920 ± 1,824	8,300-15,000	24
Vitamin D (IU/kg)	6,300		1
α-Tocopherol (ppm)	37.6	31.1-44.0	2
Thiamine (ppm)	17.2 ± 1.8	14.0-21.0	(b) 23
Riboflavin (ppm)	6.9	6.1-7.4	2
Niacin (ppm)	75	65-85	2
Pantothenic acid (ppm)	30.2	29.8-30.5	2
Pyridoxine (ppm)	7.2	5.6-8.8	2
Folic acid (ppm)	2.1	1.8-2.4	2
Biotin (ppm)	0.24	0.21-0.27	2
Vitamin B_{12} (ppb)	12.8	10.6-15.0	2
Choline (ppm)	3,315	3,200-3,430	2
Minerals			
Calcium (percent)	1.28 ± 0.18	1.08-1.69	24
Phosphorus (percent)	0.99 ± 0.06	0.88-1.10	24
Potassium (percent)	0.809	0.772-0.846	2
Chloride (percent)	0.557	0.479-0.635	2
Sodium (percent)	0.304	0.258-0.349	2
Magnesium (percent)	0.172	0.166-0.177	2
Sulfur (percent)	0.278	0.270-0.285	2
Iron (ppm)	418	409-426	2
Manganese (ppm)	90.8	86.0-95.5	2
Zinc (ppm)	55.1	54.2-56.0	2
Copper (ppm)	12.68	9.65-15.70	2
Iodine (ppm)	2.58	1.52-3.64	2
Chromium (ppm)	1.86	1.79-1.93	2
Cobalt (ppm)	0.57	0.49-0.65	2

(a) One or two batches of feed analyzed for nutrients reported in this table were manufactured in January and/or April 1983.
(b) One batch (July 22, 1981) was not analyzed for thiamine.

TABLE Q4. CONTAMINANT LEVELS IN NIH 07 RAT AND MOUSE RATION

Contaminant	Mean ± Standard Deviation	Range	No. of Samples
Arsenic (ppm)	0.44 ± 0.19	<0.05-1.06	24
Cadmium (ppm)	<0.10		24
Lead (ppm)	1.00 ± 0.73	0.42-3.37	24
Mercury (ppm) (a)	< 0.05		
Selenium (ppm)	0.31 ± 0.07	0.14-0.52	24
Aflatoxins (ppb) (a,b)	<10	<5.0-<10.0	24
Nitrate nitrogen (ppm) (c)	8.70 ± 3.67	2.1-17.0	24
Nitrite nitrogen (ppm) (c)	2.20 ± 1.59	0.4-6.9	24
BHA (ppm) (d, e)	6.02 ± 4.57	<0.5-16.0	24
BHT (ppm) (d)	3.03 ± 1.82	0.8-7.0	24
Aerobic plate count (CFU/g)	35,950 ± 27,857	4,900-88,000	24
Coliform (MPN/g) (f)	27.4 ± 52.6	<3-240	22
Coliform (MPN/g) (g)	90.9 ± 237.9	<3-1,100	24
E. coli (MPN/g) (h)	<3		24
Total nitrosamines (ppb) (h, i)	6.48 ± 5.82	0.8-18.5	21
Total nitrosamines (ppb) (i, j)	28.76 ± 64.88	0.8-273.2	24
N-Nitrosodimethylamine (ppb) (h, i)	5.24 ± 5.66	0.8-16.5	21
N-Nitrosodimethylamine (ppb) (i, j)	27.29 ± 64.45	0.8-272	24
N-Nitrosopyrrolidine (ppb)	1.23 ± 0.79	0.3-3.5	24
Pesticides (ppm)			
α-BHC (a, k)	<0.01		24
β-BHC (a)	<0.02		24
γ-BHC-Lindane (a)	<0.01		24
δ-BHC (a)	<0.01		24
Heptachlor (a)	<0.01		24
Aldrin (a)	<0.01		24
Heptachlor epoxide (a)	<0.01		24
DDE (a)	<0.01		24
DDD (a)	<0.01		24
DDT (a)	<0.01		24
HCB (a)	<0.01		24
Mirex (a)	<0.01		24
Methoxychlor (a, l)	<0.05	0.09 (8/26/81)	24
Dieldrin (a)	<0.01		24
Endrin (a)	<0.01		24
Telodrin (a)	<0.01		24
Chlordane (a)	<0.05		24
Toxaphene (a)	<0.1		24
Estimated PCB's (a)	<0.2		24
Ronnel (a)	<0.01		24
Ethion (a)	<0.02		24
Trithion (a)	<0.05		24
Diazinon (a, m)	<0.1	0.2 (4/27/81)	24
Methyl parathion (a)	<0.02		24
Ethyl parathion (a)	<0.02		24
Malathion (a, m)	0.09 ± 0.06	<0.05-0.27	24
Endosulfan I (a)	<0.01		24
Endosulfan II (a)	<0.01		24
Endosulfan sulfate (a)	<0.03		24

TABLE Q4. CONTAMINANT LEVELS IN NIH 07 RAT AND MOUSE RATION (Continued)

(a) All values were less than the detection limit, which is given in the table as the mean.
(b) Detection limit was reduced from 10 ppb to 5 ppb after 7/81.
(c) Source of contamination: Alfalfa, grains, and fish meal
(d) Source of contamination: Soy oil and fish meal
(e) Two batches contained less than 0.5 ppm.
(f) Mean, standard deviation, and range exclude one very high value of 1,100 obtained in the batch produced on 12/16/80 and one high value of 460 obtained in the batch produced on 9/23/82.
(g) Mean, standard deviation, and range include the high values listed in footnote (f).
(h) Mean, standard deviation, and range exclude three extreme values in the range of 115 - 273.2 ppb obtained in batches produced on 1/26/81, 2/23/81, and 4/27/81.
(i) All values were corrected for percent recovery.
(j) Mean, standard deviation, and range include the extreme value given in footnote h.
(k) BHC = hexachlorocyclohexane or benzene hexachloride
(l) One observation was above the detection limit. The value and the date it was obtained are listed under the range.
(m) Eleven batches contained more than 0.05 ppm.

APPENDIX R

SENTINEL ANIMAL PROGRAM

APPENDIX R. SENTINEL ANIMAL PROGRAM

I. Methods

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

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

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

II. Results

Results are presented in Table R1.

TABLE R1. MURINE VIRUS ANTIBODY DETERMINATIONS FOR MICE IN THE TWO-YEAR DERMAL STUDIES OF MARINE DIESEL FUEL AND JP-5 NAVY FUEL (a)

Interval (months)	No. of Animals	Positive Serologic Reaction for
Marine Diesel Fuel		
6	--	None positive
12	Not tested	--
18	3/8	MHV
24	10/10	MHV
JP-5 Navy Fuel		
6	--	None positive
12	3/10	MHV
18	3/8	MHV
24	--	None positive

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

APPENDIX S

DATA AUDIT SUMMARY

APPENDIX S. DATA AUDIT SUMMARY

The experimental data, laboratory records, pathology materials, and summary tables for the NTP toxicology and carcinogenesis studies of marine diesel fuel and JP-5 navy fuel were examined for completeness, consistency, and accuracy and for procedures consistent with Good Laboratory Practice requirements by Argus Research Laboratories, Inc. (marine diesel fuel), and by ImmuQuest Laboratories, Inc. (JP-5 navy fuel), under a contract with the NIEHS. The individuals involved in the audit for marine diesel fuel were J. Goeke, Ph.D., V. Everline, B.S., E. Feussner, V.M.D., J. Hills, B.A., D. Willett, B.S., and D. Copeland, V.M.D., and for JP-5 navy fuel were P. Errico, M.A., L. Brennecke, V.M.D., C. Reese, and K. Witkin, Ph.D. The 2-year studies in mice were begun in January 1981 and completed in January 1983 (marine diesel fuel) or were begun in December 1980 and completed in December 1982 (JP-5 navy fuel) at Litton Bionetics, Inc., Kensington, Maryland, under a subcontract from the National Cancer Institute with Tracor Jitco, Inc.

The full report of the NTP audit is on file at the NIEHS, Research Triangle Park, North Carolina. The audit included, but was not limited to, a review of the records of the inlife portion of the studies for 10% of the animals, 100% of the available chemistry data, and a random 50% sample of the chemical mix calculations. All Individual Animal Data Records were examined for correspondence between necropsy observations and histopathologic findings. All wet tissue bags were counted and 10% were reviewed for animal identification and the presence of untrimmed lesions. A complete slide-block match for each sex of both studies in the high dose and vehicle control groups was performed.

The audit for marine diesel fuel indicated that the inlife and chemistry portions were complete and without problems that would influence interpretation of study results. The pathology audit indicated that 3/55 animals sampled were incorrectly identified individually but could be properly identified by dose group and cage number. The results of the study were not affected, since the tumor analyses by group were unchanged.

In the JP-5 navy fuel audit, the inlife and chemistry portions were complete and without problems that would influence interpretation of study results. The pathology audit indicated that 1/40 animals were incorrectly identified individually but properly identified by dose group and cage. There were some cases of noncorrelation between gross and microscopic observations, but none of these involved target organs and could not have affected interpretation of the study.

Although not every item identified in the audits was fully resolved, it was concluded that the data reported were adequate to support the conclusions presented in this Technical Report.

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