

**NATIONAL TOXICOLOGY PROGRAM  
Technical Report Series  
No. 210**



**CARCINOGENESIS BIOASSAY  
OF  
1,2-DIBROMOETHANE  
(CAS NO. 106-93-4)  
IN F344 RATS AND B6C3F<sub>1</sub> MICE  
(INHALATION STUDY)**

**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 chemically induced 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 comprised of four charter DHHS agencies: the National Cancer Institute, National Institutes of Health; the National Institute of Environmental Health Sciences, National Institutes of Health; the National Center for Toxicological Research, Food and Drug Administration; and the National Institute for Occupational Safety and Health, Centers for Disease Control. In June 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS.

**NTP Technical Report**  
**on the**  
**CARCINOGENESIS BIOASSAY**  
**of**  
**1,2-DIBROMOETHANE**  
**(CAS NO. 106-93-4)**  
**IN F344 RATS AND B6C3F<sub>1</sub> MICE**  
**(INHALATION STUDY)**



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

## NOTE TO THE READER

This is one of the series of experiments designed to determine whether selected chemicals produce cancer in animals. Chemicals selected for testing in the NTP carcinogenesis bioassay 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 is a potential 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.

This study was initiated by the National Cancer Institute's Carcinogenesis Testing Program, now part of the National Institute of Environmental Health Sciences, National Toxicology Program.

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).

Comments and questions about the National Toxicology Program Technical Reports on Carcinogenesis Bioassays should be directed to the National Toxicology Program, located at Room A-306, Landow Building, Bethesda, MD 20205 (301-496-1152) or at Research Triangle Park, NC 27709 (919-541-3991).

Although every effort is made to prepare the Technical Reports as accurately as possible, mistakes may occur. Readers are requested to communicate any mistakes to the Deputy Director, NTP (P.O. Box 12233, Research Triangle Park, NC 27709), 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.

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## ABSTRACT

A carcinogenesis bioassay of 1,2-dibromoethane, a widely used nematocide and leaded gasoline additive, was conducted by exposing groups of 50 F344 rats and B6C3F1 mice of each sex by inhalation to concentrations of 10 or 40 ppm of the 1,2-dibromoethane for 78-103 weeks. Untreated controls consisted of 50 rats and 50 mice of each sex exposed in chambers to ambient air.

Throughout the study, mean body weights of high-dose rats and high-dose mice of either sex were lower than those of the corresponding untreated controls. Survival of the high-dose rats of either sex and of the low- and high-dose female mice was significantly shorter than that in the corresponding controls.

The principal cause of early death in control and dosed male mice was ascending, suppurative urinary tract infection that resulted in necrotic, ulcerative lesions around the urethral opening, chronic or suppurative cystitis (often with urinary tract obstruction), and ascending suppurative pyelonephritis.

Carcinomas and adenocarcinomas of the nasal cavity were observed with significantly increased incidences ( $P < 0.001$ ) in high-dose rats of either sex relative to controls. The incidences of adenocarcinomas and adenomas of the nasal cavity were also significantly increased ( $P < 0.001$ ) in low-dose rats of either sex. Adenomatous polyps of the nasal cavity showed significantly increased incidence ( $P < 0.001$ ) in low-dose male rats. The combined incidence of alveolar/bronchiolar adenomas and carcinomas was statistically significant ( $P=0.024$ ) for high-dose female rats.

Hemangiosarcomas of the circulatory system (mainly spleen) and mesotheliomas of the tunica vaginalis occurred in high-dose male rats with significantly increased incidences ( $P < 0.001$ ) relative to controls.

The incidence of fibroadenomas of the mammary gland was significantly elevated ( $P < 0.001$ ) in dosed female rats relative to controls.

The incidences of alveolar/bronchiolar carcinoma and alveolar/bronchiolar adenoma were significantly increased ( $P < 0.001$ ) in high-dose male mice relative to controls. These tumors were also increased in high-dose female mice ( $P = 0.007$  for adenomas and  $P < 0.001$  for carcinomas).

Hemangiosarcomas occurred in low- and high-dose female mice at incidences significantly greater ( $P < 0.001$ ) than the incidence in the controls (0/50). High-dose female mice also had significantly increased incidences of subcutaneous fibrosarcomas ( $P < 0.001$ ) and of nasal cavity carcinomas ( $P=0.013$ ). Low-dose female mice also showed a significantly increased incidence ( $P < 0.001$ ) of mammary gland adenocarcinomas.

Exposure to 1,2-dibromoethane was also associated with hepatic necrosis and toxic nephropathy in rats of either sex, testicular degeneration in male rats, retinal degeneration in female rats, and epithelial hyperplasia of the respiratory system in mice.

Under the conditions of this bioassay, 1,2-dibromoethane was carcinogenic for F344 rats, causing increased incidences of carcinomas, adenocarcinomas, adenomas of the nasal cavity, and hemangiosarcomas of the circulatory system in males and females; mesotheliomas of the tunica vaginalis and adenomatous polyps of the nasal cavity in males; and fibroadenomas of the mammary gland and alveolar/bronchiolar adenomas and carcinomas (combined) in females. 1,2-Dibromoethane was carcinogenic for B6C3F1 mice, causing alveolar/bronchiolar carcinomas and alveolar/bronchiolar adenomas in males and females; and hemangiosarcomas of the circulatory system, fibrosarcomas in the subcutaneous tissue, carcinomas of the nasal cavity, and adenocarcinomas of the mammary gland in females.

## CONTRIBUTORS

This bioassay of 1,2-dibromoethane was conducted from July 1976 to July 1978 by Hazleton Laboratories America, Inc., Vienna, Virginia, initially under direct contract to NCI and subsequently under a subcontract to Tracor Jitco, Inc., Rockville, Maryland, prime contractor for the NCI Carcinogenesis Testing Program.

The persons responsible for selecting the protocols used in this bioassay were Drs. O. G. Fitzhugh (1,2), C. Wessel (1,3), N. Page (4,5), and C. Cueto (4,6); representatives of Shell Oil Co., Dow Chemical Co., and the Ethyl Corp. participated in the dose selection. The principal investigators were Drs. M. B. Powers (7,4), R. W. Voelker (8), and W. B. Coate (8). Ms. K. J. Petrovics (8) was responsible for data management, and Mr. R. Hardy (8) was the supervisor of animal care. Histopathologic examinations were performed by Drs. D. A. Banas (8) and R. W. Voelker (8). The pathology report and selected slides were evaluated as described in Ward et al. (1978). The diagnoses represent a consensus of contracting pathologists and the NCI Pathology Working Group, with final approval by the NCI Pathology Working Group.

Animal pathology tables and survival tables were compiled at EG&G Mason Research Institute (9). Statistical analyses were performed by Dr. J. R. Joiner (1) and Ms. S. Vatsan (1), using methods selected for the bioassay program by Dr. J. J. Gart (10).

Chemicals used in this bioassay were analyzed at Midwest Research Institute (11), and concentrations of the test chemical in the exposure chambers were monitored at Hazleton Laboratories under the direction of Dr. W. B. Coate.

This report was prepared at Tracor Jitco in collaboration with Hazleton Laboratories and reviewed by NTP. Those responsible for the report at Tracor Jitco (1) were Dr. L. A. Campbell, Acting Director of the Bioassay Program; Dr. S. S. Olin, Associate Director; Dr. R. L. Schueler, pathologist; Dr. D. J. Beach, reports manager; Dr. A. C. Jacobs, bioscience writer; and Dr. W. D. Theriault and Ms. M. W. Glasser, technical editors.

The following scientists at NTP (4) were responsible for evaluating the bioassay, interpreting the results, and reporting the findings: Dr. J. Fielding Douglas, Dr. Richard A. Griesemer, Dr. Charles K. Grieshaber, Dr. Larry Hart, Dr. Joseph Haseman, Dr. James E. Huff, Dr. Ernest E. McConnell, Dr. John A. Moore, Dr. Marcelina B. Powers, Dr. Sherman F. Stinson, Dr. Raymond Tennant, and Dr. Jerrold M. Ward.

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## PEER REVIEW PANEL AND COMMENTS

On June 27, 1980, this report underwent peer review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The review meeting began at 9 a.m. in room 1331, Switzer Building, 330 C Street, S.W., Washington, D.C. Members of the Subcommittee are: Drs. Margaret Hitchcock (Chairperson), Curtis Harper, Thomas Shepard, and Alice Whittemore. Members of the Panel are: Drs. Norman Breslow, Joseph Highland, Charles Irving, Frank Mirer, Sheldon Murphy, Svend Nielsen, Bernard Schwetz, Roy Shore, James Swenberg, and Gary Williams. Drs. Highland, Schwetz, and Swenberg were unable to attend the review.

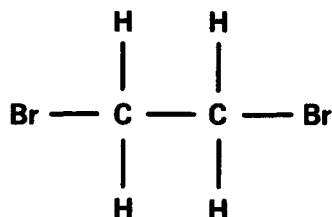
Dr. Shore, a principal reviewer for the report on the bioassay of 1,2-dibromoethane, agreed with the conclusion that 1,2-dibromoethane, under the conditions of the test, was carcinogenic in F344 rats and in B6C3F1 mice. 1,2-Dibromoethane induced tumors of the nasal cavity, circulatory system, and pituitary gland in male and female rats, mesotheliomas in the tunica vaginalis in males, and alveolar/bronchiolar carcinomas or adenomas and fibroadenomas of the mammary glands in female rats. 1,2-Dibromoethane induced alveolar/bronchiolar adenomas or carcinomas in male and female mice and fibrosarcomas in the subcutaneous tissues, hemangiosarcomas of the circulatory system, tumors of the nasal cavity, and adenocarcinomas of the mammary glands in female mice. Dr. Shore thought that the dose-related increase in carcinomas of the respiratory tract was particularly notable. Further, there were clear, dose-related increases in total numbers of malignant tumors in males and females of both species. A high rate of mortality induced by infectious disease in male mice may have suppressed group differences in late appearing tumors. Otherwise, the experimental design was judged adequate. As the second principal reviewer, Dr. Harper agreed with the conclusion.

There was considerable discussion about the selection of the inhalation route for this bioassay, since a previous bioassay by the gavage route had already demonstrated the carcinogenicity of 1,2-dibromoethane. Dr. Norton Nelson, Chairperson of the NTP Board of Scientific Counselors, and Dr. Williams said there should be side by side statements in the report comparing the findings. This procedure should also be followed in future reports in which a chemical is studied by different routes.

Dr. Shore moved that the report on the bioassay of 1,2-dibromoethane be accepted. Dr. Harper seconded the motion, and the report was approved unanimously by the Peer Review Panel.



## I. INTRODUCTION



### 1,2-DIBROMOETHANE

Molecular Formula:  $\text{C}_2\text{H}_4\text{Br}_2$  Molecular Weight: 187.9

1,2-Dibromoethane (CAS No. 106-93-4) (ethylene dibromide, EDB, ethylene bromide) is a colorless, volatile liquid used primarily as a lead scavenger in leaded gasolines and as a soil fumigant (Kirk-Othmer, 1965, 1968). The use of 1,2-dibromoethane as a fuel additive appears to be decreasing as leaded gasoline for automobiles is being phased out. However, more than 100 formulated pesticides contain 1,2-dibromoethane (EPA, 1976). In 1977, 244 million pounds were produced in the United States (U. S. International Trade Commission, 1978).

1,2-Dibromoethane, a dye intermediate in the preparation of Vat Blue 16 (CI 71205) and Vat Blue 53 (CI 71205) (Society of Dyers and Colourists, 1971), is also used as an industrial solvent for resins, gums, and waxes (IARC, 1977) and in some fire extinguishers (Clayton and Clayton, 1981).

1,2-Dibromoethane is mixed with an "inert" solvent for soil application as a nematocide and insecticide and mixed with carbon tetrachloride and ethylene dichloride for mill, warehouse, or household fumigation (Farm Chemicals Handbook, 1979). 1,2-Dibromoethane is degraded in soil or water. Two months after application to soil, 1,2-dibromoethane is converted almost quantitatively to ethylene by mixed microbial cultures -- primarily Pseudomonas and Flavobacteria (Castro, 1977). In water, 1,2-dibromoethane hydrolyzes to ethylene glycol and bromoethanol; the half-time for the process at ambient temperature is 5-10 days (Leinster et al., 1979).

Until 1958, 1,2-dibromoethane was used extensively as a grain storage fumigant in Minnesota, the Dakotas, Kansas, Iowa, Nebraska, Texas, and Oklahoma (Grain fumigants, 1958) and it is exempted from the tolerances set for organic bromide residues when applied after harvest on barley, corn, oats, popcorn, rice, rye, sorghum, and wheat. Tolerances for inorganic

bromides were set at 50 ppm (CFR, 1977). Unchanged 1,2-dibromoethane residues (up to 3.3 ppm) have been found in insufficiently aired feed grains up to 2 months after fumigation (Berck, 1974).

1,2-Dibromoethane has been used as a fumigant on all fruit imported from Hawaii (Malling, 1969). Because of its effectiveness in the control of the Mediterranean fruit fly, 1,2-dibromoethane is used for post-harvest application to beans, cantaloupe, bananas, citrus fruits, cucumbers, peppers, pineapples, and zucchini; residue tolerances of inorganic bromides were set at 10 ppm. Tolerances of 25 ppm for residues of total bromine have been set for cherries and plums (CFR, 1977).

Human exposure to 1,2-dibromoethane by inhalation can cause respiratory tract irritation, damage to the liver, kidney, spleen, and lungs; and irritation to skin and eyes (Deichmann and Gerarde, 1969). NIOSH (1977) recommended that no employee be exposed in the workplace to concentrations greater than  $1.0 \text{ mg/m}^3$  (0.13 ppm) in any 15-minute period.

The reported oral  $\text{LD}_{50}$  (gavage) of 1,2-dibromoethane is 420 mg/kg for female mice, 146 mg/kg for male albino rats, 117 mg/kg for female rats, and 110 mg/kg for guinea pigs (Rowe et al., 1952; and McCollister et al., 1956). Fifty percent of the rats exposed to air containing 200 ppm 1,2-dibromoethane died within 2 hours and 50% exposed to 50 ppm for 7 hours a day, 5 days per week died within 6 months (Rowe et al., 1952). Inhalation exposure to 1,2-dibromoethane is reported to cause lung irritation and increased liver and kidney weights in rats; fatty degeneration of the liver in guinea pigs, rabbits, and monkeys; congestion and parenchymatous degeneration of the kidneys in guinea pigs; and decreased weight of the spleen and testes in rats (Rowe, et al., 1952). 1,2-Dibromoethane causes degeneration of the spermatozoa of bulls fed 2 mg/kg body weight (Amir and Volcani, 1965).

The supernatant of rat liver homogenates contains an enzyme that catalyzes the reaction between glutathione and 1,2-dibromoethane (Nachtomi and Sarma, 1971), and Watanabe et al. (1978) calculated that 20 mg 1,2-dibromoethane would deplete the rat liver of glutathione.

According to Edwards et al. (1970), the small intestine, liver, kidney, and fat of male RF/Hiraki rats contained most of the radioactivity 3 hours after intraperitoneal injections of  $[1,2-^{14}\text{C}]$ -dibromoethane (40 mg/kg).



When rats were given intraperitoneal injections of  $[1,2-^{14}\text{C}]$ -dibromoethane (4.2 mol) and killed after 24 hours, the largest amount of radioactivity was bound to protein, DNA, and RNA in the liver and kidney, and intermediate amounts were found in the lung, testes, stomach, and large and small intestines. Bromoacetaldehyde, an alkylating agent identified as a metabolite of 1,2-dibromoethane in rats, has been suggested to be the compound involved in the irreversible binding to protein and nucleic acid (Hill et al., 1978).

1,2-Dibromoethane has been found to affect liver microsomes, DNA, and sperm. When liver microsomes from B6C3F1 mice and when DNA from salmon sperm were incubated with  $^{14}\text{C}$ -bromoacetaldehyde and  $^{14}\text{C}$ -bromoethanol, these metabolites of 1,2-dibromoethane were bound covalently to protein and DNA to a greater extent than was 1,2-dibromoethane (Kline et al., 1979). After Nachtomi and Sarma (1977) administered single doses of 0, 5.0, 7.5, 10, 15, or 22 mg/100 g body weight 1,2-dibromoethane in corn oil by gavage to male Wistar rats, liver DNA of dosed rats sedimented more slowly than that of untreated rats. Nachtomi and Sarma postulated that the slower sedimentation rate was caused by single strand breaks in the DNA.

1,2-Dibromoethane was mutagenic for Salmonella typhimurium G46, TA1530, and TA1535, without prior metabolic activation (Buselmaier et al., 1973, and Brem et al., 1974); for Drosophila melanogaster, (Vogel and Chandler, 1974); and for the plant Tradescantia (Sparrow et al. 1974).

1,2-Dibromoethane by the gavage route was carcinogenic in Osborne-Mendel rats, causing squamous-cell carcinomas of the forestomach in both sexes, hepatocellular carcinomas or neoplastic nodules in females, and hemangiosarcomas of the circulatory system in males; and in B6C3F1 mice, causing squamous-cell carcinomas of the forestomach and alveolar/bronchiolar adenomas in both sexes (Olson et al., 1973; Powers et al., 1975; IARC, 1977; NCI, 1978).

Other related chemicals undergoing toxicology and carcinogenesis bioassays include: bromoethane (ethyl bromide), bromodichloromethane, chlorodibromomethane, and 2,3-dibromo-1-propanol.

1,2-Dibromoethane was tested again by the Carcinogenesis Testing Program, this time using the inhalation route to determine the effects by this method, because workers and the general population are exposed to airborne 1,2-dibromoethane.

## II. MATERIALS AND METHODS

### A. Chemical

1,2-Dibromoethane (CAS No. 106-93-4) was obtained from Dow Chemical (Midland, Mich.) as a single batch (Lot No. 10065). Purity and identity analyses were performed at Midwest Research Institute, Kansas City, Missouri (Appendix E). Results of the elemental analyses agreed with the theoretical values. The infrared and nuclear magnetic resonance spectra were consistent with the structure and the literature spectra (Sadtler Standard Spectra). Results of vapor-phase chromatography, which were consistent with Dow's report that the material was 99.3%-99.4% 1,2-dibromoethane, indicated the presence of two major impurities comprising 0.26% and 0.38%, respectively, of the area of the major peak. All other impurities were present at levels of less than 0.05%.

In additional tests at Midwest Research Institute, residual chemical remaining in the generation flask after 4 weeks of generating airborne 1,2-dibromoethane was analyzed by vapor-phase chromatography and mass spectrometry. When the results were compared with a sample of the same lot number that had been stored at Hazleton Laboratories (Appendix F), a greater number of less volatile impurities with higher molecular weight were detected in the residue. Some of the impurities identified in the residue and their respective concentrations were bis(2-bromoethyl)ether, 3%; 1,2-dibromobutane less than 0.01%; 1,2-dibromo-3-chloropropane, 0.04%; and bromochlorobenzene (isomer not determined), 0.01%. Some of the impurities identified in the stored sample that were more volatile than 1,2-dibromoethane were vinyl bromide, comprising 0.04% of the major peak, and bromoethane, 0.06% of the major peak. Other impurities identified and their relative areas were 1,2-dibromo-3-chloropropane, 0.02%, and bis(2-bromoethyl)ether, 0.01%.

### B. Generation of 1,2-Dibromoethane Air Mixtures

1,2-Dibromoethane in air was generated by bubbling metered, filtered dried air, regulated at 10 psi, through a 1,000-ml glass globe flask that

was wrapped with black tape to reduce light exposure and contained at least 500 ml of the test chemical. The resultant mixture was forced into the make-up air input ducts of inhalation chambers through 8 feet of 1/4-inch interior diameter Teflon<sup>®</sup> tubing attached to the makeup air input duct. Each chamber had a separate flask and generation system. Each flask was located in a Plexiglas<sup>®</sup> box and equipped with an air line attached to its chamber exhaust duct and thus was under negative pressure with respect to the chamber room.

Before animal exposures began, the presence of aerosol during generation of 1,2-dibromoethane was assessed with a Royco Model 230 photometer. No aerosol was detected. The inhalation chambers were continuously monitored using a Miran<sup>®</sup> II (Wilks Scientific Corp., South Norwalk, Connecticut) infrared analyzer to detect any fluctuations during the day from the target concentrations. Actual concentrations of 1,2-dibromoethane in each inhalation chamber were determined 4 times per day by analyzing samples obtained from a closed-loop system sample line with a gas syringe. The gas samples were discharged into 15-ml test tubes containing 1.0 ml isopropanol. Aliquots of the mixed isopropanol solutions were injected directly into a Varian 600-D gas chromatograph equipped with an electron capture detector. Fresh standards of 1,2-dibromoethane were prepared daily and used for calibration of the gas chromatograph (Appendix G).

The chamber concentrations were usually within 10% of the target concentrations. The mean of 103 weekly mean vapor concentrations for the low-concentration chamber was  $10.02 \pm 0.84$  ppm (range 7.1-13.38 ppm) compared with a target concentration of 10 ppm. For the high-concentration chamber, the mean of 92 weekly mean chamber concentrations was  $38.93 \pm 2.55$  ppm (range 29.17-49.4 ppm) compared with a target concentration of 40 ppm.

### C. Animals

Five-week-old Fischer 344 rats and 4-week-old B6C3F1 mice obtained from the NCI Frederick Cancer Research Center, Frederick, Maryland, were marked for individual identification and assigned to dosed or control groups according to a published table of random permutations. All animals were held in their chambers for observation for 1 week before the start of the

bioassay. The control groups were shared with an inhalation study of 1,2-dibromo-3-chloropropane that started 2 weeks later.

#### D. Animal Maintenance

Male rats were housed three per cage, female rats were housed four per cage, and mice were housed four per cage in stainless steel wire mesh cages suspended in three tiers on aluminum racks inside the inhalation chambers (mice were on the bottom tier). Waste collection pans were placed beneath the two top tiers to catch urine, feces, and dropped food.

Animal cages were changed once per month initially and later twice per month (at the same time the animals were weighed). Soiled cages were sanitized in an industrial cage washer at 99°C using Acclaim® (Economics Laboratories). Water bottles were changed and sanitized weekly in a bottle washer. The inhalation chambers and waste pans were flushed of wastes daily using tap water after first removing the animals from the chambers. The chambers were washed with Zep® Formula 7961 (Zep Manufacturing Company) initially once per month and later twice per month when the animals were being weighed. The chamber room floor was hosed down with tap water and dried with a squeegee daily.

The food (Wayne Lab Blox®, Allied Mills, Inc., Chicago, Ill.) was placed in the chambers 1 hour after the end of the exposure period each weekday and was removed the following morning before the start of the exposure period. Food was available ad libitum on weekends. Water was available from water bottles equipped with stainless steel lick tubes. The animals lived in the inhalation chambers continuously, except when being weighed or observed. Animals in the control groups lived in identical inhalation chambers in the same room and were exposed to charcoal and HEPA-filtered, conditioned air. The temperature was maintained at 22.2<sup>o</sup>+1<sup>o</sup>C and the humidity at 50%. Fluorescent lighting was provided 12 hours per day.

Airflow into the cubical glass and stainless steel inhalation chambers (6 cubic meters) was maintained at 1,000 liters per minute and was monitored by flow calibrated Magnehelic® or Photohelic® pressure gauges. Entering air was drawn through HEPA filters (Cambridge®) and charcoal beds. Exhaust air was filtered through two 6-inch charcoal beds before entering a dilution

system and exiting the building via a stack. The chambers were maintained under negative pressure relative to the chamber rooms by individual positive displacement exhaust pumps.

#### E. Subchronic Studies

In subchronic inhalation studies conducted to determine the concentrations of 1,2-dibromoethane to be used in the chronic studies, groups of 4 or 5 male rats, 5 or 6 female rats, 10 male mice, and 10 female mice were exposed to 1,2-dibromoethane by inhalation at concentrations of 0, 3, 15, or 75 ppm for 6 hours per day, 5 days per week for 13 weeks. Animals were observed twice daily for mortality and for signs of toxicity or abnormal behavior. Individual animal weights were recorded weekly. After 13 weeks, all surviving animals were killed by intraperitoneal injections of sodium pentobarbital (Diabotal<sup>®</sup>, Diamond Laboratories, Inc., Des Moines, Iowa) and necropsied. Representative tissues were examined microscopically as described in the section on chronic studies. Exposure concentrations, survival, and mean body weights of the dosed and control groups are shown in Tables 1 and 2.

Rats: No deaths occurred in rats at any of the exposure concentrations tested. There was a dose-related depression in weight gain for male rats. In female rats, weight gain compared with the controls was depressed only at the 75 ppm dose. Furthermore, in rats exposed to 75 ppm, swelling and/or vacuolation of the adrenal cortical cells of the zona fasciculata were detected in 8/10, and slight decreases in follicular size in the thyroid were found in 6/10. Therefore, based on the toxicity observed at the 75-ppm level, concentrations of 1,2-dibromoethane selected for rats for the chronic study were 10 and 40 ppm.

Mice: Four of 10 male mice exposed to 3 ppm and 1/10 female mice exposed to the 75 ppm dose died. A dose-related depression in weight gain was observed for male and female mice. Eye irritation during weeks 12 and 13 was evident in mice exposed to 75 ppm. Megalocytic cells were found lining the bronchioles in 3/10 male mice and 9/10 female mice exposed to the highest concentration. Based on the toxicities observed at the 75 ppm

Table 1. Exposure Concentrations, Survival, and Mean Body Weights of Rats Receiving 1,2-Dibromoethane by Inhalation for 90 Days

Exposure Conc.(a) (ppm)	Survival(b)	Mean Body Weights (grams)			Weight Change(c) Relative to Controls (Percent)
		Initial	Final	Gain	
<b>Male</b>					
0	5/5	153.2	343.8	190.6	
3	4/4	109.2	283.8	174.6	- 8
15	5/5	146.2	284.8	138.6	-27
75	5/5	124.8	235.8	111.0	-42
<b>Female</b>					
0	5/5	115.0	172.8	57.8	
3	6/6	111.0	186.2	75.2	+30
15	5/5	110.4	177.2	66.8	+16
75	5/5	116.4	153.6	37.2	-36

(a) Exposure was 6 hours per day, 5 days per week

(b) Number surviving/number per group

(c) Weight Change relative to controls =

$$\frac{\text{Weight Gain (Dosed Group)} - \text{Weight Gain (Control Group)}}{\text{Weight Gain (Control Group)}} \times 100$$

Table 2. Exposure Concentrations, Survival, and Mean Body Weights of Mice Receiving 1,2-Dibromoethane by Inhalation for 90 Days

Exposure Conc.(a) (ppm)	Survival(b)	Mean Body Weights (grams)			Weight Change(c) Relative to Controls (Percent)
		Initial	Final	Gain	
<b>Male</b>					
0	10/10	17.4	31.7	14.3	
3	6/10	16.0	29.8	13.8	- 3
15	10/10	16.6	27.9	11.3	-21
75	10/10	16.6	25.8	9.2	-36
<b>Female</b>					
0	10/10	16.6	24.7	8.1	
3	10/10	17.0	23.9	6.9	-15
15	10/10	17.5	24.4	6.9	-15
75	9/10	15.3	21.4	6.1	-25

(a) Exposure was 6 hours per day, 5 days per week

(b) Number surviving/number per group

(c) Weight Change Relative to Controls =

$$\frac{\text{Weight Gain (Dosed Group)} - \text{Weight Gain (Control Group)}}{\text{Weight Gain (Control Group)}} \times 100$$



level, the concentrations of 1,2-dibromoethane selected for mice for the chronic inhalation study were 10 and 40 ppm.

#### F. Chronic Studies

The test groups, exposure concentrations, and durations of the chronic studies are shown in Table 3.

#### G. Clinical Examinations and Pathology

Animals were observed twice daily. Examinations of animals for clinical signs and the presence of palpable masses were recorded weekly. Animals were initially weighed monthly and then twice monthly beginning at week 80.

Moribund animals and those that survived to the end of the study were anesthetized by intraperitoneal injections of sodium pentobarbital (Diabutal,<sup>®</sup> Diamond Laboratories, Inc., Des Moines, Iowa), killed, and necropsied.

Gross and microscopic examinations were performed on all major tissues, organs, and gross lesions. The following tissues and organs were taken from killed animals and, when feasible, from animals found dead unless precluded in whole or part by autolysis or cannibalization: brain, pituitary, lymph nodes (cervical and mesenteric), spleen, thyroid, parathyroid, salivary glands, lung, trachea, heart, diaphragm, stomach, duodenum, jejunum or ileum, large intestine, pancreas, adrenal, kidney, liver, skin, ovary or testis, urinary bladder, prostate or uterus, and femur. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, routinely stained with hematoxylin and eosin, and examined histopathologically. An occasional section was subjected to special staining techniques for more definitive diagnosis.

Since the nasal cavity was a major target area, special processing was conducted. Nasal cavity and sinuses were fixed whole in neutral buffered 10% formalin, and/or in Bouin's solution, and decalcified using Perenyi's

Table 3. Experimental Design of Chronic Inhalation Studies with 1,2-Dibromoethane in Rats and Mice

Test Group	Initial No. of Animals	1,2-Dibromoethane Concentration(a) (ppm)	Time on Study	
			Exposed (weeks)	Observed (weeks)
<u>Male Rats</u>				
Control (b)	50	0	0	104-106
Low-Dose	50	10	103	1
High-Dose	50	40	88	0-1
<u>Female Rats</u>				
Control (b)	50	0	0	104-106
Low-Dose	50	10	103	1
High-Dose	50	40	91	0-1
<u>Male Mice</u>				
Control (b)	50	0	0	79
Low-Dose	50	10	78	0-1
High-Dose	50	40	78	0-1
<u>Female Mice</u>				
Control (b)	50	0	0	104-106
Low-Dose	50	10	103	1
High-Dose	50	40	90	0-1

- (a) Rats and mice were exposed to 1,2-dibromoethane 6 hours per day, 5 days per week.
- (b) Control groups in this study also served as controls in the bioassay of 1,2-dibromo-3-chloropropane, which started 2 weeks after this study.

method. Step cuts were made from the nostril to the cranial vault to ensure adequate tissue sampling and to enable visualization of the extent of tumor.

The number of animals from which particular organs or tissues were examined microscopically varies and does not necessarily represent the number of animals that were placed on study in each group.

#### H. Data Recording and Statistical Analyses

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

Probabilities of survival were estimated by the product-limit procedure of Kaplan and Meier (1958) and are presented in this report in the form of graphs. Animals were statistically censored as of the time that they died of other than natural causes or were found to be missing; animals dying from natural causes were not statistically 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) extensions of Cox's methods for testing for a dose-related trend. One-tailed P values are reported for all tests except the departure from linearity test, which is reported only when its two-tailed P value is less than 0.05.

The incidence of neoplastic or nonneoplastic lesions has been presented as the ratio of the number of animals bearing such lesions at a specific anatomic site (numerator) to the number of animals in which that site is examined (denominator). In most instances, the denominators included only those animals for which that site was examined histologically. However, when macroscopic examination was required to detect lesions (e.g., skin or mammary tumors) before histologic sampling or when lesions could have appeared at multiple sites (e.g., lymphomas), the denominators consist of the numbers of animals necropsied.

The statistical analyses of tumor incidence are intended to determine whether animals receiving the test chemical developed a significantly higher proportion of tumors than did the control animals. As a part of these

analyses, the one-tailed Fisher exact test (Cox, 1970) was used to compare the tumor incidence of a control group with that of a group of dosed animals at each dose level. When results for two dosed groups are compared simultaneously with those for a control group, a correction to ensure an overall significance level of 0.05 may be made. The Bonferroni test for inequality (Miller, 1966) requires that the P value for any comparison be less than or equal to 0.025. When this correction was used, it is discussed in the narrative section. It is not, however, presented in the tables where the Fisher exact P values are shown.

The Cochran-Armitage test for linear trend in proportions, with continuity correction (Armitage, 1971), was also used. Under the assumption of a linear trend, this test determines if the slope of the dose-response curve is different from zero at the one-tailed 0.05 level of significance. Unless otherwise noted, the direction of the significant trend is a positive dose relationship. This method also provides a two-tailed test of departure from linear trend.

The approximate 95% confidence interval for the relative risk of each dosed group compared with its control was calculated from the exact interval on the odds ratio (Gart, 1971). The lower and upper limits of the confidence interval of the relative risk have been included in the tables of statistical analyses. The interpretation of the limits is that, in approximately 95% of a large number of identical experiments, the true ratio of the risk in a dosed group of animals to that in a control group would be within the interval calculated from the experiment. When the lower limit of the confidence interval is greater than one, it can be inferred that a statistically significant result has occurred (P less than 0.025 one-tailed test when the control incidence is not zero, P less than 0.050 when the control incidence is zero). When the lower limit is less than unity but the upper limit is greater than unity, the lower limit indicates the absence of a significant result while the upper limit indicates that there is a theoretical possibility of the induction of tumors by the test chemical which could not be detected under the conditions of this test.

### III. RESULTS - RATS

#### A. Body Weights and Clinical Signs (Rats)

Mean body weights of high-dose rats of either sex were lower than those of the untreated controls throughout the study (Figure 1). Beginning at week 52, an increasing number of high-dose animals exhibited weakness of the limbs or body.

#### B. Survival (Rats)

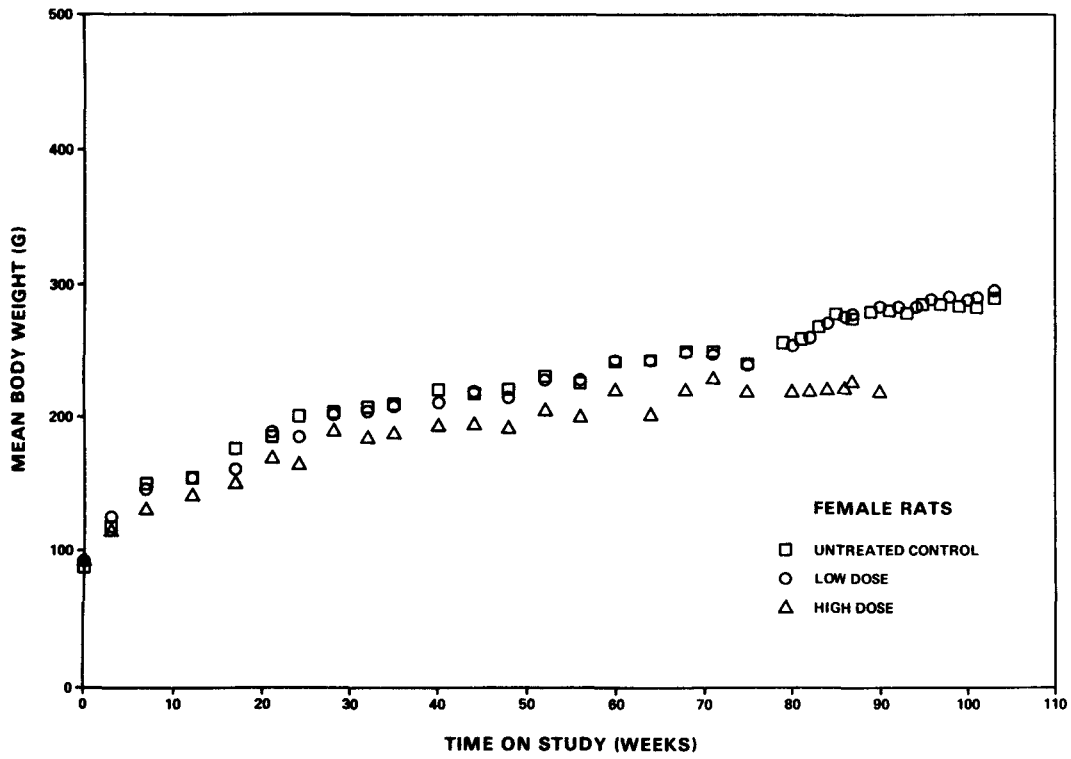
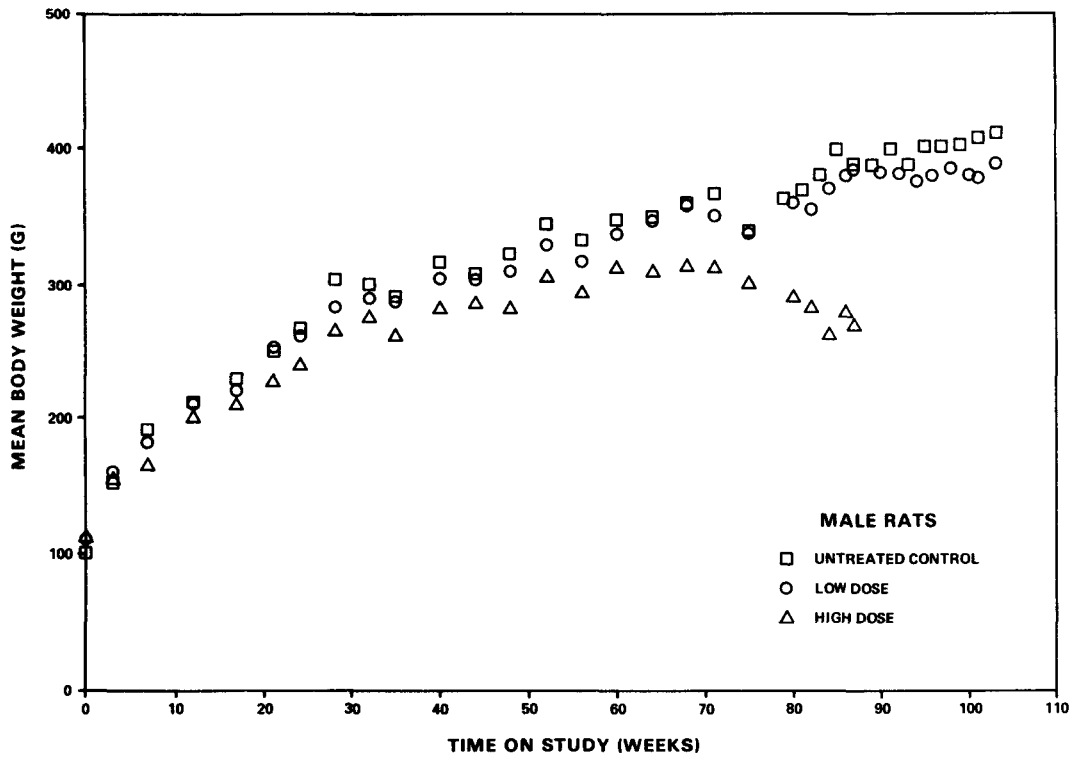
Estimates of the probabilities of survival for male and female rats administered 1,2-dibromoethane by inhalation at the concentrations of this bioassay, with those of the controls, are shown by the Kaplan and Meier curves in Figure 2. The Tarone test for positive dose-related trend in mortality is significant ( $P < 0.001$ ) in both sexes due to shortened survival in the high-dose group when compared with the low-dose group or the control group; however, survival in the control group and the low-dose group is comparable in both sexes.

In male rats, 38/50 (76%) of the control group and 35/50 (70%) of the low-dose group lived to the end of the study at 104-106 weeks. The high-dose group was killed at week 89, at which time 5/50 (10%) were still alive. In female rats, 38/50 (76%) of the control group and 39/50 (78%) of the low-dose group lived to the end of the study at 104-106 weeks. The high-dose female rats were killed at week 91, at which time 8/50 (16%) were still alive.

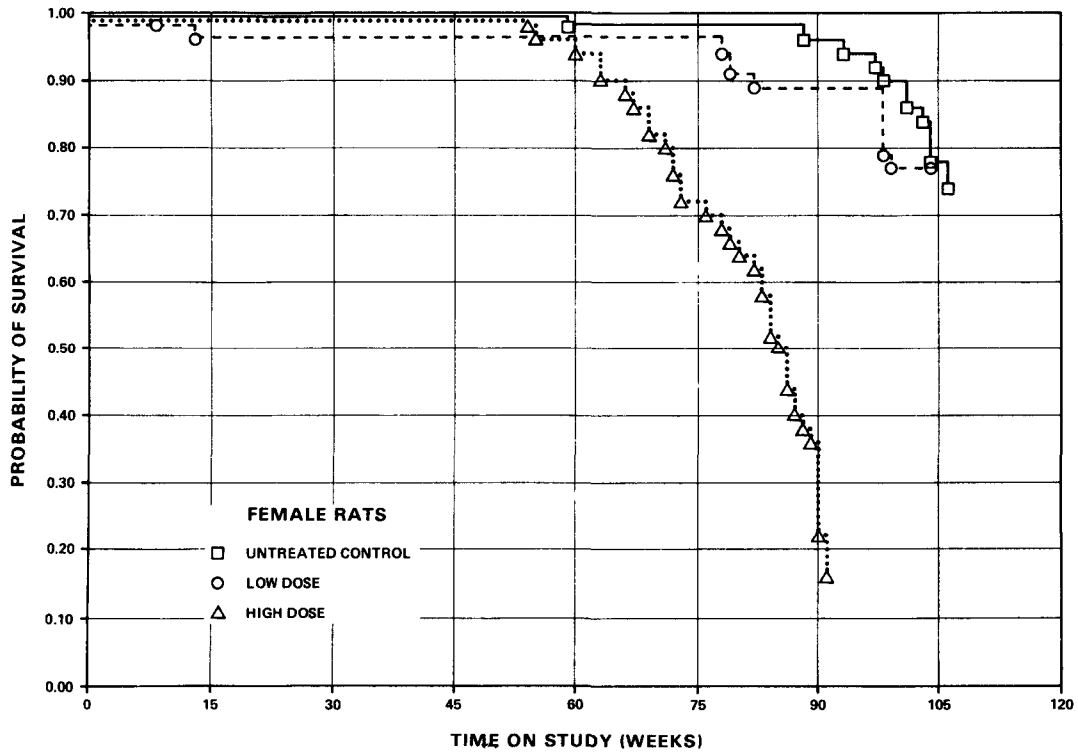
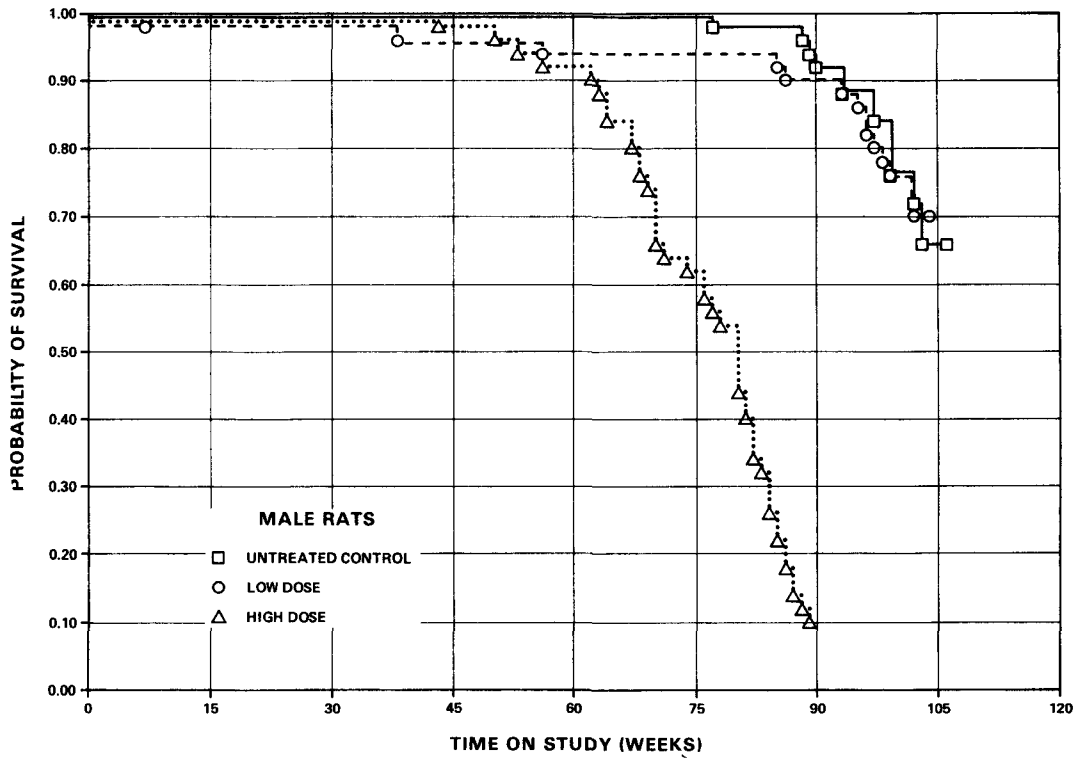
The early mortality observed among high-dose animals of both sexes may have curtailed the number of late-appearing tumors.

#### C. Pathology (Rats)

Histopathologic findings on neoplasms in rats are summarized in Appendix A, Tables A1 and A2; findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2.



**Figure 1. Growth Curves for Rats Exposed to Air Containing 1,2-Dibromoethane**



**Figure 2. Survival Curves for Rats Exposed to Air Containing 1, 2-Dibromoethane**

Nasal tumors were classified according to morphological appearance (Table 4). Adenomatous polyps occurred as small polypoid protrusions of well-differentiated nasal epithelium (usually with glandular structures) that extended into the nasal passages and that were attached by slender stalks to the underlying mucosa. Adenomas were also well differentiated, but they tended to be more globose and to have broader bases than those observed in the polyps. Small gland-like structures were present that resembled the normal acinar features of the nasal mucosa. The basal lamina was intact beneath these lesions. Adenocarcinomas were usually larger than adenomas, had a very broad base of attachment, and usually demonstrated invasion into the underlying tissue. The cells were occasionally more anaplastic than those observed in adenomas, but they were often fairly well-differentiated and consistently demonstrated a glandular appearance. Carcinomas varied from well-differentiated cells growing in solid sheets and cords to anaplastic neoplasms invading adjacent bone and extending through the cribiform plate into the olfactory lobes of the cerebrum. Although some neoplasms had areas resembling adenocarcinomas, other portions of the same tumors were less organized. These neoplasms occurred only in high-dose rats. Squamous-cell carcinomas were less common.

Epithelial hyperplasia, squamous metaplasia, and suppurative inflammation were prominent in the respiratory system. Hemangiosarcomas in the spleen were also associated with inhalation of 1,2-dibromoethane. These neoplasms were present in 1 low-dose male, 15 high-dose males, and 5 high-dose females. They were usually cavernous and hemorrhagic with prominent thrombosis.

In male rats, mesotheliomas involving either the tunica vaginalis of the testis only or multiple organs occurred in 1 control, 13 low-dose, and 26 high-dose rats. Mesothelial hyperplasia was noted in the tunica vaginalis of two high-dose males. In female rats, the incidence of mammary fibroadenomas was increased significantly (control-4/50, low dose-29/50, high dose-24/50).

Nonneoplastic lesions related to the inhalation of 1,2-dibromoethane occurred in the respiratory system, liver, kidney, testis, eye, and adrenal cortex. Hepatic necrosis (including that designated as focal or centrilobular) was present in 2 control, 6 low-dose, and 19 high-dose males and in 2 control, 3 low-dose, and 13 high-dose females. Toxic nephropathy was present



Table 4. Summary of the Incidences of Rats with Tumors of the Respiratory System after Exposure to 1,2-Dibromoethane by Inhalation

Site	Male			Female		
	Control 0 ppm	Low Dose 10 ppm	High Dose 40 ppm	Control 0 ppm	Low Dose 10 ppm	High Dose 40 ppm
<b>NASAL CAVITY</b>						
Number examined	50	50	50	50	50	50
Adenomatous polyp	0	18	5	0	5	5
Adenoma	0	11	0	0	11	3
Adenocarcinoma	0	20	28	0	20	29
Carcinoma	0	0	21	0	0	25
Squamous cell carcinoma	<u>0</u>	<u>3</u>	<u>3</u>	<u>1</u>	<u>1</u>	<u>5</u>
Total number with primary nasal cavity tumors	0	39(a)	41(a)	1	34(a)	43(a)
Brain carcinoma, invasive from nasal cavity	0	0	10	0	0	11
<b>LUNG/BRONCHUS</b>						
Number examined	50	50	50	50	48	47
Adenomatous polyp	0	0	1	0	0	0
<b>LUNG</b>						
Number examined	50	50	50	50	48	47
Alveolar/bronchiolar adenoma	0	1	1	0	0	1
Alveolar/bronchiolar carcinoma	<u>1</u>	<u>1</u>	<u>0</u>	<u>0</u>	<u>0</u>	<u>4</u>
Total number with lung tumors	1	2	1	0	0	5

(a) The incidence of tumors is greater than the incidence of animals with tumors since more than one type of tumor was detected in some of the same animals.

in no control, 4 low-dose and 28 high-dose males and in 8 high-dose females. Mineralization was present in four high-dose females.

Testicular degeneration (1/50, 10/50, 18/49) and atrophy (1/50, 2/50, 5/49) occurred with greater frequency in the dosed rats. However, many cases of atrophy in high-dose rats were associated with testicular tumors and mesotheliomas and may not have been a direct result of chemical toxicity. Spermatocytic granulomas were also noted more frequently in high-dose males. Degeneration of the adrenal cortex was observed in no control, 1 low-dose, and 1 high-dose male; and in 4 control, 7 low-dose, and 13 high-dose females. Retinal degeneration was noted in 1 male and 1 female control; retinal atrophy occurred in 1 low-dose male, 10 low-dose females, and 5 high-dose females.

Decreased incidences of age-related neoplasms and spontaneous disease lesions were noted in high-dose rats. These included interstitial-cell tumors, monocytic leukemia, pituitary tumors, pheochromocytomas, and chronic nephropathy. This decrease appears to be due to the poor survival of high-dose animals -- 45 males and 42 females either died or were killed in a moribund condition during the course of the experiment.

The results of histopathologic examination indicated that, under the conditions of this bioassay, 1,2-dibromoethane was carcinogenic in F344 rats, inducing neoplasms of the nasal cavity, mesothelium, spleen, and mammary gland. Hyperplastic and toxic lesions were also induced in a variety of tissues.

#### D. Statistical Analyses of Results (Rats)

Tables 5 and 6 contain the statistical analysis of those primary tumors that occurred in at least two animals of one group and at an incidence of at least 5% in one or more than one group.

In both sexes, the incidence of animals with nasal cavity tumors was significant in both the low- and high-dose groups ( $P < 0.001$ ). The combined incidence for nasal cavity tumors equalled 0/50 male controls, 39/50 low-dose males, 41/50 high-dose males, 1/50 female controls, 34/50 low-dose females, and 43/50 high-dose females.

For nasal cavity carcinomas, significant ( $P < 0.001$ ) positive dose-related trends and significantly higher ( $P < 0.001$ ) incidences in the high-dose group compared with the control group occurred in both sexes. The Cochran-Armitage test indicates a significant ( $P < 0.001$ ) positive linear trend in the incidence of adenocarcinomas in the nasal cavity in both sexes. The incidences of adenocarcinomas in each of the dosed groups in either sex are also significantly higher ( $P < 0.001$ ) than those in the control group.

For the combined incidence of alveolar/bronchiolar carcinomas and adenomas, a significant ( $P = 0.001$ ) positive trend in relation to increasing dose and a significantly higher ( $P = 0.024$ ) incidence occurred in the high-dose in female rats.

Hemangiosarcomas occurred with positive linear trends ( $P < 0.001$  in males and  $P = 0.002$  in females) in rats of both sexes. The incidences of this lesion were higher in the high-dose groups ( $P < 0.001$  in males and  $P = 0.028$  in females) than in the controls.

The incidence of dosed male rats with mesotheliomas in the tunica vaginalis is significantly higher ( $P = 0.006$  and  $P < 0.001$ , respectively) than that in the control groups, and a significant ( $P < 0.001$ ) dose-related trend is present.

In females, the Cochran-Armitage test indicates a significant ( $P = 0.002$ ) positive trend with a departure from linearity ( $P < 0.001$ ) in the incidence of animals with fibroadenomas in the mammary gland. Direct comparisons of the incidence in each dosed group with that of the control group are also significant ( $P < 0.001$ ).

The incidence of animals with adenomatous polyps in the nasal cavity was higher in dosed groups ( $P < 0.001$  for low-dose males,  $P = 0.028$  for high-dose males, and  $P = 0.028$  in each female dosed group).

The incidence of animals with adenomas in the nasal cavity is significantly higher ( $P = 0.001$ ) in the low-dose group than in the controls of either sex.

Dose-related positive linear trends are indicated in the incidences of follicular-cell adenomas or carcinomas in the thyroid gland ( $P = 0.011$ ) and of sarcomas that were unspecified or invasive in the salivary gland ( $P = 0.038$ ) in male rats; and in the incidences of fibroma or fibrosarcoma of the subcutaneous tissue ( $P = 0.005$ ), hepatocellular carcinomas ( $P = 0.038$ ), squamous

cell carcinomas of the nasal cavity ( $P=0.022$ ), and adenocarcinomas of the mammary gland ( $P=0.028$ ) in females; but since none of the Fisher exact tests applied to these incidences are significant, the relationship of these tumors to exposure to 1,2-dibromoethane is not clear.

There are departures from linear trend in the incidences of papillary adenomas of the nasal cavity ( $P=0.006$ ), C-cell adenomas of the thyroid gland ( $P=0.021$ ), and malignant mesotheliomas in multiple organs ( $P=0.008$ ) in males and of papillary adenomas of the nasal cavity ( $P=0.018$ ) in females. These departures from linear trend are a consequence of increased incidence in the low-dose group compared with the other two groups. Shortened survival may have reduced development of these tumors in the high-dose groups.

The incidence of male animals with adenomas in the pituitary gland was significantly higher ( $P=0.008$ ) in the low-dose group than in the control group. The historical incidence for spontaneous pituitary gland adenomas in male F344 rats in the Bioassay Program is 134/2,130 (6%) -- higher than the control group incidence of 0/45 (0%). The historical incidence at this laboratory is 0/200 for pituitary adenomas, NOS, and 16/200 (8%) for pituitary chromophobe adenomas. In females, there is a significantly higher incidence in the low-dose group ( $P<0.001$ ) when compared with the control group. The incidence observed in the female rat control group of this study (1/50, 2%) is lower than the historical incidence of 252/2,094 (12%) in the Bioassay Program for pituitary gland adenomas. The historical incidence at this laboratory is 1/200 for pituitary adenomas, NOS, and 70/200 (35%) for pituitary chromophobe adenomas. The shortened survival in the high-dose groups and the presence of other tumors may have affected the development of this tumor in those groups.

A negative trend ( $P<0.001$ ) with a significantly lower incidence in the high-dose male group ( $P<0.001$ ) when compared with the control group is indicated for the incidence of interstitial-cell tumors in the testis, but the result of the Fisher exact test is significant ( $P=0.011$ ) in the positive direction in the low-dose group. The low incidence in the high-dose group (10/49, 20%), as compared with the incidence in the low-dose group (45/50, 90%), was due primarily to early mortality in the former. This is a commonly occurring spontaneous tumor in aging Fischer 344 male rats.

Historical incidences in control groups in the Bioassay Program are usually between 80% and 100%.

Negative trends are also observed in the incidence of pheochromocytomas of the adrenal glands in male rats and of leukemia in both sexes. A significant ( $P=0.001$  in males and  $P<0.001$ ) dose-related trend in a negative direction was indicated by the Cochran-Armitage test for the incidence of chromophobe adenomas of the pituitary in either sex. The results of the Fisher exact test for the incidences of animals with chromophobe adenomas are also in the negative direction, and such results are influenced by the higher incidence in the control groups (10/45, 22%, in males and 20/50, 40%, in females) as compared with the historical incidence (161/2,130, 8%, in males and 389/2,094, 19%, in females).

In summary, the statistical analysis indicates that there is a dose-related increase in the incidences of nasal cavity tumors with the administration of 1,2-dibromoethane by inhalation in either sex. The occurrence of alveolar/bronchiolar carcinomas or adenomas in the lung of females, mesotheliomas in multiple organs and tunica vaginalis of males, and hemangiosarcomas in the circulatory system in both sexes is also related to exposure to 1,2-dibromoethane.

Table 5. Analyses of the Incidence of Primary Tumors In Male Rats Exposed to 1,2-Dibromoethane by Inhalation (a)

Topography: Morphology	Control	Low Dose	High Dose
Subcutaneous Tissue: Fibroma (b)	3/50 (6)	6/50 (12)	8/50 (16)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		2.000	2.667
Lower Limit		0.454	0.685
Upper Limit		11.761	14.816
Weeks to First Observed Tumor	104	102	77
Nasal Cavity: Carcinoma, NOS (b)	0/50 (0)	0/50 (0)	21/50 (42)
P Values (c,d)	P<0.001	N.S.	P<0.001
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	6.811
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	56
Nasal Cavity: Squamous Cell Carcinoma (b)	0/50(0)	3/50(6)	3/50(6)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.601	0.601
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	104	80

Table 5. Analyses of the Incidence of Primary Tumors In Male Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Nasal Cavity: Squamous Cell Carcinoma or Papilloma (b)	0/50(0)	4/50(8)	3/50(6)
P Values (c, d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.927	0.601
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	104	80
Nasal Cavity: Adenoma, NOS (b)	0/50 (0)	11/50 (22)	0/50 (0)
P Values (c,d)	N.S.	P=0.001	N.S.
Departure from Linear Trend (f)	P<0.001		
Relative Risk (Control) (e)		Infinite	--
Lower Limit		3.320	--
Upper Limit		Infinite	--
Weeks to First Observed Tumor	--	97	--
Nasal Cavity: Adenocarcinoma, NOS (b)	0/50 (0)	20/50 (40)	28/50 (56)
P Values (c,d)	P<0.001	P<0.001	P<0.001
Departure from Linear Trend (f)	P=0.002		
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		6.459	9.292
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	96	68

Table 5. Analyses of the Incidence of Primary Tumors In Male Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Nasal Cavity: Adenomatous Polyp, NOS (b)	0/50 (0)	18/50 (36)	5/50 (10)
P Values (c,d)	N.S.	P<0.001	P=0.028
Departure from Linear Trend (f)	P<0.001		
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		5.758	1.261
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	98	43
Nasal Cavity: Papillary Adenoma (b)	0/50(0)	4/50(8)	0/50(0)
P Values (c,d)	N.S.	N.S.	N.S.
Departure from Linear Trend (f)	P=0.006		
Relative Risk (Control) (e)		Infinite	--
Lower Limit		0.927	--
Upper Limit		Infinite	--
Weeks to First Observed Tumor	--	102	--
Nasal Cavity Tumors (Nose and Nasal Cavity), Adenoma, NOS, Adenocarcinoma, NOS, Adenomatous Polyp, NOS, Squamous Cell Carcinoma, Papillary Adenoma, Squamous Cell Papilloma, and Carcinoma, NOS (b)	0/50 (0)	39/50 (78)	41/50 (82)
P Values (c,d)	P<0.001	P<0.001	P<0.001
Departure from Linear Trend (f)	P<0.001		
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		13.372	14.180
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	96	43



Table 5. Analyses of the Incidence of Primary Tumors In Male Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
<hr/>			
Hematopoietic System: Monocytic Leukemia (b)	6/50 (12)	7/50 (14)	1/50 (2)
P Values (c,d)	P=0.026 (N)	N.S.	N.S.
Relative Risk (Control) (e)		1.167	0.167
Lower Limit		0.361	0.004
Upper Limit		3.911	1.302
Weeks to First Observed Tumor	88	97	87
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Hematopoietic System: Leukemia or Lymphoma (b)	6/50(12)	9/50(18)	2/50(4)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.500	0.333
Lower Limit		0.517	0.034
Upper Limit		4.749	1.758
Weeks to First Observed Tumor	88	7	84
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Circulatory System: Hemangiosarcoma (b)	0/50 (0)	1/50 (2)	15/50 (30)
P Values (c,d)	P<0.001	N.S.	P<0.001
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.054	4.710
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	96	50
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Table 5. Analyses of the Incidence of Primary Tumors In Male Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Salivary Gland: Sarcoma, NOS or Sarcoma, NOS, Invasive (b)	0/49(0)	1/50(2)	3/48(6)
P Values (c,d)	P=0.038	N.S.	N.S.
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.053	0.614
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	95	78
Pituitary: Adenoma, NOS (b)	0/45 (0)	7/48 (15)	2/47 (4)
P Values (c,d)	N.S.	P=0.008	N.S.
Departure from Linear Trend (f)	P=0.004		
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		1.826	0.284
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	86	78
Pituitary: Chromophobe Adenoma (b)	10/45 (22)	0/48 (0)	0/47 (0)
P Values (c,d)	P=0.001 (N)	P<0.001(N)	P<0.001(N)
Departure from Linear Trend (f)	P<0.001		
Relative Risk (Control) (e)		0.000	0.000
Lower Limit		0.000	0.000
Upper Limit		0.314	0.321
Weeks to First Observed Tumor	103	--	--

Table 5. Analyses of the Incidence of Primary Tumors In Male Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Adrenal: Pheochromocytoma (b)	4/49 (8)	5/49 (10)	0/48 (0)
P Values (c,d)	P=0.029 (N)	N.S.	N.S.
Relative Risk (Control) (e)		1.250	0.000
Lower Limit		0.286	0.000
Upper Limit		5.947	1.100
Weeks to First Observed Tumor	90	96	--
Thyroid: Follicular-cell Adenoma or Carcinoma (b)	0/48 (0)	0/50 (0)	3/46 (7)
P Values (c,d)	P=0.011	N.S.	N.S.
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	0.629
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	80
Thyroid: C-cell Adenoma (b)	0/48 (0)	3/50 (6)	0/46 (0)
P Values (c,d)	N.S.	N.S.	N.S.
Departure from Linear Trend (f)	P=0.021		
Relative Risk (Control) (e)		Infinite	--
Lower Limit		0.578	--
Upper Limit		Infinite	--
Weeks to First Observed Tumor	--	96	--

Table 5. Analyses of the Incidence of Primary Tumors In Male Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Thyroid: G-Cell Carcinoma (b)	3/48 (6)	2/50 (4)	1/46 (2)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.640	0.348
Lower Limit		0.055	0.007
Upper Limit		5.345	4.143
Weeks to First Observed Tumor	103	104	69
Thyroid: C-cell Adenoma or Carcinoma (b)	3/48 (6)	5/50 (10)	1/46 (2)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.600	0.348
Lower Limit		0.330	0.007
Upper Limit		9.811	4.143
Weeks to First Observed Tumor	103	96	69
Testis: Interstitial-cell Tumor (b)	35/50 (70)	45/50 (90)	10/49 (20)
P Values (c,d)	P<0.001 (N)	P=0.011	P<0.001 (N)
Departure from Linear Trend (f)	P<0.001		
Relative Risk (Control) (e)		1.286	0.292
Lower Limit		1.032	0.156
Upper Limit		1.511	0.516
Weeks to First Observed Tumor	93	85	64

**Table 5. Analyses of the Incidence of Primary Tumors In Male Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)**

Topography: Morphology	Control	Low Dose	High Dose
Epididymis: Mesothelioma, NOS or Invasive (b)	3/50(6)	0/50(0)	0/50(0)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.000	0.000
Lower Limit		0.000	0.000
Upper Limit		1.663	1.663
Weeks to First Observed Tumor	104	--	--
Tunica Vaginalis: Mesothelioma, NOS (b)	0/50 (0)	7/50 (14)	25/50 (50)
P Values (c,d)	P<0.001	P=0.006	P<0.001
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		1.941	8.224
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	96	50
Tunica Vaginalis: Mesothelioma, NOS or Malignant (b)	1/50(2)	8/50(16)	25/50(50)
P Values (c,d)	P<0.001	P=0.015	P<0.001
Relative Risk (Control) (e)		8.000	25.000
Lower Limit		1.136	4.425
Upper Limit		346.825	986.323
Weeks to First Observed Tumor	104	96	50

Table 5. Analyses of the Incidence of Primary Tumors In Male Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Multiple Organs: Mesothelioma, Malignant (b)	0/50 (0)	5/50 (10)	1/50 (2)
P Values (c,d)	N.S.	P=0.028	N.S.
Departure from Linear Trend (f)	P=0.008		
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		1.261	0.054
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	98	80

- (a) Dosed groups were exposed to concentrations of 10 or 40 ppm by inhalation.  
(b) Number of tumor-bearing animals/number of animals examined at site (percent).  
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.  
(d) A negative trend (N) indicates a lower incidence in a dosed group than in a control group.  
(e) The 95 percent confidence interval of the relative risk between each dosed group and the control group.  
(f) The probability level for departure from linear trend is given when P is less than 0.05 for any comparison.

Table 6. Analyses of the Incidence of Primary Tumors In Female Rats Exposed to 1,2-Dibromoethane by Inhalation (a)

Topography: Morphology	Control	Low Dose	High Dose
Subcutaneous Tissue: Fibroma (b)	0/50 (0)	0/50 (0)	3/50 (6)
P Values (c,d)	P=0.013	N.S.	N.S.
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	0.601
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	76
Subcutaneous Tissue: Fibroma or Fibrosarcoma (b)	0/50 (0)	0/50 (0)	4/50 (8)
P Values (c, d)	P=0.005	N.S.	N.S.
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	0.927
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	76
Nasal Cavity: Carcinoma, NOS (b)	0/50 (0)	0/50 (0)	25/50 (50)
P Values (c,d)	P < 0.001	N.S.	P < 0.001
Departure from Linear Trend (f)	P=0.050		
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	8.224
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	60

Table 6. Analyses of the Incidence of Primary Tumors In Female Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Nasal Cavity: Squamous Cell Carcinoma (b)	1/50 (2)	1/50 (2)	5/50 (10)
P Values (c,d)	P=0.022	N.S.	N.S.
Relative Risk (Control) (e)		1.000	5.000
Lower Limit		0.013	0.588
Upper Limit		76.970	231.346
Weeks to First Observed Tumor	97	99	79
Nasal Cavity: Adenoma, NOS (b)	0/50 (0)	11/50 (22)	3/50 (6)
P Values (c,d)	N.S.	P<0.001	N.S.
Departure from Linear Trend (f)	P<0.001		
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		3.320	0.601
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	98	91
Nasal Cavity: Adenocarcinoma, NOS (b)	0/50 (0)	20/50 (40)	29/50 (58)
P Values (c,d)	P<0.001	P<0.001	P<0.001
Departure from Linear Trend (f)	P=0.003		
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		6.459	9.651
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	52	63



Table 6. Analyses of the Incidence of Primary Tumors In Female Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Nasal Cavity: Adenomatous Polyp, NOS(b)	0/50 (0)	5/50 (10)	5/50 (10)
P Values (c,d)	N.S.	P=0.028	P=0.028
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		1.261	1.261
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	98	83
Nasal Cavity: Papillary Adenoma (b)	0/50 (0)	3/50 (6)	0/50 (0)
P Values (c,d)	N.S.	N.S.	N.S.
Departure from Linear Trend (f)	P=0.018		
Relative Risk (Control) (e)		Infinite	--
Lower Limit		0.601	--
Upper Limit		Infinite	--
Weeks to First Observed Tumor	--	104	--
Nasal Cavity Tumors : Adenoma, NOS, Carcinoma, NOS, Adenocarcinoma, NOS, Papillary Adenoma, Adenomatous Polyp, NOS, and Squamous Cell Carcinoma (b)	1/50 (2)	34/50 (68)	43/50 (86)
P Values (c,d)	P<0.001	P<0.001	P<0.001
Departure from Linear Trend (f)	P<0.001		
Relative Risk (Control) (e)		34.000	43.000
Lower Limit		6.275	8.415
Upper Limit		1297.564	1494.521
Weeks to First Observed Tumor	97	52	60

Table 6. Analyses of the Incidence of Primary Tumors In Female Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Carcinoma (b)	0/50 (0)	0/48 (0)	4/47 (9)
P Values (c,d)	P=0.004	N.S.	N.S.
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	0.987
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	85
Lung: Alveolar/Bronchiolar Carcinoma or Adenoma	0/50 (0)	0/48 (0)	5/47 (11)
P Values (c,d)	P=0.001	N.S.	P=0.024
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	1.342
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	85
Hematopoietic System: All Leukemias (b)	6/50 (12)	7/50 (14)	1/50 (2)
P Values (c,d)	P=0.026 (N)	N.S.	N.S.
Relative Risk (Control) (e)		1.167	0.167
Lower Limit		0.361	0.004
Upper Limit		3.911	1.302
Weeks to First Observed Tumor	88	8	91

Table 6. Analyses of the Incidence of Primary Tumors In Female Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
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Hematopoietic System: Monocytic Leukemia (b)	6/50 (12)	5/50 (10)	1/50 (2)
P Values (c,d)	P=0.032 (N)	N.S.	N.S.
Relative Risk (Control) (e)		0.833	0.167
Lower Limit		0.215	0.004
Upper Limit		3.064	1.302
Weeks to First Observed Tumor	88	104	91
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Circulatory System: Hemangiosarcoma (b)	0/50 (0)	0/50 (0)	5/50 (10)
P Values (c,d)	P=0.002	N.S.	P=0.028
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	1.261
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	73
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Circulatory System: Hemangiosarcoma or Hemangiosarcoma Invasive (b)	0/50 (0)	0/50 (0)	5/50 (10)
P Values (c,d)	P=0.002	N.S.	P=0.028
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	1.261
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	73
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Table 6. Analyses of the Incidence of Primary Tumors In Female Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Liver: Neoplastic Nodule (b)	2/50 (4)	0/49 (0)	3/48 (6)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.000	1.563
Lower Limit		0.000	0.187
Upper Limit		3.448	18.028
Weeks to First Observed Tumor	104	--	90
Liver: Hepatocellular Carcinoma (b)	0/50 (0)	1/49 (2)	3/48 (6)
P Values (c,d)	P=0.038	N.S.	N.S.
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.055	0.627
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	104	89
Liver: Neoplastic Nodule or Hepatocellular Carcinoma (b)	2/50 (4)	1/49 (2)	5/48 (10)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.510	2.604
Lower Limit		0.009	0.451
Upper Limit		9.474	26.304
Weeks to First Observed Tumor	104	104	89

Table 6. Analyses of the Incidence of Primary Tumors In Female Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Pituitary: Adenoma, NOS (b)	1/50 (2)	18/49 (37)	4/45 (9)
P Values (c,d)	N.S.	P < 0.001	N.S.
Departure from Linear Trend (f)	P<0.001		
Relative Risk (Control) (e)		18.367	4.444
Lower Limit		3.112	0.462
Upper Limit		741.072	213.732
Weeks to First Observed Tumor	106	52	83
Pituitary: Chromophobe Adenoma (b)	20/50 (40)	0/49 (0)	0/45 (0)
P Values (c,d)	P<0.001(N)	P<0.001(N)	P<0.001(N)
Departure from Linear Trend (f)	P<0.001		
Relative Risk (Control) (e)		0.000	0.000
Lower Limit		0.000	0.000
Upper Limit		0.158	0.171
Weeks to First Observed Tumor	93	--	--
Adrenal: Pheochromocytoma (b)	3/50 (6)	1/49 (2)	0/47 (0)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.340	0.000
Lower Limit		0.007	0.000
Upper Limit		4.062	1.766
Weeks to First Observed Tumor	103	104	--

Table 6. Analyses of the Incidence of Primary Tumors In Female Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Thyroid: C-cell Carcinoma (b)	1/49 (2)	3/48 (6)	1/45 (2)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		3.063	1.089
Lower Limit		0.257	0.014
Upper Limit		157.336	83.619
Weeks to First Observed Tumor	104	104	91
Mammary Gland: Adenocarcinoma, NOS(b)	1/50 (2)	0/50 (0)	4/50 (8)
P Values (c,d)	P=0.028	N.S.	N.S.
Relative Risk (Control) (e)		0.000	4.000
Lower Limit		0.000	0.415
Upper Limit		18.658	192.805
Weeks to First Observed Tumor	106	--	73
Mammary Gland: Fibroadenoma (b)	4/50 (8)	29/50 (58)	24/50 (48)
P Values (c,d)	P=0.002	P<0.001	P<0.001
Departure from Linear Trend (f)	P<0.001		
Relative Risk (Control) (e)		7.250	6.000
Lower Limit		2.844	2.280
Upper Limit		25.443	21.715
Weeks to First Observed Tumor	104	52	63

Table 6. Analyses of the Incidence of Primary Tumors In Female Rats  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Clitoral Gland: Carcinoma, NOS(b)	0/50 (0)	3/50 (6)	1/50 (2)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.601	0.054
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	104	91
Uterus: Endometrial Stromal Polyps(b)	6/50 (12)	3/49 (6)	4/48 (8)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.510	0.694
Lower Limit		0.087	0.153
Upper Limit		2.243	2.739
Weeks to First Observed Tumor	101	104	80

- (a) Dosed groups were exposed to concentrations of 10 or 40 ppm by inhalation.  
(b) Number of tumor-bearing animals/number of animals examined at site (percent).  
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.  
(d) A negative trend (N) indicates a lower incidence in a dosed group than in a control group.  
(e) The 95 percent confidence interval of the relative risk between each dosed group and the control group.  
(f) The probability level for departure from linear trend is given when P is less than 0.05 for any comparison.





#### IV. RESULTS - MICE

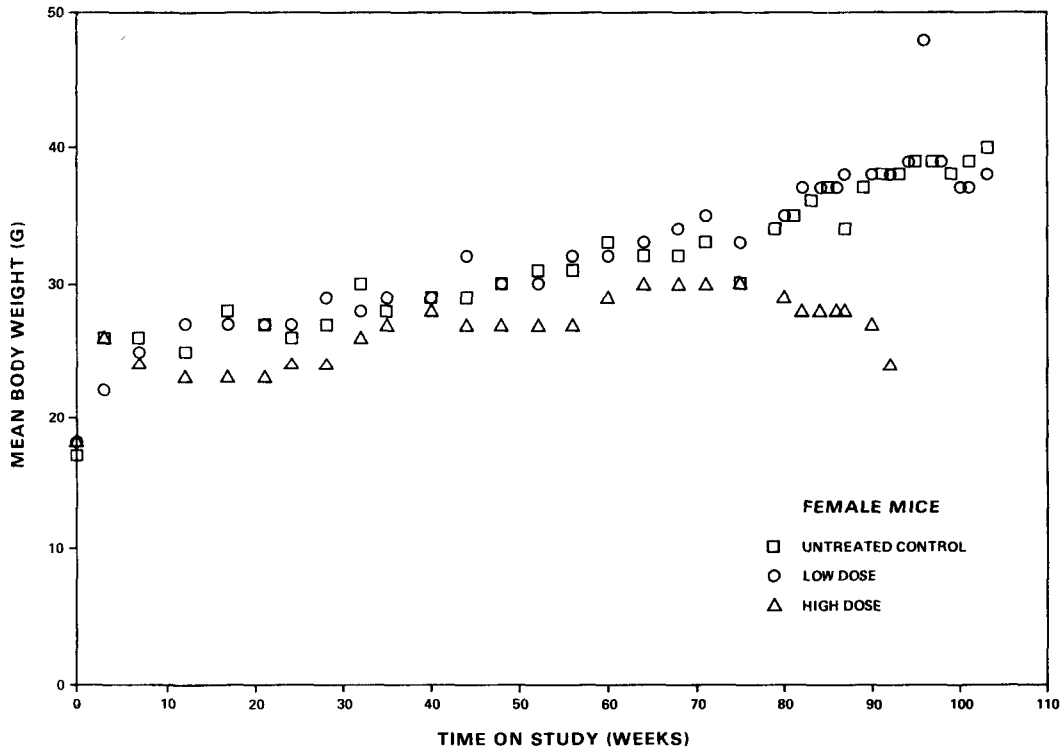
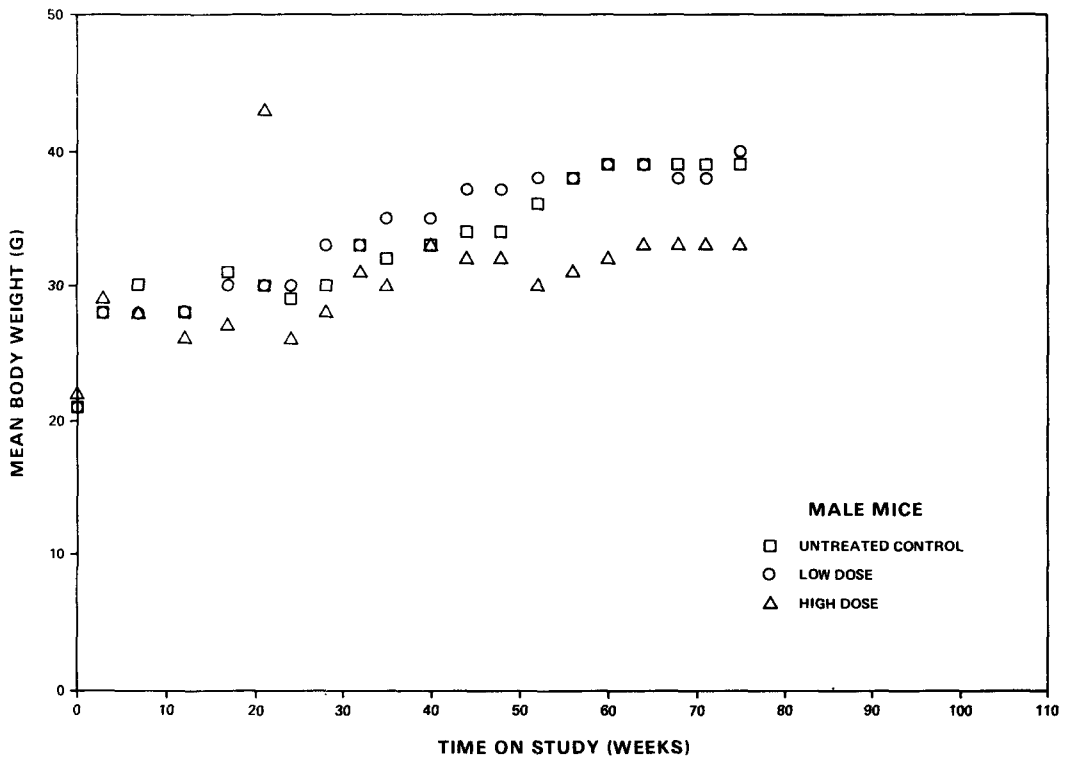
##### A. Body Weights and Clinical Signs (Mice)

Mean body weights of high-dose mice of either sex were lower than those of the corresponding untreated controls throughout the study (Figure 3). During the second year of the study, an increasing number of high-dose animals exhibited weakness of the limbs or body.

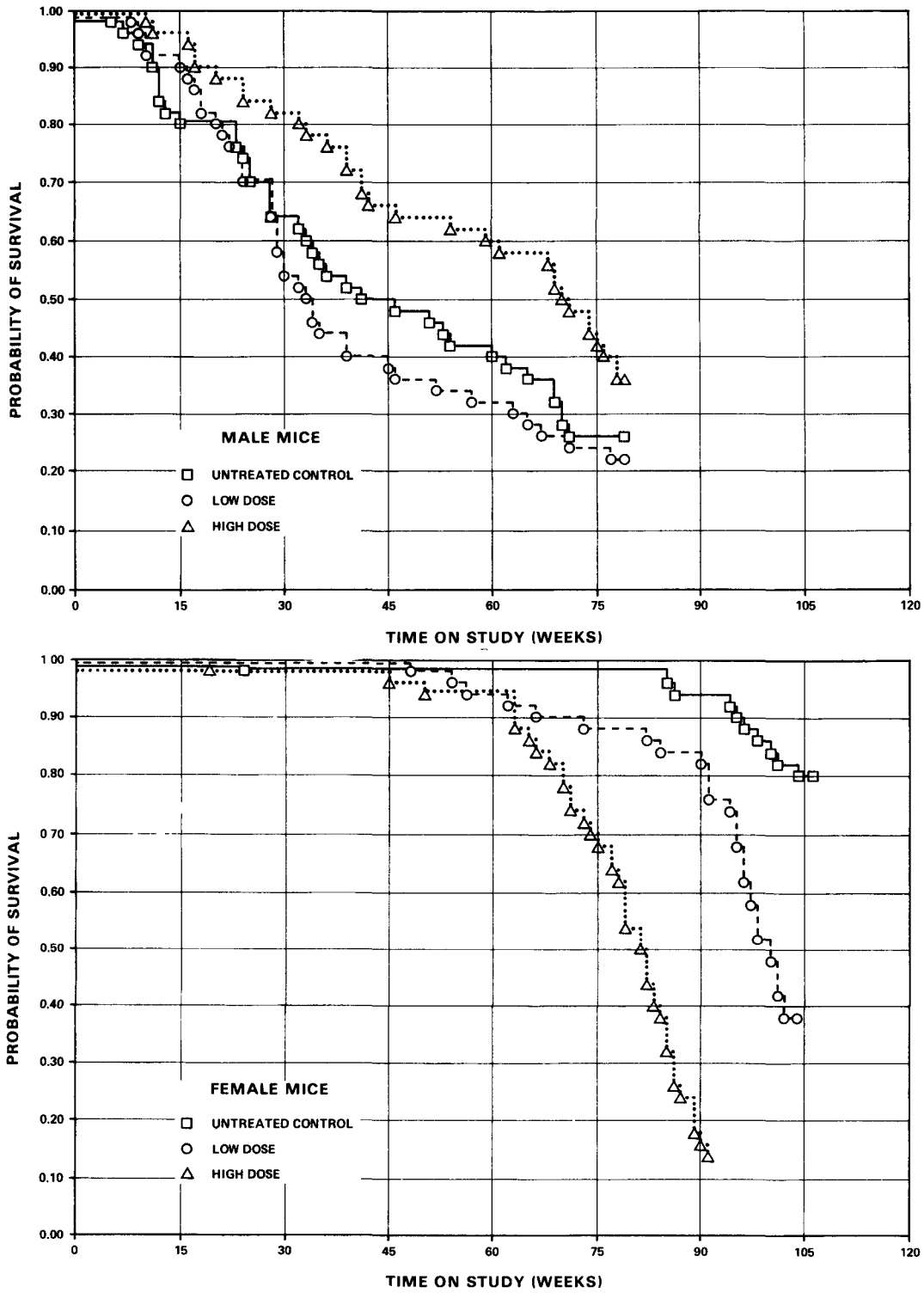
##### B. Survival (Mice)

Estimates of the probabilities of survival for male and female mice administered 1,2-dibromoethane by inhalation at the doses of this bioassay, together with those for the controls, are shown by the Kaplan and Meier curves in Figure 4. The results of the Tarone test of mortality are significant in both sexes ( $P=0.031$  in males and  $P < 0.001$  in females) due to shortened survival in the low-dose group of males and in the high-dose group of females. Direct comparisons of survival between each of the dosed groups and the control group and between the two dosed groups are also significantly different ( $P < 0.001$  in each instance) in females due to shortened survival in the dosed groups than in the controls and shorter survival in the high-dose group than in the low-dose group.

In male mice, 13/50 (26%) of the control group, 11/50 (22%) of the low-dose group, and 18/50 (36%) of the high-dose group lived to the end of the study at week 79. In females, 40/50 (80%) of the control group and 19/50 (38%) of the low-dose group lived to the end of the study at 104-106 weeks. The high-dose female mice were killed at week 91, when 7/50 (14%) were alive. Late-appearing tumors in the low-dose group of males and in the high-dose group of females may have been curtailed by early mortality.



**Figure 3. Growth Curves for Mice Exposed to Air Containing 1, 2-Dibromoethane**



**Figure 4. Survival Curves for Mice Exposed to Air Containing 1, 2-Dibromoethane**

### C. Pathology (Mice)

Histopathologic findings on neoplasms in mice are summarized in Appendix B, Tables B1 and B2; findings on nonneoplastic lesions are summarized in Appendix D, Tables D1 and D2.

A variety of neoplasms were seen in both control and dosed mice. Except for those of the respiratory and circulatory systems, mammary glands, and connective tissues, all were unrelated to chemical administration.

The respiratory neoplasms (Table 7) were classified according to morphologic appearance. Adenomatous polyps noted in the trachea, bronchi, or bronchioles were small benign neoplasms on slender stalks extending into the respiratory passages. The epithelium comprising these lesions was well differentiated. Alveolar/bronchiolar adenomas consisted of proliferations of well-differentiated alveolar/bronchiolar epithelium forming expanding masses with internal papillary-like projections. These neoplasms tended to be small and did not invade the adjacent parenchyma but tended to cause compression. Adenomas derived from the bronchial epithelium had a similar appearance, whereas carcinomas in the bronchi were invasive.

Alveolar/bronchiolar carcinomas consisted of two types. The well-differentiated neoplasms differed from alveolar/bronchiolar adenomas by their invasion of adjacent structures, large size, or early evidence of anaplasia. Some of these neoplasms encompassed entire lung lobes with evidence of intrapulmonary metastases via "seeding." Other tumors were much more anaplastic with solid cords and sheets of cells, some of which had an almost epithelioid appearance. These tumors were poorly circumscribed. It was not unusual to have multiple tumors of both types as well as adenomas, polyps, and epithelial hyperplasias in the same lung, particularly in the high-dose females.

Tumors of the nasal cavity consisted of adenomatous polyps, adenomas, and carcinomas arising from the nasal epithelium. The polyps were slender papillary proliferations, while the adenomas were more globose with a broader attachment area. Carcinomas were more anaplastic and tended to form solid sheets of cells. Invasion of adjacent connective tissue and bone was common.

Table 7. Summary of the Incidences of Mice with Tumors of the Respiratory System after Exposure to 1,2-Dibromoethane by Inhalation(a)

Topography: Morphology	Male			Female		
	Control 0 ppm	Low Dose 10 ppm	High Dose 40 ppm	Control 0 ppm	Low Dose 10 ppm	High Dose 40 ppm
<b>NASAL CAVITY</b>						
Number examined	45	50	50	50	50	50
Carcinoma	0	0	0	0	0	6
Adenoma	0	0	0	0	0	2
Adenomatous polyp	<u>0</u>	<u>0</u>	<u>0</u>	<u>0</u>	<u>0</u>	<u>3</u>
Total number with these tumors	0	0	0	0	0	11
<b>TRACHEA</b>						
Number examined	38	47	45	49	50	48
Adenomatous polyp	0	0	0	0	0	1
Carcinosarcoma	0	0	0	0	1	0
<b>LUNG/BRONCHUS</b>						
Number examined	41	48	46	49	49	50
Carcinoma	0	0	0	0	1	4
Adenoma	0	0	2	0	0	5
Adenomatous polyp	0	0	3	0	0	1
<b>LUNG/BRONCHIOLE</b>						
Number examined	41	48	46	49	49	50
Adenomatous polyp	0	0	2	0	1	2
<b>LUNG</b>						
Number examined	41	48	46	49	49	50
Alveolar/bronchiolar adenoma	0	0	11	3	7	13
Alveolar/bronchiolar carcinoma	<u>0</u>	<u>3</u>	<u>19</u>	<u>1</u>	<u>5</u>	<u>37</u>
Total number with tumors of lung, bronchus or bronchiole	0	3(b)	25(b)	4	11(b)	42(b)

(a) The tumors identified in the table represent diagnoses by pathologists at the contracting laboratories.

(b) The incidence of tumors is greater than the incidence of animals with tumors since more than one type of tumor was detected in some of the same animals.

Epithelial hyperplasia occurring throughout the respiratory system was a prominent feature in mice inhaling 1,2-dibromoethane, particularly in those surviving the longest. Serous and suppurative inflammation of the nasal cavity was also related to inhalation of 1,2-dibromoethane.

The occurrence of hemangiomas and hemangiosarcomas was related to the inhalation of 1,2-dibromoethane by B6C3F1 mice. These neoplasms were not observed in control mice, whereas hemangiosarcomas occurred in 2 high-dose males and in 11 low-dose and 23 high-dose females and hemangiomas occurred in 2 high-dose males and in 1 low-dose and 4 high-dose females. These neoplasms occurred predominantly in the retroperitoneal area of female mice, involving tissues adjacent to the adrenals, kidneys, ovaries, and uterus and occasionally invading these organs.

The occurrence of fibrosarcomas was also related to 1,2-dibromoethane inhalation. Two tumors were noted in high-dose males, 5 in low-dose females, and 15 in high-dose females. Lung metastases were noted in two low-dose and one high-dose female, and invasion of adjacent tissues was also noted in some neoplasms. The majority of the fibrosarcomas (2 in high-dose males, 4 in low-dose females, and 11 in high-dose females) were located in the subcutaneous tissues.

Malignant mammary neoplasms occurred with increased frequency in 1,2-dibromoethane-treated female mice. Adenocarcinomas were diagnosed in 2 controls and 14 low-dose and 8 high-dose mice; adenocarcinoma with squamous metaplasia in 1 high-dose mouse; and adenosquamous carcinoma in 4 low-dose and 1 high-dose mice.

In all compound-related alterations, the incidence of lesions in female mice greatly exceeded that in male mice. This does not appear to be a true sex-related trend, however, because the majority of male mice, both control and treated, died during the experiment and the remainder were killed at week 79. By contrast, the surviving high-dose females were not killed until week 91 and the surviving control and low-dose females were not killed until weeks 106 and 104, respectively. The principal cause of death in male mice of all groups was ascending, suppurative urinary tract infections that resulted in necrotic, ulcerative lesions around the urethral opening, chronic or suppurative cystitis often with urinary tract obstruction, and ascending suppurative pyelonephritis.

The results of histopathologic examination indicated that, under the conditions of this bioassay, 1,2-dibromoethane was carcinogenic in B6C3F1 mice, inducing neoplasms of the nasal cavity, lung neoplasms, and tumors of the blood vessels, mammary gland, and connective tissue. Hyperplastic lesions were also seen in the respiratory tract.

#### D. Statistical Analyses of Results (Mice)

Tables 8 and 9 contain the statistical analyses of the incidences of those primary tumors that occurred in at least two animals of one group and at an incidence of at least 5% in one or more than one group.

In both sexes, the incidence of animals with some form of respiratory tumor was significant in the high-dose groups ( $P < 0.001$ ). The following paragraphs contain the analysis of the specific respiratory tumors that occurred in significant incidences.

In males, a dose-related trend ( $P=0.005$ ) was observed in the incidence of animals with either hemangiomas or hemangiosarcomas in the circulatory system. In female mice, a significant ( $P < 0.001$ ) positive linear trend and a significantly higher ( $P < 0.001$ ) incidence of animals with hemangiosarcomas were seen in each of the dosed groups when compared with the control groups. Several of the females had multiple hemangiosarcomas.

A significant ( $P < 0.001$ ) positive dose-related trend in the incidence of animals with alveolar/bronchiolar adenomas or carcinomas was seen in either sex. The direct comparison of the incidence in either the male or female high-dose group with that of their control groups indicates a significant increase in tumors in the dosed groups ( $P < 0.001$ ).

The Cochran-Armitage test indicates significant positive trends in relation to increasing dose in the incidences of female mice with fibrosarcomas in subcutaneous tissue ( $P < 0.001$ ) and with carcinomas or adenomas in the nasal cavity ( $P < 0.001$ ) and in the lung/bronchus ( $P < 0.001$ ). The incidence of fibrosarcomas in subcutaneous tissue in the high-dose group of female mice is significantly higher ( $P < 0.001$ ) than the control group incidence. Several female mice in the low- and high-dose groups had multiple fibrosarcomas. Significantly higher incidences are also observed in animals

with carcinomas or adenomas in the nasal cavity ( $P=0.003$ ) and in the lung/bronchus ( $P=0.001$ ) of the high-dose group of female mice.

The Fisher exact test shows that the incidence of adenocarcinomas in the mammary gland of female mice is significantly higher ( $P=0.001$  in the low-dose group and  $P=0.046$  in the high-dose group) in the dosed groups than in the control group, but a dose-related linear trend is not indicated, since there is a departure from linear trend due to the higher incidence in the low-dose group (14/50, 28%) than in the high-dose group (8/50, 16%). The lower incidence in the high-dose group, compared with the low-dose group, may be a result of the shortened survival in the high-dose group.

The Cochran-Armitage test indicates significant dose-related trends in the incidence of adenomatous polyps of the lung/bronchus/bronchiole in male mice ( $P=0.002$ ) and in the incidences of adenomatous polyps or adenoma of the nasal cavity ( $P=0.002$ ) and of hemangiomas of the circulatory system ( $P=0.015$ ) in females.

The incidence of female mice with either adenomas or adenomatous polyps of the lung/bronchus is significantly higher ( $P=0.014$ ) in the high-dose group than in the control group. A positive dose-related trend ( $P=0.001$ ) is also observed.

A departure from linear trend ( $P=0.047$ ) has been indicated in the incidence of female mice with hepatocellular carcinomas or adenomas as a result of the higher incidence (6/50, 12%) observed in the low-dose group than in the high-dose group (1/50, 2%). A departure from linear trend ( $P=0.021$ ) is also observed in the incidence of animals with adenosquamous carcinomas in the mammary gland in females due to the higher incidence in the low-dose group (4/50, 8%) than in the high-dose group (1/50, 2%). These departures may be due to early mortality in the high-dose group of female mice from respiratory tumors.

A significant ( $P=0.005$ ) negative dose-related trend with a departure from linearity ( $P=0.027$ ) in the incidence of adenomas in the pituitary gland of female mice was detected with the Cochran-Armitage test. The results of the Fisher exact test in each of the dosed groups also indicate significantly lower ( $P=0.018$  and  $P=0.006$ , respectively) incidences in the dosed groups than in the control group. The historical incidence in female B6C3F1 mice for this lesion is 43/2,767 (2%), which is lower than the



control group incidence of 8/48 (17%). Significant results in the negative direction are also observed in the incidence of female mice with either lymphomas or leukemia.

In summary, the results of statistical analysis indicate a dose-related increase in the incidence of lung tumors in both sexes and in the incidences of fibrosarcomas of subcutaneous tissue or rib, of nasal cavity tumors, of hemangiosarcomas of the circulatory system, and of adenocarcinomas in the mammary gland of female mice. The incidence of hemangiomas in the circulatory system in females may also be associated with the administration of 1,2-dibromoethane.

**Table 8. Analyses of the Incidence of Primary Tumors In Male Mice Exposed to 1,2-Dibromoethane by Inhalation (a)**

Topography: Morphology	Control	Low Dose	High Dose
Lung/Bronchus: Adenomatous Polyp, NOS (b)	0/41 (0)	0/48 (0)	3/46 (7)
P Values (c)	P=0.014	N.S.	N.S.
Relative Risk (Control) (d)		--	Infinite
Lower Limit		--	0.539
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	78
Lung/Bronchus: Adenomatous Polyp, NOS, or Adenoma, NOS (b)	0/41(0)	0/48(0)	5/46(11)
P Values (c)	P=0.002	N.S.	P=0.037
Relative Risk (Control) (d)		--	Infinite
Lower Limit		--	1.131
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	78
Lung/Bronchus/Bronchiole: Adenomatous Polyp, NOS (b)	0/41 (0)	0/48 (0)	5/46(11)
P Values (c)	P=0.002	N.S.	P=0.037
Relative Risk (Control) (d)		--	Infinite
Lower Limit		--	1.131
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	78

Table 8. Analyses of the Incidence of Primary Tumors In Male Mice  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma (b)	0/41 (0)	0/48 (0)	11/46 (24)
P Values (c)	P<0.001	N.S.	P<0.001
Relative Risk (Control) (d)		--	Infinite
Lower Limit		--	2.980
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	68
Lung: Alveolar/Bronchiolar Carcinoma (b)	0/41 (0)	3/48 (6)	19/46 (41)
P Values (c)	P<0.001	N.S.	P<0.001
Relative Risk (Control) (d)		Infinite	Infinite
Lower Limit		0.517	5.488
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	65	69
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma (b)	0/41 (0)	3/48 (6)	23/46 (50)
P Values (c)	P<0.001	N.S.	P<0.001
Relative Risk (Control) (d)		Infinite	Infinite
Lower Limit		0.517	6.757
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	65	68

Table 8. Analyses of the Incidence of Primary Tumors In Male Mice  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Respiratory Tumors (Lung, Bronchus, and Bronchiole): Adenoma, NOS, Adenomatous Polyp, NOS, Alveolar/Bronchiolar Adenoma, and Alveolar/Bronchiolar Carcinoma (b)	0/41 (0)	3/48 (6)	25/46 (54)
P Values (c)	P<0.001	N.S.	P<0.001
Relative Risk (Control) (d)		Infinite	Infinite
Lower Limit		0.517	7.396
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	65	68
Circulatory System: Hemangioma or Hemangiosarcoma (b)	0/45 (0)	0/50 (0)	4/50 (8)
P Values (c)	P=0.005	N.S.	N.S.
Relative Risk (Control) (d)		--	Infinite
Lower Limit		--	0.837
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	39
Liver: Hepatocellular Carcinoma (b)	3/41 (7)	1/48 (2)	1/46 (2)
P Values (c)	N.S.	N.S.	N.S.
Relative Risk (Control) (d)		0.285	0.297
Lower Limit		0.006	0.006
Upper Limit		3.390	3.532
Weeks to First Observed Tumor	71	79	79

**Table 8. Analyses of the Incidence of Primary Tumors In Male Mice Exposed to 1,2-Dibromoethane by Inhalation (a)**  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Liver: Hepatocellular Carcinoma or Adenoma (b)	3/41 (7)	1/48 (2)	3/46 (7)
P Values (c)	N.S.	N.S.	N.S.
Relative Risk (Control) (d)		0.285	0.891
Lower Limit		0.006	0.126
Upper Limit		3.390	6.321
Weeks to First Observed Tumor	71	79	79

- (a) Dosed groups were exposed to concentrations of 10 or 40 ppm by inhalation.
- (b) Number of tumor-bearing animals/number of animals examined at site (percent).
- (c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.
- (d) The 95 percent confidence interval of the relative risk between each dosed group and the control group.

Table 9. Analyses of the Incidence of Primary Tumors In Female Mice Exposed to 1,2-Dibromoethane by Inhalation (a)

Topography: Morphology	Control	Low Dose	High Dose
Subcutaneous Tissue or Rib: Fibrosarcoma (b)	0/50 (0)	5/50 (8)	11/50 (22)
P Values (c,d)	P<0.001	P=0.028	P<0.001
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		1.261	3.320
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	54	50
Nasal Cavity: Carcinoma, NOS (b)	0/50 (0)	0/50 (0)	6/50 (12)
P Values (c,d)	P=0.001	N.S.	P=0.013
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	1.600
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	45
Nasal Cavity: Carcinoma, NOS, or Adenoma, NOS (b)	0/50 (0)	0/50 (0)	8/50 (16)
P Values (c), (d)	P<0.001	N.S.	P=0.003
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	2.284
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	45

Table 9. Analyses of the Incidence of Primary Tumors In Female Mice Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Nasal Cavity: Adenomatous Polyp, NOS (b)	0/50 (0)	0/50 (0)	3/50 (6)
P Values (c,d)	P=0.013	N.S.	N.S.
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	0.601
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	78
Nasal Cavity: Adenomatous Polyp, NOS or Adenoma, NOS (b)	0/50 (0)	0/50 (0)	5/50 (10)
P Values (c,d)	P=0.002	N.S.	P=0.028
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	1.261
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	75
Nasal Cavity Tumor: Adenoma, NOS Carcinoma, NOS, Adenomatous Polyp, NOS, and Hemangiosarcoma, NOS (b)	0/50 (0)	0/50 (0)	12/50 (24)
P Values (c,d)	P<0.001	N.S.	P<0.001
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	3.667
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	45

Table 9. Analyses of the Incidence of Primary Tumors In Female Mice Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Lung/Bronchus: Carcinoma, NOS(b)	0/49 (0)	1/49 (2)	4/50 (8)
P Values (c,d)	P=0.016	N.S.	N.S.
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.054	0.909
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	97	71
Lung/Bronchus: Adenoma, NOS (b)	0/49 (0)	0/49 (0)	5/50 (10)
P Values (c,d)	P=0.002	N.S.	P=0.030
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	1.237
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	77
Lung/Bronchus: Carcinoma, NOS or Adenoma, NOS (b)	0/49 (0)	1/49 (2)	9/50 (18)
P Values (c), (d)	P<0.001	N.S.	P=0.001
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.054	2.577
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	97	71



Table 9. Analyses of the Incidence of Primary Tumors In Female Mice  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Lung/Bronchus: Adenoma, NOS or Adenomatous Polyp, NOS (b)	0/49 (0)	0/49 (0)	6/50 (12)
P Values (c,d)	P=0.001	N.S.	P=0.014
Relative Risk (Control) (e)		--	Infinite
Lower Limit		--	1.569
Upper Limit		--	Infinite
Weeks to First Observed Tumor	--	--	77
Lung: Alveolar/Bronchiolar Adenoma (b)	3/49 (6)	7/49 (14)	13/50 (26)
P Values (c,d)	P=0.004	N.S.	P=0.007
Relative Risk (Control) (e)		2.333	4.247
Lower Limit		0.569	1.263
Upper Limit		13.275	21.916
Weeks to First Observed Tumor	104	96	63
Lung: Alveolar/Bronchiolar Carcinoma (b)	1/49 (2)	5/49 (10)	37/50 (74)
P Values (c,d)	P<0.001	N.S.	P<0.001
Relative Risk (Control) (e)		5.000	36.260
Lower Limit		0.589	6.799
Upper Limit		231.287	1359.586
Weeks to First Observed Tumor	104	84	50

Table 9. Analyses of the Incidence of Primary Tumors In Female Mice  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma (b)	4/49 (8)	11/49 (22)	41/50 (82)
P Values (c,d)	P<0.001	P=0.045	P<0.001
Relative Risk (Control) (e)		2.750	10.045
Lower Limit		0.883	4.260
Upper Limit		11.076	30.537
Weeks to First Observed Tumor	104	84	50
Respiratory Tumors (Bronchus, Bronchiole, and Lung): Adenoma, NOS, Carcinoma, NOS, Adenomatous Polyp, NOS, Alveolar/Bronchiolar Adenoma, and Alveolar/Bronchiolar Carcinoma	4/49 (8)	11/49 (22)	42/50 (84)
P Values (c, d)	P<0.001	P=0.045	P<0.001
Relative Risk (Control) (e)		2.750	10.290
Lower Limit		0.883	4.404
Upper Limit		11.076	30.407
Weeks to First Observed Tumors	104	84	50
Hematopoietic System: Malignant Lymphoma, Undifferentiated-Type (b)	3/50 (6)	0/50 (0)	0/50 (0)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.000	0.000
Lower Limit		0.000	0.000
Upper Limit		1.663	1.663
Weeks to First Observed Tumor	86	--	--

Table 9. Analyses of the Incidence of Primary Tumors In Female Mice  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Hematopoietic System: Malignant Lymphoma, Lymphocytic Type (b)	2/50 (4)	3/50 (6)	0/50 (0)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.500	0.000
Lower Limit		0.180	0.000
Upper Limit		17.329	3.381
Weeks to First Observed Tumor	104	100	--
Hematopoietic System: Malignant Lymphoma, Histiocytic - Type (b)	1/50 (2)	3/50 (6)	0/50 (0)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		3.000	0.000
Lower Limit		0.251	0.000
Upper Limit		154.270	18.658
Weeks to First Observed Tumor	104	91	--
Hematopoietic System: All Lymphomas (b)	8/50 (16)	6/50 (12)	0/50 (0)
P Values (c,d)	P=0.003 (N)	N.S.	P=0.003 (N)
Relative Risk (Control) (e)		0.750	0.000
Lower Limit		0.231	0.000
Upper Limit		2.281	0.438
Weeks to First Observed Tumor	86	91	--

Table 9. Analyses of the Incidence of Primary Tumors In Female Mice  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Hematopoietic System: Lymphoma or Leukemia (b)	8/50 (16)	7/50 (14)	1/50 (2)
P Values (c,d)	P=0.009 (N)	N.S.	P=0.015 (N)
Relative Risk (Control) (e)		0.875	0.125
Lower Limit		0.292	0.003
Upper Limit		2.549	0.880
Weeks to First Observed Tumor	86	73	84
Circulatory System: Hemangioma (b)	0/50 (0)	1/50 (2)	4/50 (8)
P Values (c,d)	P=0.015	N.S.	N.S.
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.054	0.927
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	94	79
Circulatory System: Hemangiosarcoma (b)	0/50 (0)	11/50 (22)	23/50 (46)
P Values (c,d)	P<0.001	P<0.001	P<0.001
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		3.320	7.515
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	90	63

Table 9. Analyses of the Incidence of Primary Tumors In Female Mice Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Circulatory System: Hemangioma or Hemangiosarcoma (b)	0/50 (0)	12/50 (24)	27/50 (54)
P Values (c,d)	P<0.001	P<0.001	P<0.001
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		3.667	8.935
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	90	63
Liver: Hepatocellular Carcinoma (b)	2/50 (4)	5/50 (10)	1/50 (2)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		2.500	0.500
Lower Limit		0.432	0.009
Upper Limit		25.286	9.290
Weeks to First Observed Tumor	104	66	79
Liver: Hepatocellular Carcinoma or Adenoma (b)	2/50 (4)	6/50 (12)	1/50 (2)
P Values (c,d)	N.S.	N.S.	N.S.
Departure from Linear Trend (f)	P=0.047		
Relative Risk (Control) (e)		3.000	0.500
Lower Limit		0.569	0.009
Upper Limit		29.254	9.290
Weeks to First Observed Tumor	104	66	79

Table 9. Analyses of the Incidence of Primary Tumors In Female Mice  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Pituitary: Adenoma, NOS (b)	8/48 (17)	1/46 (2)	0/40 (0)
P Values (c,d)	P=0.005 (N)	P=0.018 (N)	P=0.006 (N)
Departure from Linear Trend (f)	P=0.027		
Relative Risk (Control) (e)		0.130	0.000
Lower Limit		0.003	0.000
Upper Limit		0.915	0.522
Weeks to First Observed Tumor	104	62	--
Mammary Gland: Adenocarcinoma, NOS (b)	2/50 (4)	14/50 (28)	8/50 (16)
P Values (c,d)	N.S.	P=0.001	P=0.046
Departure from Linear Trend (f)	P=0.002		
Relative Risk (Control) (e)		7.000	4.000
Lower Limit		1.730	0.851
Upper Limit		60.610	37.147
Weeks to First Observed Tumors	101	48	70
Mammary Gland: Adenosquamous Carcinoma (b)	0/50 (0)	4/50 (8)	1/50 (2)
P Values (c, d)	N.S.	N.S.	N.S.
Departure from Linear Trend (f)	P=0.021		
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.927	0.054
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	94	19

Table 9. Analyses of the Incidence of Primary Tumors In Female Mice  
Exposed to 1,2-Dibromoethane by Inhalation (a)  
(continued)

Topography: Morphology	Control	Low Dose	High Dose
Harderian Gland: Adenoma NOS (b)	0/50 (0)	3/50 (6)	1/50 (2)
P Values (c,d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		Infinite	Infinite
Lower Limit		0.601	0.054
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	96	91

- (a) Dosed groups were exposed to concentrations of 10 or 40 ppm by inhalation.  
(b) Number of tumor-bearing animals/number of animals examined at site (percent).  
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.  
(d) A negative trend (N) indicates a lower incidence in a dosed group than in a control group.  
(e) The 95 percent confidence interval of the relative risk between each dosed group and the control group.  
(f) The probability level for departure from linear trend is given when P is less than 0.05 for any comparison.





## V. DISCUSSION

Mean body weights of high-dose male and female rats were lower than those of corresponding untreated controls throughout the study, and survival in the same high-dose groups was significantly shorter than that of controls.

Tumors of the respiratory tract and tumors of the mammary gland were found at significantly increased incidences in dosed rats. Carcinomas, adenomatous polyps, and adenocarcinomas of the nasal cavity and hemangiosarcomas of the circulatory system in high-dose rats of either sex occurred at incidences higher than those in the corresponding controls. Mesotheliomas of the tunica vaginalis in high-dose male rats and mammary gland fibroadenomas and the combined incidence of alveolar/bronchiolar carcinomas and adenomas in high-dose female rats all occurred at incidences higher than those in the corresponding controls.

A previous gavage study (NCI TR 86, 1978), conducted in the same laboratory as the present study, reported increased incidences of squamous cell carcinomas of the forestomach in Osborne-Mendel rats of both sexes, hepatocellular carcinomas or neoplastic nodules in females, and hemangiosarcomas (primarily of the spleen) in males. The time-weighted average dosages administered in this study for low- and high-dose groups were 38 and 41 mg/kg body weight for male rats and 37 and 39 mg/kg for females.

Among the compound-related nonneoplastic lesions observed in the present study were hepatic necrosis and toxic nephropathy in rats of either sex, testicular degeneration and atrophy, and retinal degeneration in female rats. A 91-day study by Rowe et al. (1952) reported compound-related nonneoplastic lesions in some of the same organs when rats were exposed to 1,2-dibromoethane in air at a concentration of 385 mg/m<sup>3</sup> for 7 hours per day, 5 days per week.

Mean body weights of high-dose mice were lower than those of corresponding controls throughout the study, and survival in dosed females was significantly shorter than that of controls. Control and dosed male mice had poor survival, the principal cause of death being an ascending suppurative urinary tract infection that was unrelated to compound administration.

Epithelial hyperplasia of the respiratory system was among the compound-related nonneoplastic lesions observed in dosed mice in the present study.

In mice, as in dosed rats, tumors of the respiratory tract, (both sexes), hemangiosarcomas of the circulatory system (female only), and tumors of the mammary gland (female only) were found at significantly increased incidences. Alveolar/bronchiolar adenomas and alveolar/bronchiolar carcinomas in high-dose male and female mice, and the combined incidence of carcinomas and adenomas of the nasal cavity, fibrosarcomas of the subcutaneous tissue, and hemangiosarcomas of the circulatory system in high-dose female mice, occurred at incidences significantly higher than those in the corresponding controls.

A previous gavage study (NCI, TR 86, 1978) conducted in the same laboratory as the present study, concluded that administration of 1,2-dibromoethane was associated with an increased incidence of squamous cell carcinomas of the forestomach and alveolar/bronchiolar adenomas in B6C3F1 mice. The time-weighted-average dosages administered in this study for the low and high dose groups were 62 and 107 mg/kg. According to Van Duuren et al. (1979), long-term (62 weeks) dermal application of the test chemical to Ha:ICR Swiss mice was associated with an increased incidence of respiratory tract tumors, skin papillomas, and skin carcinomas. The results of these two studies are compared with those of the current study in Table 10.

Table 10. Comparison of Target Organs Affected In Chronic Bioassays of 1,2-Dibromoethane

Route	Species	Sex	Dose or Dose Equivalent	Duration (weeks)	Circulatory	Pituitary	Kidney	Nasal Cavity	Fore-Stomach	Con-nective	Site and Type of Lesion Observed					
											Mammary Gland	Tunica Vaginalis	Lung	Liver	Eye	Testes
Inhalation (Current Study)	Rat (F344)	M	10 or 40 ppm 6 hours per day	88 or 103	N	N	T	N				N		T	T	
		F	10 or 40 ppm 6 hours per day	91 or 103	N	N	T	N			N		N	T	T	
Inhalation (Current Study)	Mouse (B6C3F1)	M	10 or 40 ppm 6 hours per day	78	N									N		
		F	10 or 40 ppm 6 hours per day	90 or 103	N			N		N	N		N			N
Gavage (NCI, 1978)	Rat (Osborne-Mendel)	M	41 mg/kg 5 X per week	49	N											T
		F	39 mg/kg 5 X per week	61											N	
Gavage (NCI, 1978)	Mouse (B6C3F1)	M	62 or 107 mg/kg 5 X per week	78										N		T
		F	62 or 107 mg/kg 5 X per week	78 or 90										N		
Skin (Van Duuren, 1979)	Mouse (Ha:ICR)	F	50 mg in 0.2 ml acetone 2 X per week	62										N		N

(a) N = neoplastic lesion; T = toxic lesions



## VI. CONCLUSIONS

Under the conditions of this bioassay, 1,2-dibromoethane was carcinogenic for F344 rats, causing increased incidences of carcinomas, adenocarcinomas, adenomas of the nasal cavity, and hemangiosarcomas of the circulatory system in males and females; mesotheliomas of the tunica vaginalis and adenomatous polyps of the nasal cavity in males; and fibroadenomas of the mammary gland and alveolar/bronchiolar adenomas and carcinomas (combined) in females. 1,2-Dibromoethane was carcinogenic for B6C3F1 mice, causing alveolar/bronchiolar carcinomas and alveolar/bronchiolar adenomas in males and females; and hemangiosarcomas of the circulatory system, fibrosarcomas in the subcutaneous tissue, carcinomas of the nasal cavity, and adenocarcinomas of the mammary gland in females.



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**APPENDIX A**  
**SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS**  
**EXPOSED TO AIR CONTAINING 1,2-DIBROMOETHANE**



TABLE A1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS EXPOSED TO AIR CONTAINING 1,2-DIBROMOETHANE

	UNTREATED CONTROL	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)
KERATOACANTHOMA			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	
BASAL-CELL CARCINOMA		1 (2%)	
TRICHOEPITHELIOMA			1 (2%)
SARCOMA, NOS		1 (2%)	2 (4%)
FIBROMA	3 (6%)	6 (12%)	8 (16%)
FIBROSARCOMA	1 (2%)		
LIPOMA	1 (2%)		
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
CARCINOMA, NOS			21 (42%)
SQUAMOUS CELL PAPILLOMA		1 (2%)	
SQUAMOUS CELL CARCINOMA		3 (6%)	3 (6%)
ADENOMA, NOS		11 (22%)	-
ADENOCARCINOMA, NOS		20 (40%)	28 (56%)
ADENOMATOUS POLYP, NOS		18 (36%)	5 (10%)
PAPILLARY ADENOMA		4 (8%)	
*NOSE	(50)	(50)	(50)
SQUAMOUS CELL PAPILLOMA		1 (2%)	
#LUNG/BRONCHUS	(50)	(50)	(50)
ADENOMATOUS POLYP, NOS			1 (2%)
#LUNG	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR ADENOMA		1 (2%)	1 (2%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)	1 (2%)	

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
 \* NUMBER OF ANIMALS NECROPSIED

**TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
PHEOCHROMOCYTOMA, METASTATIC	1 (2%)		
SARCOMA, NOS, METASTATIC		1 (2%)	
<b>HEMATOPOIETIC SYSTEM</b>			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIG.LYMPHOMA, UNDIFFER-TYPE		2 (4%)	
MONOCYTIC LEUKEMIA	6 (12%)	7 (14%)	1 (2%)
#BONE MARROW	(50)	(49)	(49)
PHEOCHROMOCYTOMA, METASTATIC	1 (2%)		
#SPLEEN	(50)	(50)	(49)
PHEOCHROMOCYTOMA, METASTATIC	1 (2%)		
#CERVICAL LYMPH NODE	(50)	(49)	(48)
CARCINOMA, NOS, METASTATIC			1 (2%)
PHEOCHROMOCYTOMA, METASTATIC	1 (2%)		
MALIG.LYMPHOMA, UNDIFFER-TYPE			1 (2%)
<b>CIRCULATORY SYSTEM</b>			
*DIAPHRAGM	(50)	(50)	(50)
HEMANGIOSARCOMA, INVASIVE			1 (2%)
*ABDOMINAL CAVITY	(50)	(50)	(50)
HEMANGIOSARCOMA, INVASIVE			1 (2%)
#SPLEEN	(50)	(50)	(49)
HEMANGIOSARCOMA		1 (2%)	15 (31%)
*BLOOD VESSEL	(50)	(50)	(50)
MESOTHELIOMA, METASTATIC		1 (2%)	
#PANCREAS	(49)	(50)	(48)
HEMANGIOSARCOMA, INVASIVE			1 (2%)
*MESENTERY	(50)	(50)	(50)
HEMANGIOSARCOMA, INVASIVE			1 (2%)
<b>DIGESTIVE SYSTEM</b>			
*ORAL CAVITY	(50)	(50)	(50)
AMELOBLASTIC ODONTOMA		1 (2%)	

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

**TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
*TONGUE SQUAMOUS CELL CARCINOMA	(50)	(50) 1 (2%)	(50)
#SALIVARY GLAND SARCOMA, NOS SARCOMA, NOS, INVASIVE	(49)	(50) 1 (2%)	(48) 2 (4%) 1 (2%)
#LIVER HEPATOCELLULAR CARCINOMA	(50)	(50) 1 (2%)	(50) 1 (2%)
#PANCREAS ACINAR-CELL ADENOMA	(49)	(50) 1 (2%)	(48)
#SMALL INTESTINE MUCINOUS ADENOCARCINOMA	(50)	(45)	(49) 1 (2%)
#JEJUNUM ADENOCARCINOMA, NOS	(50) 1 (2%)	(45)	(49)
#LARGE INTESTINE ADENOCARCINOMA, NOS	(49)	(49) 1 (2%)	(50)
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY CARCINOMA, NOS ADENOMA, NOS CHROMOPHOBE ADENOMA	(45) 1 (2%) 10 (22%)	(48) 2 (4%) 7 (15%)	(47) 2 (4%)
#ADRENAL CORTICAL ADENOMA CORTICAL CARCINOMA PHEOCHROMOCYTOMA PHEOCHROMOCYTOMA, MALIGNANT	(49) 1 (2%) 4 (8%) 1 (2%)	(49) 1 (2%) 5 (10%)	(48) 1 (2%)
#THYROID FOLLICULAR-CELL ADENOMA FOLLICULAR-CELL CARCINOMA	(48)	(50)	(46) 2 (4%) 1 (2%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
\* NUMBER OF ANIMALS NECROPSIED

**TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
C-CELL ADENOMA		3 (6%)	
C-CELL CARCINOMA	3 (6%)	2 (4%)	1 (2%)
#PANCREATIC ISLETS	(49)	(50)	(48)
ISLET-CELL CARCINOMA	1 (2%)		1 (2%)
<b>REPRODUCTIVE SYSTEM</b>			
*MAMMARY GLAND ADENOMA, NOS	(50)	(50)	(50) 1 (2%)
*PREPUTIAL GLAND CARCINOMA, NOS	(50) 1 (2%)	(50) 2 (4%)	(50) 2 (4%)
SQUAMOUS CELL CARCINOMA	1 (2%)		
#TESTIS	(50)	(50)	(49)
INTERSTITIAL-CELL TUMOR	35 (70%)	45 (90%)	10 (20%)
*EPIDIDYMIS	(50)	(50)	(50)
MESOTHELIOMA, NOS	2 (4%)		
MESOTHELIOMA, INVASIVE	1 (2%)		
*SCROTUM	(50)	(50)	(50)
MESOTHELIOMA, INVASIVE	1 (2%)		
<b>NERVOUS SYSTEM</b>			
#CEREBRUM	(50)	(50)	(49)
CARCINOMA, NOS, METASTATIC	1 (2%)		
#BRAIN	(50)	(50)	(49)
CARCINOMA, NOS, INVASIVE **			10 (20%)
GRANULAR-CELL TUMOR, BENIGN			1 (2%)
GLIOBLASTOMA MULTIFORME			1 (2%)
*CERVICAL SPINAL CORD	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, INVASIV		1 (2%)	
<b>SPECIAL SENSE ORGANS</b>			
*ZYMBAL'S GLAND	(50)	(50)	(50)
CARCINOMA, NOS		1 (2%)	

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

\*\* FROM NASAL CAVITY



**TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
<b>MUSCULOSKELETAL SYSTEM</b>			
*SKULL SQUAMOUS CELL CARCINOMA, INVASIV	(50) 1 (2%)	(50) 1 (2%)	(50)
*CERVICAL VERTEBRA OT SQUAMOUS CELL CARCINOMA, INVASIV	(50) 1 (2%)	(50) 1 (2%)	(50)
*STERNUM LIPOMA	(50) 1 (2%)	(50)	(50)
*MUSCLE OF NECK SQUAMOUS CELL CARCINOMA, INVASIV	(50) 1 (2%)	(50) 1 (2%)	(50)
*MUSCLE OF PERINEUM MESOTHELIOMA, INVASIVE	(50) 1 (2%)	(50)	(50)
<b>BODY CAVITIES</b>			
*PERITONEUM MESOTHELIOMA, INVASIVE	(50) 1 (2%)	(50)	(50)
*TUNICA VAGINALIS MESOTHELIOMA, NOS MESOTHELIOMA, MALIGNANT	(50) 1 (2%)	(50) 7 (14%) 1 (2%)	(50) 25 (50%)
<b>ALL OTHER SYSTEMS</b>			
*MULTIPLE ORGANS MESOTHELIOMA, MALIGNANT	(50)	(50) 5 (10%)	(50) 1 (2%)
<b>ANIMAL DISPOSITION SUMMARY</b>			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH <sup>a</sup>	5	10	37
MORIBUND SACRIFICE	7	5	8
SCHEDULED SACRIFICE	19		
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	19	35	5
ANIMAL MISSING			
<sup>a</sup> INCLUDES AUTOLYZED ANIMALS			
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY			
* NUMBER OF ANIMALS NECROPSIED			

**TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	45	50	49
TOTAL PRIMARY TUMORS	75	165	141
TOTAL ANIMALS WITH BENIGN TUMORS	40	47	26
TOTAL BENIGN TUMORS	55	104	34
TOTAL ANIMALS WITH MALIGNANT TUMORS	18	39	43
TOTAL MALIGNANT TUMORS	18	54	82
TOTAL ANIMALS WITH SECONDARY TUMORS#	3	3	14
TOTAL SECONDARY TUMORS	9	7	16
TOTAL ANIMALS WITH TUMORS UNCERTAIN- BENIGN OR MALIGNANT	2	7	25
TOTAL UNCERTAIN TUMORS	2	7	25
TOTAL ANIMALS WITH TUMORS UNCERTAIN- PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			
* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS			
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN			

TABLE A2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS EXPOSED  
TO AIR CONTAINING 1,2-DIBROMOETHANE

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	49
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
KERATOACANTHOMA			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
FIBROMA			3 (6%)
FIBROSARCOMA			1 (2%)
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
CARCINOMA, NOS			25 (50%)
SQUAMOUS CELL CARCINOMA	1 (2%)	1 (2%)	5 (10%)
ADENOMA, NOS		11 (22%)	3 (6%)
ADENOCARCINOMA, NOS		20 (40%)	29 (58%)
ADENOMATOUS POLYP, NOS		5 (10%)	5 (10%)
PAPILLARY ADENOMA		3 (6%)	
#LUNG	(50)	(48)	(47)
SQUAMOUS CELL CARCINOMA			1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA			1 (2%)
ALVEOLAR/BRONCHIOLAR CARCINOMA			4 (9%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MYELOMONOCYTIC LEUKEMIA		2 (4%)	
MONOCYTIC LEUKEMIA	6 (12%)	5 (10%)	1 (2%)
CIRCULATORY SYSTEM			
#SPLEEN	(50)	(49)	(48)
HEMANGIOSARCOMA			5 (10%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
\* NUMBER OF ANIMALS NECROPSIED

**TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
*MESENTERY HEMANGIOSARCOMA, INVASIVE	(50)	(50)	(50) 1 (2%)
<b>DIGESTIVE SYSTEM</b>			
*HARD PALATE SQUAMOUS CELL CARCINOMA NEUROFIBROSARCOMA	(50)	(50) 1 (2%)	(50) 1 (2%)
*ROOT OF TONGUE SQUAMOUS CELL CARCINOMA	(50)	(50) 1 (2%)	(50)
#LIVER NEOPLASTIC NODULE HEPATOCELLULAR CARCINOMA	(50) 2 (4%)	(49) 1 (2%)	(48) 3 (6%) 3 (6%)
*PHARYNX SQUAMOUS CELL CARCINOMA, INVASIV	(50) 1 (2%)	(50)	(50)
<b>URINARY SYSTEM</b>			
#KIDNEY NEPHROBLASTOMA	(50)	(49)	(48) 1 (2%)
<b>ENDOCRINE SYSTEM</b>			
#PITUITARY CARCINOMA, NOS ADENOMA, NOS CHRONOPHOBE ADENOMA	(50) 1 (2%) 1 (2%) 20 (40%)	(49) 18 (37%)	(45) 4 (9%)
#ADRENAL CORTICAL ADENOMA PHEOCHROMOCYTOMA	(50) 3 (6%)	(49) 1 (2%) 1 (2%)	(47) 1 (2%)
#THYROID FOLLICULAR-CELL ADENOMA FOLLICULAR-CELL CARCINOMA C-CELL CARCINOMA	(49) 1 (2%)	(48) 3 (6%)	(45) 1 (2%) 1 (2%) 1 (2%)
<b>REPRODUCTIVE SYSTEM</b>			
*MAMMARY GLAND ADENOMA, NOS	(50)	(50) 1 (2%)	(50) 1 (2%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

**TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ADENOCARCINOMA, NOS	1 (2%)		4 (8%)
ADENOMATOUS POLYP. NOS			1 (2%)
FIBROADENOMA	4 (8%)	29 (58%)	24 (48%)
*CLITORAL GLAND CARCINOMA, NOS	(50)	(50)	(50)
ADEHOMA, NOS		3 (6%)	1 (2%)
			1 (2%)
*VAGINA	(50)	(50)	(50)
SQUAMOUS CELL PAPILLOMA			1 (2%)
FIBROMA		1 (2%)	
#UTERUS	(50)	(49)	(48)
ENDOMETRIAL STROMAL POLYP	6 (12%)	3 (6%)	4 (8%)
#RIGHT OVARY	(50)	(48)	(48)
THECOMA		1 (2%)	
NERVOUS SYSTEM			
#CEREBRUM	(50)	(50)	(48)
CARCINOMA, NOS, INVASIVE	1 (2%)		
#BRAIN	(50)	(50)	(48)
CARCINOMA, NOS, INVASIVE **			11 (23%)
*OLFACTORY NERVE	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, INVASIV	1 (2%)		
SPECIAL SENSE ORGANS			
*EYE/IRIS	(50)	(50)	(50)
LEIOMYOMA			1 (2%)
*ZYMBAI'S GLAND	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*SKULL	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, INVASIV		1 (2%)	
*MUSCLE OF NECK	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, INVASIV	1 (2%)		

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

\*\* FROM NASAL CAVITY

**TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
<b>BODY CAVITIES</b>			
NONE			
<b>ALL OTHER SYSTEMS</b>			
NONE			
<b>ANIMAL DISPOSITION SUMMARY</b>			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH <sup>a</sup>	7	6	29
MORIBUND SACRIFICE	5	5	13
SCHEDULED SACRIFICE	18	1	
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	20	38	8
ANIMAL MISSING			
<sup>a</sup> INCLUDES AUTOLYZED ANIMALS			
<b>TUMOR SUMMARY</b>			
TOTAL ANIMALS WITH PRIMARY TUMORS*	33	49	46
TOTAL PRIMARY TUMORS	47	111	138
TOTAL ANIMALS WITH BENIGN TUMORS	27	41	31
TOTAL BENIGN TUMORS	34	74	52
TOTAL ANIMALS WITH MALIGNANT TUMORS	9	31	43
TOTAL MALIGNANT TUMORS	11	37	83
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	1	12
TOTAL SECONDARY TUMORS	4	1	12
TOTAL ANIMALS WITH TUMORS UNCERTAIN- BENIGN OR MALIGNANT	2		3
TOTAL UNCERTAIN TUMORS	2		3
TOTAL ANIMALS WITH TUMORS UNCERTAIN- PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			
* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS			
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN			

**APPENDIX B**  
**SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE**  
**EXPOSED TO AIR CONTAINING 1,2-DIBROMOETHANE**





TABLE B1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE EXPOSED  
TO AIR CONTAINING 1,2-DIBROMOETHANE

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	45	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	44	48	46
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE FIBROSARCOMA	(45)	(50)	(50) 2 (4%)
RESPIRATORY SYSTEM			
#LUNG/BRONCHUS ADENOMA, NOS ADENOMATOUS POLYP, NOS	(41)	(48)	(46) 2 (4%) 3 (7%)
#LUNG/BRONCHIOLE ADENOMATOUS POLYP, NOS	(41)	(48)	(46) 2 (4%)
#LUNG ALVEOLAR/BRONCHIOLAR ADENOMA ALVEOLAR/BRONCHIOLAR CARCINOMA	(41)	(48) 3 (6%)	(46) 11 (24%) 19 (41%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS MALIG.LYMPHOMA, LYMPHOCYTIC TYPE MAST-CELL LEUKEMIA	(45)	(50) 1 (2%)	(50) 1 (2%)
CIRCULATORY SYSTEM			
*SUBCUT TISSUE HEMANGIOMA HEMANGIOSARCOMA	(45)	(50)	(50) 1 (2%) 1 (2%)
#PROSTATE HEMANGIOMA	(41)	(46)	(41) 1 (2%)
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY			
* NUMBER OF ANIMALS NECROPSIED			

**TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#PERIADRENAL TISSUE HEMANGIOSARCOMA	(34)	(46)	(43) 1 (2%)
<b>DIGESTIVE SYSTEM</b>			
#LIVER	(41)	(48)	(46)
HEPATOCELLULAR ADENOMA			2 (4%)
HEPATOCELLULAR CARCINOMA	3 (7%)	1 (2%)	1 (2%)
<b>URINARY SYSTEM</b>			
#URINARY BLADDER TRANSITIONAL-CELL PAPILLOMA	(41)	(48)	(45) 2 (4%)
<b>ENDOCRINE SYSTEM</b>			
NONE			
<b>REPRODUCTIVE SYSTEM</b>			
NONE			
<b>NERVOUS SYSTEM</b>			
NONE			
<b>SPECIAL SENSE ORGANS</b>			
*HARDERIAN GLAND ADENOMA, NOS	(45)	(50)	(50) 1 (2%)
<b>MUSCULOSKELETAL SYSTEM</b>			
NONE			
<b>BODY CAVITIES</b>			
NONE			

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
\* NUMBER OF ANIMALS NECROPSIED

**TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH <sup>a</sup>	34	36	27
MORIBUND SACRIFICE	3	3	5
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	13	11	18
ANIMAL MISSING			
<sup>a</sup> INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	3	5	27
TOTAL PRIMARY TUMORS	3	5	50
TOTAL ANIMALS WITH BENIGN TUMORS			20
TOTAL BENIGN TUMORS			25
TOTAL ANIMALS WITH MALIGNANT TUMORS	3	5	20
TOTAL MALIGNANT TUMORS	3	5	25
TOTAL ANIMALS WITH SECONDARY TUMORS#			
TOTAL SECONDARY TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN- BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN- PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			
* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS			
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN			

TABLE B2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE EXPOSED  
TO AIR CONTAINING 1,2-DIBROMOETHANE

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(50)	(50)	(50)
NEOPLASM, NOS, MALIGNANT		1 (2%)	
KERATOACANTHOMA		1 (2%)	
FIBROSARCOMA		4 (8%)	11 (22%)
MYXOSARCOMA		1 (2%)	
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
CARCINOMA, NOS			6 (12%)
ADENOMA, NOS			2 (4%)
ADENOMATOUS POLYP, NOS			3 (6%)
#TRACHEA	(49)	(50)	(48)
ADENOMATOUS POLYP, NOS			1 (2%)
CARCINOSARCOMA, INVASIVE		1 (2%)	
#LUNG/BRONCHUS	(49)	(49)	(50)
CARCINOMA, NOS		1 (2%)	4 (8%)
ADENOMA, NOS			5 (10%)
ADENOMATOUS POLYP, NOS			1 (2%)
#LUNG/BRONCHIOLE	(49)	(49)	(50)
ADENOMATOUS POLYP, NOS		1 (2%)	2 (4%)
#LUNG	(49)	(49)	(50)
NEOPLASM, NOS, METASTATIC		1 (2%)	
ADENOCARCINOMA, NOS, METASTATIC		2 (4%)	1 (2%)
HEPATOCELLULAR CARCINOMA, METAST		1 (2%)	
ALVEOLAR/BRONCHIOLAR ADENOMA	3 (6%)	7 (14%)	13 (26%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)	5 (10%)	37 (74%)
ADENOSQUAMOUS CARCINOMA, METASTA		1 (2%)	
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY			
* NUMBER OF ANIMALS NECROPSIED			

**TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ADENOCARCINOMA/SQUAMOUS METAPLASIA, MET			1 (2%)
FIBROSARCOMA, METASTATIC		2 (4%)	1 (2%)
CARCINOSARCOMA, METASTATIC		1 (2%)	
OSTEOSARCOMA, METASTATIC	1 (2%)		
<b>HEMATOPOIETIC SYSTEM</b>			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
MALIG. LYMPHOMA, UNDIFFER-TYPE	3 (6%)		
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE	2 (4%)	2 (4%)	
MALIG. LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)	3 (6%)	
MALIGNANT LYMPHOMA, MIXED TYPE	1 (2%)		
GRANULOCYTIC LEUKEMIA		1 (2%)	1 (2%)
#CERVICAL LYMPH NODE	(49)	(42)	(45)
FIBROSARCOMA, METASTATIC		1 (2%)	
#BRONCHIAL LYMPH NODE	(49)	(42)	(45)
ALVEOLAR/BRONCHIOLAR CA, METASTA			1 (2%)
#PEYER'S PATCH	(47)	(47)	(48)
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE		1 (2%)	
<b>CIRCULATORY SYSTEM</b>			
*ABDOMINAL CAVITY	(50)	(50)	(50)
HEMANGIOMA		1 (2%)	
HEMANGIOSARCOMA			2 (4%)
*ABDOMINAL WALL	(50)	(50)	(50)
HEMANGIOSARCOMA, INVASIVE			1 (2%)
*PELVIC PERITONEAL CA	(50)	(50)	(50)
HEMANGIOSARCOMA		2 (4%)	2 (4%)
*SUBCUT TISSUE	(50)	(50)	(50)
HEMANGIOSARCOMA		1 (2%)	3 (6%)
HEMANGIOSARCOMA, UNC PRIM OR MET		1 (2%)	
#SPLEEN	(50)	(49)	(49)
HEMANGIOSARCOMA		1 (2%)	
#LYMPH NODE	(49)	(42)	(45)
HEMANGIOSARCOMA, METASTATIC		1 (2%)	

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
 \* NUMBER OF ANIMALS NECROPSIED

**TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#LUMBAR LYMPH NODE HEMANGIOSARCOMA, METASTATIC	(49)	(42) 1 (2%)	(45)
#MESENTERIC L. NODE HEMANGIOSARCOMA, INVASIVE	(49)	(42) 1 (2%)	(45)
*NASAL CAVITY HEMANGIOSARCOMA	(50)	(50)	(50) 1 (2%)
#LUNG HEMANGIOSARCOMA, METASTATIC	(49)	(49) 1 (2%)	(50)
#HEART ADENOCARCINOMA, NOS, METASTATIC ALVEOLAR/BRONCHIOLAR CA, METASTA CARCINOSARCOMA	(50)	(49) 1 (2%) 1 (2%)	(50) 1 (2%)
#LIVER HEMANGIOSARCOMA	(50)	(50)	(50) 1 (2%)
#PANCREAS HEMANGIOSARCOMA, INVASIVE	(48)	(48) 1 (2%)	(49)
*MESENTERY HEMANGIOSARCOMA	(50)	(50)	(50) 2 (4%)
#KIDNEY HEMANGIOSARCOMA, INVASIVE	(50)	(50) 1 (2%)	(50) 1 (2%)
#PERIRENAL TISSUE HEMANGIOMA HEMANGIOSARCOMA	(50)	(50) 1 (2%)	(50) 1 (2%) 2 (4%)
#PERIVESICAL TISSUE HEMANGIOSARCOMA	(48)	(47)	(45) 4 (9%)
*VAGINA HEMANGIOSARCOMA	(50)	(50)	(50) 1 (2%)
#UTERUS HEMANGIOSARCOMA HEMANGIOSARCOMA, INVASIVE	(50)	(48) 1 (2%)	(48) 2 (4%)
#BROAD LIGAMENT HEMANGIOMA	(50)	(48)	(48) 1 (2%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
\* NUMBER OF ANIMALS NECROPSIED

**TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
HEMANGIOSARCOMA		6 (13%)	3 (6%)
#OVARY/PAROVARIAN HEMANGIOMA HEMANGIOSARCOMA	(48)	(40)	(36) 1 (3%) 2 (6%)
#OVARY HEMANGIOSARCOMA HEMANGIOSARCOMA, INVASIVE	(48)	(40)	(36) 2 (6%) 1 (3%)
#PERIADRENAL TISSUE HEMANGIOMA	(48)	(46)	(49) 1 (2%)
DIGESTIVE SYSTEM			
*ORAL MUCOUS MEMBRANE SQUAMOUS CELL CARCINOMA	(50)	(50) 1 (2%)	(50)
#LIVER HEPATOCELLULAR ADENOMA HEPATOCELLULAR CARCINOMA	(50) 2 (4%)	(50) 1 (2%) 5 (10%)	(50) 1 (2%)
URINARY SYSTEM			
#KIDNEY ALVEOLAR/BRONCHIOLAR CA, METASTA OSTEOSARCOMA, METASTATIC	(50) 1 (2%)	(50)	(50) 1 (2%)
#URINARY BLADDER LEIOMYOSARCOMA, INVASIVE	(48)	(47)	(45) 1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY ADENOMA, NOS	(48) 8 (17%)	(46) 1 (2%)	(40)
#THYROID FOLLICULAR-CELL ADENOMA C-CELL CARCINOMA	(45) 1 (2%)	(43)	(37) 1 (3%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND ADENOCARCINOMA, NOS	(50) 2 (4%)	(50) 14 (28%)	(50) 8 (16%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
\* NUMBER OF ANIMALS NECROPSIED

**TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ADENOSQUAMOUS CARCINOMA		4 (8%)	1 (2%)
ADENOCARCINOMA/SQUAMOUS METAPLASIA			1 (2%)
*VAGINA	(50)	(50)	(50)
LEIOMYOSARCOMA	1 (2%)	1 (2%)	
#UTERUS	(50)	(48)	(48)
FIBROSARCOMA, METASTATIC			1 (2%)
LEIOMYOSARCOMA			1 (2%)
ENDOMETRIAL STROMAL POLYP		1 (2%)	
NERVOUS SYSTEM			
*SPINAL CORD	(50)	(50)	(50)
FIBROSARCOMA, INVASIVE			1 (2%)
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(50)
ADENOMA, NOS		3 (6%)	1 (2%)
*EAR	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	
MUSCULOSKELETAL SYSTEM			
*STERNUM	(50)	(50)	(50)
CARCINOSARCOMA, INVASIVE		1 (2%)	
*RIB	(50)	(50)	(50)
FIBROSARCOMA		1 (2%)	1 (2%)
*MUSCLE OF BACK	(50)	(50)	(50)
FIBROSARCOMA			1 (2%)
BODY CAVITIES			
*ABDOMINAL CAVITY	(50)	(50)	(50)
FIBROSARCOMA			1 (2%)
FIBROSARCOMA, METASTATIC		1 (2%)	
*ABDOMINAL WALL	(50)	(50)	(50)
FIBROSARCOMA, INVASIVE			1 (2%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED



**TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
PERIORBITAL REGION FIBROSARCOMA			1
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH <sup>a</sup>	7	27	36
MORIBUND SACRIFICE	3	4	7
SCHEDULED SACRIFICE	21		
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	19	19	7
ANIMAL MISSING			
<sup>a</sup> INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	22	45	49
TOTAL PRIMARY TUMORS	26	76	133
TOTAL ANIMALS WITH BENIGN TUMORS	12	14	22
TOTAL BENIGN TUMORS	12	16	32
TOTAL ANIMALS WITH MALIGNANT TUMORS	13	42	48
TOTAL MALIGNANT TUMORS	14	59	101
TOTAL ANIMALS WITH SECONDARY TUMORS#	1	12	10
TOTAL SECONDARY TUMORS	2	19	15
TOTAL ANIMALS WITH TUMORS UNCERTAIN- BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN- PRIMARY OR METASTATIC		1	
TOTAL UNCERTAIN TUMORS		1	
* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS			
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN			



**APPENDIX C**  
**SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN**  
**RATS EXPOSED TO AIR CONTAINING 1,2-DIBROMOETHANE**



TABLE C1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS EXPOSED TO AIR CONTAINING 1,2-DIBROMOETHANE

	UNTREATED CONTROL	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)
EPIDERMAL INCLUSION CYST	1 (2%)		
ULCER, NOS		1 (2%)	
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)	
NECROSIS, FAT	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
ABCESS, NOS			1 (2%)
INFLAMMATION, PYOGRANULOMATOUS			1 (2%)
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
CYST, NOS		1 (2%)	
CONGESTION, NOS	1 (2%)	2 (4%)	1 (2%)
HEMORRHAGE		10 (20%)	1 (2%)
INFLAMMATION, SEROUS		2 (4%)	1 (2%)
INFLAMMATION, SUPPURATIVE		8 (16%)	20 (40%)
INFLAMMATION, CHRONIC	2 (4%)	1 (2%)	
INFLAMMATION, PYOGRANULOMATOUS			1 (2%)
HYPERPLASIA, EPITHELIAL		38 (76%)	25 (50%)
HYPERPLASIA, FOCAL		1 (2%)	
ANGIECTASIS		6 (12%)	
METAPLASIA, SQUAMOUS		3 (6%)	2 (4%)
*NASAL GLAND	(50)	(50)	(50)
DISTENTION		2 (4%)	
*NASAL TURBINATE	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
*LARYNX	(50)	(50)	(50)
HYPERPLASIA, EPITHELIAL		1 (2%)	

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
 \* NUMBER OF ANIMALS NECROPSIED

**TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#TRACHEA	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			8 (16%)
HYPERPLASIA, EPITHELIAL			4 (8%)
METAPLASIA, SQUAMOUS			2 (4%)
#TRACHEAL SUBMUCOSA	(50)	(50)	(50)
DISTENTION		1 (2%)	
#LUNG/BRONCHUS	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			2 (4%)
HYPERPLASIA, EPITHELIAL		7 (14%)	13 (26%)
HYPERPLASIA, ADENOMATOUS			1 (2%)
METAPLASIA, SQUAMOUS			3 (6%)
#LUNG/BRONCHIOLE	(50)	(50)	(50)
HYPERPLASIA, EPITHELIAL		4 (8%)	4 (8%)
#LUNG	(50)	(50)	(50)
CONGESTION, NOS		4 (8%)	14 (28%)
EDEMA, NOS		1 (2%)	3 (6%)
HEMORRHAGE		1 (2%)	
BRONCHOPNEUMONIA, FOCAL			1 (2%)
INFLAMMATION, SUPPURATIVE			1 (2%)
BRONCHOPNEUMONIA SUPPURATIVE			19 (38%)
INFLAMMATION, ACUTE FOCAL			1 (2%)
INFLAMMATION, ACUTE SUPPURATIVE			1 (2%)
ABSCESS, NOS			1 (2%)
PNEUMONIA, CHRONIC MURINE	5 (10%)		
INFLAMMATION, FOCAL GRANULOMATOUS			1 (2%)
INFLAMMATION, PYOGRANULOMATOUS			1 (2%)
ALVEOLAR MACROPHAGES			1 (2%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	2 (4%)	13 (26%)	12 (24%)
METAPLASIA, OSSEOUS		1 (2%)	
HEMATOPOIETIC SYSTEM			
*RETICULOENDOTHELIAL	(50)	(50)	(50)
HYPERPLASIA, NOS	1 (2%)		
#BONE MARROW	(50)	(49)	(49)
HYPOPLASIA, NOS	1 (2%)	2 (4%)	1 (2%)
#SPLEEN	(50)	(50)	(49)
CONGESTION, NOS		1 (2%)	2 (4%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
 \* NUMBER OF ANIMALS NECROPSIED

**TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
HEMORRHAGE		1 (2%)	
PIGMENTATION, NOS	4 (8%)	1 (2%)	2 (4%)
HEMOSIDEROSIS			2 (4%)
ATROPHY, NOS			1 (2%)
HEMATOPOIESIS	2 (4%)	3 (6%)	1 (2%)
#CERVICAL LYMPH NODE	(50)	(49)	(48)
HEMORRHAGE	2 (4%)		
PIGMENTATION, NOS	1 (2%)		
PLASMACYTOSIS		3 (6%)	
HYPERPLASIA, LYMPHOID	1 (2%)		3 (6%)
#MESENTERIC L. NODE	(50)	(49)	(48)
CONGESTION, NOS			1 (2%)
HEMORRHAGE			1 (2%)
PLASMACYTOSIS		1 (2%)	
#LIVER	(50)	(50)	(50)
HEMATOPOIESIS		2 (4%)	1 (2%)
#THYMUS	(29)	(22)	(22)
CYST, NOS		1 (5%)	
CONGESTION, NOS			1 (5%)
HEMORRHAGE	1 (3%)		
INVOLUTION, NOS		1 (5%)	
HYPERPLASIA, EPITHELIAL		1 (5%)	
<b>CIRCULATORY SYSTEM</b>			
#SPLEEN	(50)	(50)	(49)
THROMBOSIS, NOS		1 (2%)	
#CERVICAL LYMPH NODE	(50)	(49)	(48)
LYMPHANGIECTASIS		1 (2%)	
#MESENTERIC L. NODE	(50)	(49)	(48)
LYMPHANGIECTASIS		1 (2%)	
#HEART	(50)	(50)	(50)
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)	
#AURICULAR APPENDAGE	(50)	(50)	(50)
THROMBOSIS, NOS			1 (2%)
#MYOCARDIUM	(50)	(50)	(50)
MINERALIZATION		1 (2%)	

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
 \* NUMBER OF ANIMALS NECROPSIED

**TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC FIBROSIS	32 (64%) 2 (4%)	34 (68%)	25 (50%)
#PANCREAS PERIARTERITIS	(49)	(50) 3 (6%)	(48)
*TESTIS PERIARTERITIS	(50) 1 (2%)	(50)	(49)
*EPIDIDYMISS PERIARTERITIS	(50) 1 (2%)	(50)	(50)
<b>DIGESTIVE SYSTEM</b>			
*HARD PALATE FOREIGN BODY, NOS ABSCESS, NOS INFLAMMATION, CHRONIC FIBROUS OSTEODYSTROPHY	(50)   1 (2%)	(50) 1 (2%) 1 (2%) 1 (2%)	(50)
*LIP ABSCESS, NOS INFLAMMATION, CHRONIC	(50) 1 (2%) 1 (2%)	(50)	(50)
*ROOT OF TOOTH INFLAMMATION, SUPPURATIVE	(50)	(50) 1 (2%)	(50)
#SALIVARY GLAND INFLAMMATION, CHRONIC FIBROSIS ATROPHY, NOS METAPLASIA, SQUAMOUS	(49)	(50)	(48) 4 (8%) 1 (2%) 1 (2%) 4 (8%)
#LIVER HERNIA, NOS CONGESTION, NOS HEMORRHAGE INFLAMMATION, GRANULOMATOUS INFLAMMATION, FOCAL GRANULOMATOUS CHOLANGIOFIBROSIS HEPATITIS, TOXIC NECROSIS, NOS NECROSIS, FOCAL INFARCT, NOS	(50) 2 (4%)   5 (10%) 2 (4%)  1 (2%) 1 (2%)	(50) 4 (8%) 4 (8%) 1 (2%) 3 (6%)   1 (2%) 1 (2%)	(50) 5 (10%) 9 (18%)   1 (2%) 5 (10%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
\* NUMBER OF ANIMALS NECROPSIED



**TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
METAMORPHOSIS FATTY	1 (2%)	6 (12%)	
FOCAL CELLULAR CHANGE	8 (16%)	8 (16%)	3 (6%)
ANGIECTASIS		1 (2%)	
#LIVER/CENTRILOBULAR NECROSIS, NOS	(50) 1 (2%)	(50) 5 (10%)	(50) 13 (26%)
#BILE DUCT FIBROSIS	(50)	(50) 1 (2%)	(50)
HYPERPLASIA, NOS	7 (14%)	6 (12%)	2 (4%)
#PANCREAS EDEMA, INTERSTITIAL	(49)	(50) 1 (2%)	(48)
HEMORRHAGE		1 (2%)	
FIBROSIS		1 (2%)	
ATROPHY, FOCAL	8 (16%)		
#PANCREATIC DUCT FIBROSIS	(49)	(50) 1 (2%)	(48)
#PANCREATIC ACINUS ATROPHY, NOS	(49)	(50) 2 (4%)	(48)
ATROPHY, FOCAL		5 (10%)	
HYPERPLASIA, NODULAR		1 (2%)	
*OROPHARYNX DEGENERATION, CYSTIC	(50)	(50) 1 (2%)	(50)
#ESOPHAGUS HYPERKERATOSIS	(48) 1 (2%)	(31)	(49) 1 (2%)
#STOMACH ULCER, NOS	(50) 1 (2%)	(49)	(49)
ULCER, FOCAL			2 (4%)
INFLAMMATION, CHRONIC	1 (2%)		1 (2%)
HYPERPLASIA, BASAL CELL		1 (2%)	2 (4%)
HYPERKERATOSIS			2 (4%)
ACANTHOSIS	1 (2%)		2 (4%)
#GASTRIC MUCOSA MINERALIZATION	(50)	(49) 1 (2%)	(49)
#GASTRIC SUBMUCOSA EDEMA, NOS	(50)	(49) 1 (2%)	(49) 2 (4%)
#LARGE INTESTINE PARASITISM	(49) 5 (10%)	(49) 6 (12%)	(50) 1 (2%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

**TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
<b>URINARY SYSTEM</b>			
#KIDNEY	(50)	(50)	(50)
CALCULUS, NOS		1 (2%)	
MINERALIZATION		4 (8%)	5 (10%)
CONGESTION, NOS		2 (4%)	1 (2%)
INFLAMMATION, CHRONIC	43 (86%)	40 (80%)	2 (4%)
NEPHROPATHY, TOXIC		4 (8%)	28 (56%)
PIGMENTATION, NOS	1 (2%)		
#KIDNEY/TUBULE	(50)	(50)	(50)
PIGMENTATION, NOS		2 (4%)	
#KIDNEY/PELVIS	(50)	(50)	(50)
NECROSIS, NOS		1 (2%)	
#URINARY BLADDER	(48)	(47)	(44)
CONGESTION, NOS			1 (2%)
<b>ENDOCRINE SYSTEM</b>			
#PITUITARY	(45)	(48)	(47)
CYST, NOS		4 (8%)	2 (4%)
HEMORRHAGE	1 (2%)		
HYPERPLASIA, FOCAL	5 (11%)		
HYPERPLASIA, CHROMOPHOBE-CELL		3 (6%)	
ANGIECTASIS		4 (8%)	1 (2%)
#ADRENAL	(49)	(49)	(48)
METAMORPHOSIS FATTY			1 (2%)
#ADRENAL CORTEX	(49)	(49)	(48)
DEGENERATION, NOS		1 (2%)	1 (2%)
METAMORPHOSIS FATTY	5 (10%)	7 (14%)	7 (15%)
HYPERPLASIA, FOCAL	1 (2%)		
#ADRENAL MEDULLA	(49)	(49)	(48)
HYPERPLASIA, NOS	2 (4%)		
HYPERPLASIA, FOCAL	2 (4%)	1 (2%)	2 (4%)
#THYROID	(48)	(50)	(46)
FOLLICULAR CYST, NOS	3 (6%)	1 (2%)	
HYPERPLASIA, C-CELL		1 (2%)	

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
 \* NUMBER OF ANIMALS NECROPSIED

**TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#PANCREATIC ISLETS	(49)	(50)	(48)
HYPERPLASIA, NOS	1 (2%)	3 (6%)	
HYPERPLASIA, FOCAL			1 (2%)
<b>REPRODUCTIVE SYSTEM</b>			
*MAMMARY GLAND	(50)	(50)	(50)
GALACTOCELE	1 (2%)		
CYSTIC DUCTS	1 (2%)		
HYPERPLASIA, EPITHELIAL		2 (4%)	
LACTATION		3 (6%)	
*PREPUTIAL GLAND	(50)	(50)	(50)
CYST, NOS			3 (6%)
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, CHRONIC		1 (2%)	
#PROSTATE	(48)	(45)	(50)
INFLAMMATION, SUPPURATIVE			2 (4%)
ABSCESS, NOS	4 (8%)		1 (2%)
INFLAMMATION, CHRONIC	11 (23%)	10 (22%)	4 (8%)
INFLAMMATION, CHRONIC FOCAL	2 (4%)		
*SEMINAL VESICLE	(50)	(50)	(50)
CYST, NOS			1 (2%)
INFLAMMATION, SUPPURATIVE			1 (2%)
ABSCESS, NOS			1 (2%)
ATROPHY, NOS		11 (22%)	
#TESTIS	(50)	(50)	(49)
MINERALIZATION		2 (4%)	1 (2%)
CYST, NOS			1 (2%)
GRANULOMA, SPERMATIC			2 (4%)
DEGENERATION, NOS	1 (2%)	10 (20%)	18 (37%)
NECROSIS, NOS	1 (2%)		
INFARCT, NOS	1 (2%)		
CALCIFICATION, NOS		1 (2%)	
ATROPHY, NOS	1 (2%)	2 (4%)	5 (10%)
HYPERPLASIA, INTERSTITIAL CELL	41 (82%)	1 (2%)	6 (12%)
*EPIDIDYIMIS	(50)	(50)	(50)
INFLAMMATION, CHRONIC		1 (2%)	1 (2%)
GRANULOMA, SPERMATIC	1 (2%)		7 (14%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

**TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
*VAS DEFERENS GRANULOMA, SPERMATIC	(50)	(50)	(50) 2 (4%)
NERVOUS SYSTEM			
#CEREBRUM HEMORRHAGE	(50) 1 (2%)	(50)	(49)
#BRAIN COMPRESSION MINERALIZATION GLIOSIS MALACIA	(50)	(50) 2 (4%)	(49) 1 (2%) 1 (2%) 4 (8%)
SPECIAL SENSE ORGANS			
*EYE SYNECHIA, ANTERIOR SYNECHIA, POSTERIOR CATARACT	(50) 1 (2%) 1 (2%) 1 (2%)	(50)	(50)
*EYE/CORNEA INFLAMMATION, CHRONIC	(50) 1 (2%)	(50)	(50)
*EYE/RETINA DEGENERATION, NOS ATROPHY, NOS	(50) 1 (2%)	(50) 1 (2%)	(50)
*EYE/CONJUNCTIVA INFLAMMATION, CHRONIC	(50) 1 (2%)	(50)	(50)
MUSCULOSKELETAL SYSTEM			
*SKULL INFLAMMATION, SUPPURATIVE	(50)	(50)	(50) 1 (2%)
BODY CAVITIES			
*ABDOMINAL CAVITY NECROSIS, FAT	(50)	(50)	(50) 1 (2%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
\* NUMBER OF ANIMALS NECROPSIED

**TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	<b>UNTREATED CONTROL</b>	<b>LOW DOSE</b>	<b>HIGH DOSE</b>
*PLEURA INFLAMMATION, CHRONIC	(50) 1 (2%)	(50)	(50)
*TUNICA VAGINALIS HYPERPLASIA, MESOTHELIAL	(50)	(50)	(50) 2 (4%)
ALL OTHER SYSTEMS			
CHEEK INFLAMMATION, CHRONIC	1		
SPECIAL MORPHOLOGY SUMMARY			
NONE			
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY			
* NUMBER OF ANIMALS NECROPSIED			

**TABLE C2.**

**SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS EXPOSED TO AIR CONTAINING 1,2-DIBROMOETHANE**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	49
<b>INTEGUMENTARY SYSTEM</b>			
*SKIN	(50)	(50)	(50)
ABSCESS, NOS	1 (2%)		1 (2%)
<b>RESPIRATORY SYSTEM</b>			
*NASAL CAVITY	(50)	(50)	(50)
HEMORRHAGE		2 (4%)	1 (2%)
INFLAMMATION, SEROUS		4 (8%)	1 (2%)
INFLAMMATION, SUPPURATIVE		1 (2%)	15 (30%)
INFLAMMATION, ACUTE	2 (4%)		
ABSCESS, NOS	1 (2%)		
INFLAMMATION, CHRONIC		2 (4%)	1 (2%)
HYPERPLASIA, EPITHELIAL		27 (54%)	31 (62%)
ANGIECTASIS			1 (2%)
METAPLASIA, SQUAMOUS		4 (8%)	3 (6%)
*NASAL TURBINATE	(50)	(50)	(50)
HYPERPLASIA, FOCAL	1 (2%)		
*LARYNX	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		4 (8%)
METAPLASIA, SQUAMOUS			2 (4%)
#TRACHEA	(50)	(49)	(47)
INFLAMMATION, SUPPURATIVE			20 (43%)
HYPERPLASIA, EPITHELIAL			6 (13%)
METAPLASIA, SQUAMOUS			9 (19%)
#LUNG/BRONCHUS	(50)	(48)	(47)
HYPERPLASIA, EPITHELIAL			8 (17%)
HYPERPLASIA, ADENOMATOUS			1 (2%)
#LUNG/BRONCHIOLE	(50)	(48)	(47)
HYPERPLASIA, EPITHELIAL		1 (2%)	4 (9%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
 \* NUMBER OF ANIMALS NECROPSIED

**TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#LUNG	(50)	(48)	(47)
CONGESTION, NOS		1 (2%)	8 (17%)
BRONCHOPNEUMONIA, FOCAL PNEUMONIA, ASPIRATION	1 (2%)		1 (2%)
BRONCHOPNEUMONIA SUPPURATIVE INFLAMMATION, ACUTE SUPPURATIVE			25 (53%)
PNEUMONIA, CHRONIC MURINE	2 (4%)		4 (9%)
ALVEOLAR MACROPHAGES			1 (2%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	3 (6%)	5 (10%)	5 (11%)
METAPLASIA, SQUAMOUS			1 (2%)
#ALVEOLAR EPITHELIUM HYPERPLASIA, ADENOMATOUS	(50)	(48)	(47)
			1 (2%)
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(48)	(49)	(47)
HYPOPLASIA, NOS		1 (2%)	1 (2%)
#SPLEEN	(50)	(49)	(48)
CONGESTION, NOS			1 (2%)
FIBROSIS			1 (2%)
FIBROSIS, FOCAL			1 (2%)
PIGMENTATION, NOS	10 (20%)		
HEMOSIDEROSIS			2 (4%)
ATROPHY, NOS	1 (2%)		
HEMATOPOIESIS	22 (44%)	2 (4%)	1 (2%)
#THYMUS	(38)	(30)	(19)
CYST, NOS	2 (5%)		1 (5%)
#THYMIC MEDULLA	(38)	(30)	(19)
HYPERPLASIA, NOS	1 (3%)		
CIRCULATORY SYSTEM			
#LUNG	(50)	(48)	(47)
THROMBOSIS, NOS	1 (2%)		
#HEART	(50)	(49)	(48)
DILATATION, NOS		1 (2%)	
#MYOCARDIUM	(50)	(49)	(48)
INFLAMMATION, CHRONIC	36 (72%)	19 (39%)	15 (31%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

**TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
FIBROSIS	1 (2%)		
#ENDOCARDIUM FIBROSIS	(50) 3 (6%)	(49)	(48)
#PANCREAS PERIARTERITIS	(50) 1 (2%)	(46)	(47)
*MESENTERY PERIARTERITIS	(50)	(50)	(50) 1 (2%)
<b>DIGESTIVE SYSTEM</b>			
#SALIVARY GLAND INFLAMMATION, SUPPURATIVE METAPLASIA, SQUAMOUS	(49)	(48)	(44) 1 (2%) 1 (2%)
#LIVER	(50)	(49)	(48)
HERNIA, NOS	2 (4%)	5 (10%)	6 (13%)
CONGESTION, NOS			3 (6%)
INFLAMMATION, FOCAL GRANULOMATOUS		2 (4%)	
CHOLANGIOFIBROSIS	4 (8%)	2 (4%)	
HEPATITIS, TOXIC	6 (12%)		
NECROSIS, NOS	2 (4%)		1 (2%)
NECROSIS, FOCAL		2 (4%)	5 (10%)
INFARCT, NOS			1 (2%)
METAMORPHOSIS FATTY	2 (4%)	1 (2%)	
FOCAL CELLULAR CHANGE	39 (78%)	28 (57%)	17 (35%)
ANGIECTASIS		1 (2%)	
#LIVER/CENTRILOBULAR NECROSIS, NOS	(50)	(49) 1 (2%)	(48) 7 (15%)
#BILE DUCT	(50)	(49)	(48)
INFLAMMATION, CHRONIC	1 (2%)		
HYPERPLASIA, NOS	5 (10%)	8 (16%)	
#PANCREAS	(50)	(46)	(47)
ATROPHY, NOS	1 (2%)		
ATROPHY, FOCAL	3 (6%)		
#PANCREATIC ACINUS ATROPHY, FOCAL	(50)	(46) 1 (2%)	(47)
*PHARYNX ABSCESS, NOS	(50) 2 (4%)	(50)	(50)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED



**TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#ESOPHAGUS	(48)	(32)	(45)
ABSCESS, NOS			1 (2%)
INFLAMMATION, CHRONIC	1 (2%)		
HYPERKERATOSIS	4 (8%)		
#STOMACH	(50)	(48)	(48)
HEMORRHAGE	1 (2%)		
ULCER, FOCAL		1 (2%)	
INFLAMMATION, ACUTE	1 (2%)		
ABSCESS, NOS	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)		
NECROSIS, NOS	1 (2%)		
NECROSIS, FOCAL	2 (4%)		
HYPERPLASIA, BASAL CELL			3 (6%)
HYPERKERATOSIS			2 (4%)
ACANTHOSIS			1 (2%)
#GASTRIC SUBMUCOSA	(50)	(48)	(48)
EDEMA, NOS			2 (4%)
#LARGE INTESTINE	(49)	(46)	(48)
PARASITISM	8 (16%)	7 (15%)	2 (4%)
URINARY SYSTEM			
#KIDNEY	(50)	(49)	(48)
MINERALIZATION			4 (8%)
HYDRONEPHROSIS	1 (2%)		
CONGESTION, NOS			3 (6%)
INFLAMMATION, CHRONIC	39 (78%)	15 (31%)	1 (2%)
NEPHROPATHY, TOXIC			8 (17%)
#KIDNEY/TUBULE	(50)	(49)	(48)
PIGMENTATION, NOS			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(50)	(49)	(45)
CYST, NOS	9 (18%)	4 (8%)	4 (9%)
HEMORRHAGIC CYST	2 (4%)		
HYPERPLASIA, FOCAL	7 (14%)		
HYPERPLASIA, CHROMOPHOBE-CELL		1 (2%)	1 (2%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

**TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ANGIECTASIS	1 (2%)	7 (14%)	3 (7%)
#ADRENAL	(50)	(49)	(47)
METAMORPHOSIS FATTY	1 (2%)	2 (4%)	
ANGIECTASIS	2 (4%)	1 (2%)	2 (4%)
#ADRENAL CORTEX	(50)	(49)	(47)
CYST, NOS		1 (2%)	
HEMORRHAGE	1 (2%)		
DEGENERATION, NOS	4 (8%)	7 (14%)	13 (28%)
METAMORPHOSIS FATTY		6 (12%)	3 (6%)
HYPERPLASIA, NOS	2 (4%)		
ANGIECTASIS			1 (2%)
#ADRENAL MEDULLA	(50)	(49)	(47)
HYPERPLASIA, NOS		1 (2%)	1 (2%)
HYPERPLASIA, FOCAL			2 (4%)
#THYROID	(49)	(48)	(45)
HYPERPLASIA, C-CELL		1 (2%)	4 (9%)
HYPERPLASIA, FOLLICULAR-CELL			1 (2%)
#PARATHYROID	(19)	(22)	(22)
HYPERPLASIA, NOS	1 (5%)		
#PANCREATIC ISLETS	(50)	(46)	(47)
HYPERPLASIA, NOS		2 (4%)	
HYPERPLASIA, FOCAL		1 (2%)	
<b>REPRODUCTIVE SYSTEM</b>			
*MAMMARY GLAND	(50)	(50)	(50)
GALACTOCELE	1 (2%)	16 (32%)	3 (6%)
CYSTIC DUCTS	7 (14%)		
FIBROSIS		2 (4%)	
HYPERPLASIA, EPITHELIAL		2 (4%)	2 (4%)
HYPERPLASIA, CYSTIC	4 (8%)		
LACTATION		9 (18%)	3 (6%)
*CLITORAL GLAND	(50)	(50)	(50)
CYST, NOS			1 (2%)
*VAGINA	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		2 (4%)	5 (10%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

**TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
HYPERKERATOSIS			1 (2%)
#UTERUS	(50)	(49)	(48)
HYDROMETRA	3 (6%)	5 (10%)	
HEMORRHAGE	1 (2%)		1 (2%)
HEMATOMA, NOS			
INFARCT, NOS		1 (2%)	
#UTERUS/ENDOMETRIUM	(50)	(49)	(48)
HYPERPLASIA, CYSTIC		2 (4%)	1 (2%)
#ENDOMETRIAL GLAND	(50)	(49)	(48)
CYST, NOS			1 (2%)
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(50)	(48)
INFLAMMATION, NOS			1 (2%)
#BRAIN	(50)	(50)	(48)
HYDROCEPHALUS, INTERNAL			1 (2%)
HEMORRHAGE			2 (4%)
INFLAMMATION, FOCAL		1 (2%)	
MALACIA			4 (8%)
#CEREBELLUM	(50)	(50)	(48)
HEMORRHAGE	1 (2%)		
SPECIAL SENSE ORGANS			
.*EYE	(50)	(50)	(50)
INFLAMMATION, ACUTE	2 (4%)		
CATARACT	1 (2%)		
NECROSIS, NOS	1 (2%)		
PHTHISIS BULBI	1 (2%)		
*SCLERA	(50)	(50)	(50)
MINERALIZATION			1 (2%)
*EYE/CORNEA	(50)	(50)	(50)
INFLAMMATION, NOS			1 (2%)
INFLAMMATION, FOCAL			1 (2%)
*EYE/RETINA	(50)	(50)	(50)
DEGENERATION, NOS	1 (2%)		

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
 \* NUMBER OF ANIMALS NECROPSIED

**TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ATROPHY, NOS		10 (20%)	5 (10%)
*EYE/CRYSTALLINE LENS MINERALIZATION CATARACT	(50)	(50)	(50) 1 (2%) 1 (2%)
*NASOLACRIMAL DUCT INFLAMMATION, SUPPURATIVE INFLAMMATION, ACUTE	(50) 1 (2%) 1 (2%)	(50)	(50)
<b>MUSCULOSKELETAL SYSTEM</b>			
*MAXILLA INFLAMMATION, CHRONIC	(50) 1 (2%)	(50)	(50)
<b>BODY CAVITIES</b>			
*ABDOMINAL CAVITY STEATITIS NECROSIS, FAT	(50) 1 (2%) 8 (16%)	(50) 5 (10%)	(50) 3 (6%)
<b>ALL OTHER SYSTEMS</b>			
NONE			
<b>SPECIAL MORPHOLOGY SUMMARY</b>			
AUTO/NECROPSY/HISTO PERF	1	1	
AUTO/NECROPSY/NO HISTO			1
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY			
* NUMBER OF ANIMALS NECROPSIED			

APPENDIX D  
SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE  
EXPOSED TO AIR CONTAINING 1,2-DIBROMOETHANE



TABLE D1.

**SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE EXPOSED TO AIR CONTAINING 1,2-DIBROMOETHANE**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	45	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	44	48	46
INTEGUMENTARY SYSTEM			
*SKIN	(45)	(50)	(50)
ULCER, FOCAL	1 (2%)		1 (2%)
INFLAMMATION, SUPPURATIVE	1 (2%)	3 (6%)	
INFLAMMATION, FOCAL GRANULOMATOUS	1 (2%)		
NECROSIS, NOS		1 (2%)	
NECROSIS, FOCAL		1 (2%)	
*SUBCUT TISSUE	(45)	(50)	(50)
STEATITIS			1 (2%)
INFLAMMATION, SUPPURATIVE		1 (2%)	
INFLAMMATION, PYOGRANULOMATOUS			1 (2%)
NECROSIS, NOS		1 (2%)	
RESPIRATORY SYSTEM			
*NASAL CAVITY	(45)	(50)	(50)
HEMORRHAGE			1 (2%)
INFLAMMATION, SEROUS		15 (30%)	22 (44%)
INFLAMMATION, SUPPURATIVE		3 (6%)	9 (18%)
INFLAMMATION, PYOGRANULOMATOUS			1 (2%)
POLYP, INFLAMMATORY			3 (6%)
#TRACHEA	(38)	(47)	(45)
HYPERPLASIA, EPITHELIAL			1 (2%)
#LUNG/BRONCHUS	(41)	(48)	(46)
HYPERPLASIA, EPITHELIAL			6 (13%)
#LUNG/BRONCHIOLE	(41)	(48)	(46)
HYPERPLASIA, EPITHELIAL		3 (6%)	29 (63%)
#LUNG	(41)	(48)	(46)
CONGESTION, NOS	14 (34%)	13 (27%)	7 (15%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
 \* NUMBER OF ANIMALS NECROPSIED

**TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
EDEMA, NOS		1 (2%)	2 (4%)
HYPERPLASIA, ADENOMATOUS			15 (33%)
HYPERPLASIA, ALVEOLAR EPITHELIUM		2 (4%)	31 (67%)
<b>HEMATOPOIETIC SYSTEM</b>			
#BONE MARROW	(35)	(46)	(44)
GRANULOPOIESIS		1 (2%)	1 (2%)
#SPLEEN	(37)	(47)	(44)
ATROPHY, NOS	1 (3%)		1 (2%)
LEUKEMOID REACTION			1 (2%)
HEMATOPOIESIS	9 (24%)	2 (4%)	1 (2%)
MYELOPOIESIS	1 (3%)		
GRANULOPOIESIS		4 (9%)	
#LYMPH NODE	(32)	(42)	(40)
HYPERPLASIA, LYMPHOID			3 (8%)
#CERVICAL LYMPH NODE	(32)	(42)	(40)
MASTOCYTOSIS			1 (3%)
#MESENTERIC L. NODE	(32)	(42)	(40)
HISTIOCYTOSIS		1 (2%)	
HYPERPLASIA, LYMPHOID	1 (3%)		
#LUNG	(41)	(48)	(46)
LEUKOCYTOSIS, NOS			2 (4%)
#LIVER	(41)	(48)	(46)
LEUKEMOID REACTION			1 (2%)
<b>CIRCULATORY SYSTEM</b>			
*SKELETAL MUSCLE	(45)	(50)	(50)
THROMBOSIS, NOS	1 (2%)		
#HEART	(41)	(48)	(46)
CALCIFICATION, FOCAL			1 (2%)
#MYOCARDIUM	(41)	(48)	(46)
INFLAMMATION, SUPPURATIVE		1 (2%)	
#KIDNEY	(40)	(48)	(46)
THROMBOSIS, NOS		3 (6%)	

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED



**TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#URINARY BLADDER PERIARTERITIS	(41) 1 (2%)	(48)	(45)
DIGESTIVE SYSTEM			
*LIP	(45)	(50)	(50)
ULCER, FOCAL	1 (2%)		
INFLAMMATION, SUPPURATIVE	1 (2%)		
ABSCESS, NOS	1 (2%)		
*ROOT OF TOOTH ABSCESS, NOS	(45) 1 (2%)	(50)	(50)
#LIVER	(41)	(48)	(46)
INFLAMMATION, SUPPURATIVE	1 (2%)		
NECROSIS, NOS			1 (2%)
NECROSIS, FOCAL	2 (5%)		
NECROSIS, COAGULATIVE		1 (2%)	
METAMORPHOSIS FATTY			1 (2%)
FOCAL CELLULAR CHANGE		1 (2%)	1 (2%)
#LIVER/CENTRIOLOBULAR NECROSIS, NOS	(41)	(48)	(46)
NECROSIS, FOCAL	1 (2%)		2 (4%)
#PANCREAS	(35)	(43)	(41)
EDEMA, INTERSTITIAL	1 (3%)		
NECROSIS, FOCAL	1 (3%)		
INFARCT, NOS		1 (2%)	
#STOMACH	(37)	(48)	(45)
ULCER, FOCAL			1 (2%)
HYPERPLASIA, EPITHELIAL			2 (4%)
URINARY SYSTEM			
#KIDNEY	(40)	(48)	(46)
MINERALIZATION			1 (2%)
HYDRONEPHROSIS		1 (2%)	
POLYCYSTIC KIDNEY			1 (2%)
PYELONEPHRITIS SUPPURATIVE	8 (20%)	16 (33%)	7 (15%)
INFLAMMATION, CHRONIC	1 (3%)	1 (2%)	

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

**TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
PYELONEPHRITIS, CHRONIC	3 (8%)		2 (4%)
NEPHROPATHY, TOXIC			1 (2%)
INFARCT, NOS		2 (4%)	
CALCIFICATION, FOCAL		3 (6%)	
HYPERPLASIA, EPITHELIAL		1 (2%)	1 (2%)
#KIDNEY/CAPSULE FIBROSIS	(40)	(48)	(46) 1 (2%)
#KIDNEY/TUBULE DILATATION, NOS	(40)	(48) 1 (2%)	(46)
#KIDNEY/PELVIS INFLAMMATION, SUPPURATIVE	(40)	(48) 5 (10%)	(46) 4 (9%)
INFLAMMATION, CHRONIC			1 (2%)
NECROSIS, NOS	2 (5%)	7 (15%)	3 (7%)
#URINARY BLADDER DISTENTION	(41) 10 (24%)	(48) 10 (21%)	(45) 10 (22%)
INFLAMMATION, SUPPURATIVE	1 (2%)	12 (25%)	4 (9%)
INFLAMMATION, HEMORRHAGIC	1 (2%)	1 (2%)	
INFLAMMATION, CHRONIC	6 (15%)	7 (15%)	7 (16%)
INFLAMMATION, CHRONIC SUPPURATIV	3 (7%)		
HYPERPLASIA, EPITHELIAL		7 (15%)	7 (16%)
<b>ENDOCRINE SYSTEM</b>			
#PERIADRENAL TISSUE INFLAMMATION, SUPPURATIVE	(34)	(46)	(43) 1 (2%)
<b>REPRODUCTIVE SYSTEM</b>			
*PÊNIS HEMORRHAGE	(45) 1 (2%)	(50)	(50)
ULCER, NOS	4 (9%)		1 (2%)
INFLAMMATION, SUPPURATIVE	5 (11%)	1 (2%)	1 (2%)
NECROSIS, NOS	1 (2%)		
NECROSIS, FOCAL		1 (2%)	
*PREPUCE ULCER, NOS	(45) 8 (18%)	(50)	(50) 4 (8%)
INFLAMMATION, SUPPURATIVE	10 (22%)	8 (16%)	3 (6%)
ABSCESS, NOS	1 (2%)		1 (2%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

**TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC NECROSIS, NOS	1 (2%)	6 (12%)	
*PREPUTIAL GLAND	(45)	(50)	(50)
CYST, NOS	3 (7%)	2 (4%)	
INFLAMMATION, SUPPURATIVE	1 (2%)	1 (2%)	3 (6%)
ABSCESS, NOS	1 (2%)	4 (8%)	6 (12%)
INFLAMMATION, CHRONIC	2 (4%)	2 (4%)	5 (10%)
FIBROSIS		1 (2%)	
NECROSIS, NOS		1 (2%)	
METAPLASIA, SQUAMOUS			2 (4%)
#PROSTATE	(41)	(46)	(41)
INFLAMMATION, SUPPURATIVE	6 (15%)	19 (41%)	13 (32%)
ABSCESS, NOS			1 (2%)
INFLAMMATION, CHRONIC	2 (5%)	1 (2%)	1 (2%)
*SEMINAL VESICLE	(45)	(50)	(50)
DISTENTION	1 (2%)	1 (2%)	
INFLAMMATION, SUPPURATIVE	2 (4%)	6 (12%)	3 (6%)
INFLAMMATION, CHRONIC			1 (2%)
FIBROSIS		2 (4%)	2 (4%)
#TESTIS	(42)	(47)	(44)
INFLAMMATION, SUPPURATIVE		3 (6%)	
DEGENERATION, NOS			1 (2%)
NECROSIS, NOS		1 (2%)	
INFARCT, NOS		1 (2%)	
CALCIFICATION, FOCAL		1 (2%)	
*EPIDIDYMIS	(45)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)	3 (6%)	
INFLAMMATION, CHRONIC	1 (2%)		
GRANULOMA, SPERMATIC		1 (2%)	
NERVOUS SYSTEM			
#BRAIN	(38)	(48)	(46)
CALCIFICATION, FOCAL	9 (24%)	5 (10%)	8 (17%)
SPECIAL SENSE ORGANS			
*EYE/CORNEA	(45)	(50)	(50)
INFLAMMATION, FOCAL			1 (2%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
 \* NUMBER OF ANIMALS NECROPSIED

**TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
*HARDERIAN GLAND INFLAMMATION, SUPPURATIVE	(45)	(50)	(50) 1 (2%)
MUSCULOSKELETAL SYSTEM			
*MANDIBLE INFLAMMATION, SUPPURATIVE	(45) 1 (2%)	(50)	(50)
*SKELETAL MUSCLE INFLAMMATION, SUPPURATIVE	(45) 1 (2%)	(50)	(50)
BODY CAVITIES			
*TUNICA VAGINALIS INFLAMMATION, SUPPURATIVE INFLAMMATION, CHRONIC	(45) 1 (2%)	(50) 2 (4%)	(50)
ALL OTHER SYSTEMS			
CHIN INFLAMMATION, PYOGRANULOMATOUS	1		
TAIL INFLAMMATION, CHRONIC		1	
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	6	3	
AUTO/NECROPSY/HISTO PERF	3		
AUTO/NECROPSY/NO HISTO	1	2	4
AUTOLYSIS/NO NECROPSY	5		
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY			
* NUMBER OF ANIMALS NECROPSIED			

TABLE D2.

**SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE EXPOSED TO AIR CONTAINING 1, 2-DIBROMOETHANE**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
<b>INTEGUMENTARY SYSTEM</b>			
*SUBCUT TISSUE	(50)	(50)	(50)
EDEMA, NOS		4 (8%)	4 (8%)
METAPLASIA, OSSEOUS		1 (2%)	
<b>RESPIRATORY SYSTEM</b>			
*NASAL CAVITY	(50)	(50)	(50)
HEMORRHAGE		6 (12%)	2 (4%)
INFLAMMATION, SEROUS		19 (38%)	14 (28%)
INFLAMMATION, SUPPURATIVE		4 (8%)	20 (40%)
HYPERPLASIA, EPITHELIAL			13 (26%)
POLYP, INFLAMMATORY			5 (10%)
ANGIECTASIS			1 (2%)
#TRACHEA	(49)	(50)	(48)
HYPERPLASIA, EPITHELIAL			3 (6%)
#LUNG/BRONCHUS	(49)	(49)	(50)
CONGESTION, NOS	1 (2%)		
HYPERPLASIA, EPITHELIAL		10 (20%)	18 (36%)
#LUNG/BRONCHIOLE	(49)	(49)	(50)
HYPERPLASIA, EPITHELIAL		13 (27%)	44 (88%)
#LUNG	(49)	(49)	(50)
CONGESTION, NOS		2 (4%)	1 (2%)
EDEMA, NOS		1 (2%)	1 (2%)
HEMORRHAGE	1 (2%)	1 (2%)	
PNEUMONIA, ASPIRATION			1 (2%)
INFLAMMATION, SUPPURATIVE			2 (4%)
HYPERPLASIA, ADENOMATOUS			37 (74%)
HYPERPLASIA, ALVEOLAR EPITHELIUM		11 (22%)	44 (88%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
 \* NUMBER OF ANIMALS NECROPSIED

**TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
METAPLASIA, OSSEOUS			1 (2%)
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(47)	(47)	(50)
FIBROUS OSTEODYSTROPHY	28 (60%)	13 (28%)	4 (8%)
ERYTHROPOIESIS		1 (2%)	
GRANULOPOIESIS		1 (2%)	1 (2%)
#SPLEEN	(50)	(49)	(49)
ATROPHY, NOS			2 (4%)
ANGIECTASIS	1 (2%)	1 (2%)	
LEUKEMOID REACTION		1 (2%)	1 (2%)
HYPERPLASIA, LYMPHOID	7 (14%)	2 (4%)	
HEMATOPOIESIS		8 (16%)	16 (33%)
GRANULOPOIESIS		2 (4%)	
#CERVICAL LYMPH NODE	(49)	(42)	(45)
HYPERPLASIA, LYMPHOID	2 (4%)		
#BRONCHIAL LYMPH NODE	(49)	(42)	(45)
HYPERPLASIA, LYMPHOID	2 (4%)	1 (2%)	
#MESENTERIC L. NODE	(49)	(42)	(45)
HYPERPLASIA, LYMPHOID	3 (6%)		
#LUNG	(49)	(49)	(50)
LEUKOCYTOSIS, NOS		2 (4%)	1 (2%)
LEUKEMOID REACTION			1 (2%)
#LIVER	(50)	(50)	(50)
LEUKEMOID REACTION		1 (2%)	1 (2%)
HEMATOPOIESIS			1 (2%)
CIRCULATORY SYSTEM			
#BRAIN	(50)	(50)	(50)
THROMBOSIS, NOS			1 (2%)
*PERITONEAL CAVITY	(50)	(50)	(50)
THROMBOSIS, NOS		1 (2%)	
#MESENTERIC L. NODE	(49)	(42)	(45)
LYMPHANGIECTASIS		1 (2%)	

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

**TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
THROMBOSIS, NOS		1 (2%)	
#HEART	(50)	(49)	(50)
THROMBOSIS, NOS			1 (2%)
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, CHRONIC			1 (2%)
#MYOCARDIUM	(50)	(49)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
#ENDOCARDIUM	(50)	(49)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)
#CARDIAC VALVE	(50)	(49)	(50)
THROMBOSIS, NOS		1 (2%)	
#SALIVARY GLAND	(47)	(48)	(47)
PERIARTERITIS		2 (4%)	
#LIVER	(50)	(50)	(50)
THROMBOSIS, NOS	1 (2%)		1 (2%)
#PERIRENAL TISSUE	(50)	(50)	(50)
THROMBOSIS, NOS		1 (2%)	
#UTERUS	(50)	(48)	(48)
THROMBOSIS, NOS		1 (2%)	
DIGESTIVE SYSTEM			
*ROOT OF TOOTH	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
#SALIVARY GLAND	(47)	(48)	(47)
EDEMA, NOS		1 (2%)	
#LIVER	(50)	(50)	(50)
INFLAMMATION, FOCAL	1 (2%)		
INFLAMMATION, GRANULOMATOUS		1 (2%)	
NECROSIS, FOCAL		2 (4%)	5 (10%)
INFARCT, NOS	1 (2%)		
INFARCT, FOCAL			1 (2%)
CALCIFICATION, FOCAL			1 (2%)
FOCAL CELLULAR CHANGE	2 (4%)	5 (10%)	1 (2%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
 \* NUMBER OF ANIMALS NECROPSIED

**TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ANGIECTASIS		3 (6%)	1 (2%)
#LIVER/CENTRILOBULAR NECROSIS, NOS	(50)	(50) 1 (2%)	(50) 2 (4%)
*GALLBLADDER CALCULUS, NOS	(50) 1 (2%)	(50)	(50)
#BILE DUCT HYPERPLASIA, NOS	(50) 1 (2%)	(50)	(50)
#PANCREAS CYSTIC DUCTS AMYLOIDOSIS METAMORPHOSIS FATTY	(48) 2 (4%) 2 (4%)	(48) 3 (6%) 1 (2%) 3 (6%)	(49)
*PHARYNX HYPERPLASIA, EPITHELIAL	(50)	(50)	(50) 1 (2%)
#STOMACH ULCER, FOCAL HYPERKERATOSIS ACANTHOSIS	(50)	(50)	(49) 1 (2%) 2 (4%) 2 (4%)
#COLON NEMATODIASIS	(49) 1 (2%)	(49)	(48)
<b>URINARY SYSTEM</b>			
#KIDNEY MINERALIZATION HYDRONEPHROSIS INFLAMMATION, SUPPURATIVE PYELONEPHRITIS SUPPURATIVE INFLAMMATION, CHRONIC INFARCT, NOS INFARCT, FOCAL PIGMENTATION, NOS	(50)  1 (2%)	(50) 1 (2%)  1 (2%)	(50) 2 (4%) 2 (4%) 2 (4%) 1 (2%) 1 (2%) 1 (2%)
#RIGHT KIDNEY HYDRONEPHROSIS	(50)	(50)	(50) 2 (4%)
#PERIRENAL TISSUE INFLAMMATION, SUPPURATIVE	(50)	(50) 1 (2%)	(50) 1 (2%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY  
\* NUMBER OF ANIMALS NECROPSIED



**TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#KIDNEY/TUBULE NECROSIS, NOS PIGMENTATION, NOS REGENERATION, NOS	(50)	(50)	(50) 1 (2%) 1 (2%) 1 (2%)
*URETER INFLAMMATION, SUPPURATIVE	(50)	(50) 1 (2%)	(50)
#URINARY BLADDER DISTENTION	(48) 1 (2%)	(47) 1 (2%)	(45)
ENDOCRINE SYSTEM			
#PITUITARY CYST, NOS INFLAMMATION, SUPPURATIVE HYPERPLASIA, NOS	(48) 1 (2%) 1 (2%)	(46) 1 (2%) 1 (2%)	(40)
#PARATHYROID CYST, NOS	(26) 1 (4%)	(20)	(16)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND INFLAMMATION, SUPPURATIVE HYPERPLASIA, EPITHELIAL LACTATION	(50) 1 (2%) 4 (8%)	(50) 1 (2%)	(50) 1 (2%) 1 (2%)
*VAGINA EDEMA, NOS INFLAMMATION, SUPPURATIVE	(50) 3 (6%) 3 (6%)	(50)	(50)
#UTERUS HYDROMETRA ANGIECTASIS	(50) 2 (4%)	(48) 1 (2%) 1 (2%)	(48) 1 (2%)
#UTERUS/ENDOMETRIUM INFLAMMATION, SUPPURATIVE HYPERPLASIA, CYSTIC	(50) 41 (82%)	(48) 2 (4%) 30 (63%)	(48) 1 (2%)
#ENDOMETRIAL GLAND CYST, NOS	(50) 2 (4%)	(48) 1 (2%)	(48) 6 (13%)

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

**TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)**

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#OVARY	(48)	(40)	(36)
CYSTIC FOLLICLES	5 (10%)	4 (10%)	
FOLLICULAR CYST, NOS	1 (2%)		
PAROVARIAN CYST	7 (15%)	2 (5%)	2 (6%)
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	
#BRAIN	(50)	(50)	(50)
COMPRESSION		1 (2%)	
CALCIFICATION, FOCAL	7 (14%)	4 (8%)	
SPECIAL SENSE ORGANS			
*EYE/CORNEA	(50)	(50)	(50)
INFLAMMATION, FOCAL	2 (4%)		1 (2%)
*HARDERIAN GLAND	(50)	(50)	(50)
HYPERPLASIA, NOS		1 (2%)	
*INTERNAL EAR	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			2 (4%)
MUSCULOSKELETAL SYSTEM			
*SKELETAL MUSCLE	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)
BODY CAVITIES			
*ABDOMINAL CAVITY	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
STEATITIS		1 (2%)	
NECROSIS, FAT		2 (4%)	
*PERITONEUM	(50)	(50)	(50)
INFLAMMATION, CHRONIC		1 (2%)	1 (2%)
INFLAMMATION, GRANULOMATOUS	1 (2%)		

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

**TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)**

	<b>UNTREATED CONTROL</b>	<b>LOW DOSE</b>	<b>HIGH DOSE</b>
<b>*MESENTERY INFLAMMATION, CHRONIC</b>	(50)	(50) 1 (2%)	(50)
<b>ALL OTHER SYSTEMS</b>			
<b>BROAD LIGAMENT ABSCESS, NOS</b>		1	
<b>SPECIAL MORPHOLOGY SUMMARY</b>			
<b>NO LESION REPORTED</b>		1	

**# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY**  
**\* NUMBER OF ANIMALS NECROPSIED**



**APPENDIX E**  
**ANALYSIS OF 1,2-DIBROMOETHANE**  
**AT MIDWEST RESEARCH INSTITUTE**



## Appendix E

### Analysis of 1,2-Dibromoethane at Midwest Research Institute

#### A. ELEMENTAL ANALYSIS

Element	C	H	Br
Theory	12.78	2.15	85.07
Determined	12.82	2.10	85.17
	12.77	2.13	85.26

#### B. VAPOR-PHASE CHROMATOGRAPHY

Instrument: Tracor MT 220  
Detector: Flame ionization  
Inlet temperature: 200°C  
Detector temperature: 250°C

#### System 1 (Table E1)

Table E1. Vapor-Phase Chromatography Data -- System 1 (a)

---

Peak	Retention Time (min)	Retention Time (Relative to 1,2-Dibromoethane)	Area (Relative to 1,2-Dibromoethane)
1	13.4	0.52	0.004
2	14.7	0.56	0.012
3	15.8	0.61	0.017
4	20.5	0.79	0.006
5	22.2	0.85	Tr
6	23.6	0.91	0.266
7	26.0	1.00	100.000
8	28.4	1.09	0.025

---

(a) Column: Porapak Q, 80/100, 1.8 m x 4 mm I.D., glass  
Oven temperature program: 60°C, 2 min; 60° to 205°C at 6°C/min; 205°C, 20 min.  
Results: Major peak and seven impurities

System 2 (Table E2)

Table E2. Vapor-Phase Chromatography Data -- System 2 (a)

Peak	Retention Time (min)	Retention Time (Relative to 1,2-Dibromoethane)	Area (Relative to 1,2-Dibromoethane)
1	4.4	0.44	< 0.02
2	6.4	0.64	trace < 0.01
3	7.4	0.73	trace < 0.01
4	8.3	0.83	0.20
5	10.1	1.0	100.00
6	17.3	1.7	0.30

(a) Column: 80/100 Porapak Q, 1.8 m x 4 mm I.D., glass  
Oven temperature program: 150°C, 5 min: 150° to 200°C at 5°C/min.

Results: Major peak and five impurities

System 3 (Table E3)

Table E3. Vapor-Phase Chromatography Data -- System 3 (a)

Peak	Retention Time (min)	Retention Time (Relative to 1,2-Dibromoethane)	Area (Relative to 1,2-Dibromoethane)
1	1.4	0.14	Tr
2	2.0	0.20	0.028
3	6.8	0.65	0.007
4	7.7	0.74	0.262
5	8.6	0.83	0.053
6	10.4	1.00	100.000
7	11.8	1.14	0.012
8	12.1	1.17	Tr
9	12.9	1.24	0.009
10	13.2	1.27	Tr
11	13.7	1.32	0.012
12	14.4	1.39	0.026
13	15.7	1.52	0.007
14	16.2	1.56	0.386
15	17.0	1.64	0.028
16	17.1	1.65	Tr
17	17.4	1.68	Tr
18	22.9	2.21	0.009



(a) Column: 20% SP 2100 + 0.1% Carbowax 20 M on Supelcoport 100/120, 1.8 m x 4 mm I.D., glass.

Oven temperature program: 50°C, 5 min; 50° to 200°C at 10°C/min

Results: Major peak and 17 impurities

C. SPECTRAL DATA

1. Infrared

System 1: Liquid spectrum      Consistent with literature spectrum (Sadtler Standard Spectra)

Instrument: Beckman IR-12

Cell: Neat, NaCl plates

Results: See Figure 5

System 2: Gas phase spectrum

Instrument: Beckman IR-12

Cell: 10 cm gas cell with NaCl windows

Spectrum seen: 1,400 to 700 cm<sup>-1</sup>

Results: See Figure 6

2. Nuclear Magnetic Resonance

Instrument: Varian HA-100      Consistent with literature spectrum (Sadtler Standard Spectra)

Solvent: Neat, tetramethylsilane  
internal standard added

Assignments: (See Figure 7)

(a) s,  $\delta = 3.67$  ppm

Integration ratios: (a) 4.00



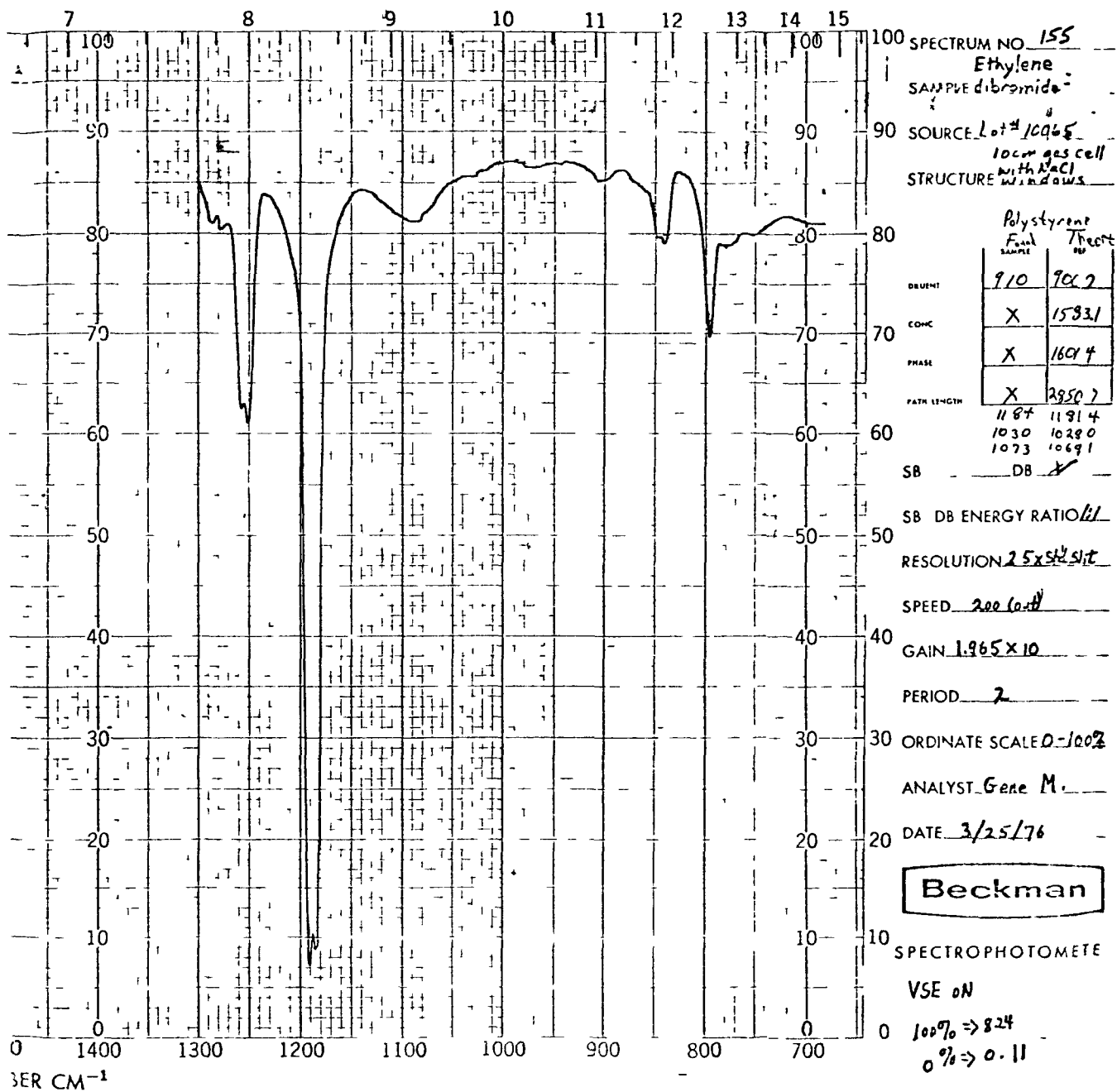


Figure 6. Infrared Absorption Spectrum (Gas) of 1,2-Dibromoethane

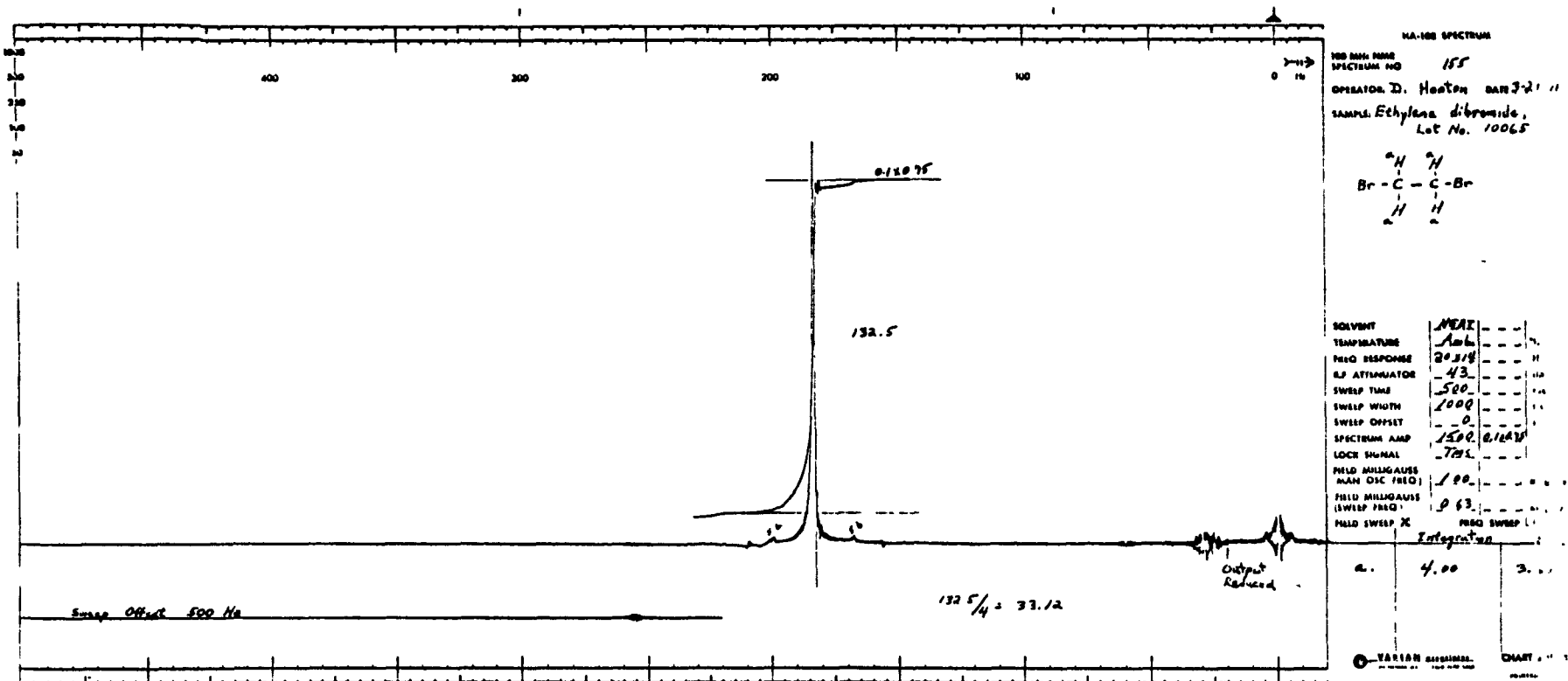


Figure 7. Nuclear Magnetic Resonance Spectrum of 1,2-Dibromoethane

D. ANALYTICAL DATA: (Table E4)

Table E4. Analytical Data (Dow Chemical)

Component	Run 1	Run 2	Average
Vinyl Bromide	0.05	0.05	0.05
Ethyl Bromide	0.06	0.06	0.06
Methylene Chloride	Not detected at limit of 0.01%		
Bromochloromethane	Not detected at limit of 0.01%		
Methylene Bromide + 1-Bromo,2-Chloroethane	0.14	0.14	0.14
1,2-Dibromoethane	99.4	99.3	99.4
2-Chloroethanol	0.01	0.04	0.03
Bromoform	0.03	0.05	0.04
2-Bromoethanol	0.05	0.04	0.05
1,1,2-Tribromoethane	0.01	0.02	0.02
Bis(2-Bromoethyl) Ether	0.18	0.19	0.19
Unknowns	0.02	0.04	0.03



**APPENDIX F**  
**ANALYSIS OF 1,2-DIBROMOETHANE RESIDUE AND**  
**COMPARISON WITH A STORED SAMPLE**





Appendix F

Analysis of 1,2-Dibromoethane Residue and  
Comparison with a Stored Sample

I. VAPOR-PHASE CHROMATOGRAPHY

Instrument: Tracor MT 220  
 Detector: Flame ionization  
 Inlet temperature: 200°C  
 Detector temperature: 250°C  
 Carrier gas: Nitrogen  
 Carrier flow: 70 ml/min

A. IMPURITY DETECTION

1. SYSTEM 1

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120  
 Supelcoport, 1.8 m x 4 mm I.D., glass  
 Oven temperature program: 50°C, 5 min; 50° to  
 170°C at 10°C/min  
 Sample injected: 2 µl Neat liquid diluted to 1% in  
 methanol to quantitate major peak

a. Residue from inhalation studies (Table F1)

Table F1. Vapor-Phase Chromatography Data -- System 1 -- Residue From  
Inhalation Studies (a)

Peak	Retention Time (min)	Retention Time (Relative to 1,2-Dibromoethane)	Area (Relative to 1,2-Dibromoethane)
1	7.4	1.0	100
2	10.7	1.4	0.02
3	11.1	1.5	trace < 0.01
4	12.6	1.7	0.2
5	13.4	1.8	0.04
6	13.8	1.9	0.01
7	14.3	1.9	3
8	15.0	2.0	0.5
9	15.3	2.1	0.02
10	15.9	2.1	0.02
11	17.0	2.3	trace < 0.01
12	17.2	2.3	0.01
13	24.3	2.3	0.05

(a) Results: Major peak and 12 impurities. One impurity has an area 3% of the major peak. The areas of the other impurities total 0.9% of the major peak.

b. Sample stored at Hazleton Laboratories (Table F2)

Table F2. Vapor-Phase Chromatography Data -- System 1 -- Sample Stored at Hazleton Laboratories (a)

Peak	Retention Time (min)	Retention Time (Relative to 1,2-Dibromoethane)	Area (Relative to 1,2-Dibromoethane)
1	0.8	0.1	0.01
2 (b)	1.0	0.1	0.04
3	1.3	0.2	0.06
4	7.4	1.0	100
5	10.5	1.4	trace < 0.01
6	12.3	1.7	0.02
7	13.1	1.8	0.02
8	13.8	1.9	0.01
9	14.7	2.0	trace < 0.01

(a) Results: Major peak and eight impurities with areas totalling less than 0.2% of the area of the major peak.

(b) Peak No. 2 was enhanced when vinyl bromide was added to the sample.

c. Conclusions: Three volatile impurities eluting before the major peak were observed in the sample stored at Hazleton. One peak was enhanced by the addition of vinyl bromide. These impurities were not observed in the residue from the inhalation studies. Compared with the stored sample, the residue contained a greater number of less volatile impurities (and of less volatile impurities of higher molecular weight) that eluted after the major peak.

2. SYSTEM 2

Column: 10% Carbowax 20 M-TPA on 80/100 Chromosorb W AW, 1.8 m x 4 mm I.D., glass

Oven temperature program: 50°C, 10 min; 50° to 200°C at 10°C/min

Sample injected: 5 µl Neat liquid diluted to 1% in hexane to quantitate major peak

a. Residue from inhalation studies (Table F3)

Table F3. Vapor-Phase Chromatography Data -- System 2 -- Residue From Inhalation Studies (a)

Peak	Retention Time (min)	Retention Time (Relative to 1,2-Dibromoethane)	Area (Relative to 1,2-Dibromoethane)
1	14.2	1.00	100
2	15.6	1.10 shoulder	< 0.01
3	15.8	1.11 shoulder	< 0.007
4	16.1	1.13 shoulder	< 0.003
5	16.8	1.18	0.02
6	17.0	1.20	0.005
7	17.6	1.24	0.01
8	17.7	1.25	shoulder
9	18.0	1.27	0.01
10	18.5	1.30	0.03
11	18.7	1.32 trace	< 0.001
12	19.0	1.34	0.2
13	19.4	1.37	0.06
14	20.0	1.41	0.08
15	20.2	1.42	2
16	20.5	1.44	0.02
17	21.0	1.48	0.1
18	21.9	1.54	0.07
19	23.4	1.65 shoulder	< 0.05

(a) Results: Major peak and 18 impurities. One impurity has an area 2% of that of the major peak. The areas of the other impurities total 0.8%.

b. Sample stored at Hazelton Laboratories (Table F4)

Table F4. Vapor-Phase Chromatography Data -- System 2 -- Sample Stored at Hazelton Laboratories (a)

Peak	Retention Time (min)	Retention Time (Relative to 1,2-Dibromoethane)	Area (Relative to 1,2-Dibromoethane)
1	0.6	0.04	0.01
2	0.8	0.06	0.008
3	0.9	0.06	0.02
4	1.1	0.08	trace < 0.001
5	1.8	0.13	0.02
6	3.0	0.21	trace < 0.001
7	14.1	1.00	100
8	16.1	1.14	0.004
9	16.7	1.18	0.001
10	17.0	1.21	trace < 0.001
11	17.4	1.23	0.001
12	17.9	1.27	0.001
13	18.8	1.33	0.01
14	19.4	1.38	0.008
15	20.0	1.42	0.01

(a) Results: Major peak and 14 impurities. The areas of the impurities total less than 0.1% of the major peak.

c. Conclusions: Five volatile impurities which eluted before the major peak were observed in the sample stored at Hazelton Laboratories and not in the residue from the inhalation studies. The residue contained more and larger less volatile impurities which eluted after the major peak.

B. QUANTITATION OF THE MAJOR COMPONENT

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120

Supelcoport, 1.8 m x 4 mm I.D., glass

Oven temperature program: 75°C, isothermal

Standard: 1,2-Dibromoethane, 99%

Aldrich Chemical Company, Lot No. MA102567

Sample injected: 7 µl 0.45% v/v solutions in methanol

Results: (a) Residue from inhalation studies: 93.8±0.9%

(b) Sample stored at Hazelton Laboratories:  
97.9±1.4%

## II. VAPOR-PHASE CHROMATOGRAPHY/MASS SPECTROMETRY

Instrument: Varian MAT CH<sub>4</sub>B mass spectrometer interfaced via a Watson-Biemann helium separator to a Tracor MT 2000 MF vapor-phase chromatograph. Data processed by a Varian 620/i computer.

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120

Supelcoport, 1.8 m x 4 mm I.D., glass

Oven temperature program: 50°C, 5 min; 50° to 170°C at 10°C/min

Inlet temperature: 170°C

Carrier gas: Helium

Carrier Flow: 30 ml/min

### A. RESIDUE FROM INHALATION STUDIES (Tables F5, F6, and F7)

Table F5. Vapor-Phase Chromatography Data -- Residue From Inhalation Studies (a)

Peak	Retention Time (min)	Retention Time (Relative to 1,2-Dibromoethane)	Corresponding Peak in Table F1 (Tentative)
1	0.9	0.1	not detected
2	13.3	1.0	1
3	15.2	1.1	2
4	15.7	1.2	not detected
5	16.1	1.2	3
6	16.8	1.2	4
7	17.8	1.3	5
8	18.5 shoulder	1.4	6
9	19.2	1.4	7
10	20.9	1.6	8
11	22.5	1.7	9
12	24.7	1.9	10
13	27.1	2.0	11
14	29.6	2.2	12
15	42	3.2	13

(a) Results: Major peak and 14 impurities

Table F6. Mass Spectrometry Data — Residue From Inhalation Studies (a)

Peak	Mass	Percent of Base Peak	Possible Identity	Literature	
				Mass	Percent of Base Peak
1	109	100			
	64	75			
	80	73			
	81	69			
	55	66			
	82	63			
	48	62			
	107	54			
	56	54			
2	107	100	1,2-Dibromoethane	107	100 ( <u>Eight</u>
	109	100		109	95 <u>Peak</u>
	27	100		27	54 <u>Index,</u>
	28	100		28	11 <u>1970)</u>
	26	100		26	8
	93	20		93	5
	188	17		188	5
	95	19		95	4
	3	143		100	Unknown
141		77			
62		37			
61		28			
145		23			
222		5			
4	55	100	1,2-Dibromobutane	55	100 ( <u>Eight</u>
	135	45		135	99 <u>Peak</u>
	137	33		137	99 <u>Index,</u>
	29	60		29	28 <u>1970)</u>
	27	805		27	28
	39	40		39	26
	41	38		41	15
	56	23		56	8
	5	57		100	Unknown
185		98			
264		85			

Table F6. Mass Spectrometry Data -- Residue From Inhalation Studies (a)

(Continued)

Peak	Mass	Percent of Base Peak	Possible Identity	Literature	
				Mass	Percent of Base Peak
5	266	78			
	80	71			
	187	69			
	183	66			
	79	65			
6	187	100	Unknown		
	185	47			
	106	41			
	189	38			
	108	38			
	266	12			
	168	8			
7	157	100	1,2-Dibromo- 3-chloro- propane	157	100 ( <u>Eight</u> <u>Peak</u> <u>Index,</u> <u>1970</u> )
	155	100		155	
	75	100		75	
	159	47		159	
	39	100		39	
	77	53		77	
	49	37		49	
	93	21		93	
8	192	96	1-Bromo- 2-chloro- benzene or the 3- chloro-or 4-chloro- isomer	192	100 ( <u>Eight</u> <u>Peak</u> <u>Index,</u> <u>1970</u> )
	190	74		190	
	111	100		111	
	75	60		75	
	194	21		194	
	113	34		113	
	50	24		50	
	74	20		74	
9	137	100	Bis (2- bromoethyl) ether	137	100 ( <u>Eight</u> <u>Peak</u> <u>Index,</u> <u>1970</u> )
	139	100		139	
	27	54		27	
	107	91		107	
	109	87		109	
	28	103		28	

Table F6. Mass Spectrometry Data — Residue From Inhalation Studies (a)

(Continued)

Peak	Mass	Percent of Base Peak	Possible Identity	Literature	
				Mass	Percent of Base Peak
9	138	4		138	17
	18	100		18	15
10	106	100	Unknown		
	108	100			
	42	78			
	44	47			
	43	40			
	123	37			
	121	36			
	95	19			
	93	20			
Masses 107, 109 obscured by previous peak.					
11	186	100	Unknown		
	184	77			
	265	49			
	263	39			
	344	35			
	346	29			
	342	27			
	171	17			
12	186	100	Unknown		
	105	95			
	184	43			
	188	38			
	265	23			
	267	23			
	104	11			
	269	7			
13	250	100	Unknown		
	252	62			
	248	46			
	323	10			



Table F6. Mass Spectrometry Data — Residue From Inhalation Studies (a)

(Continued)

Peak	Mass	Percent of Base Peak	Possible Identity	Literature	
				Mass	Percent of Base Peak
14	308	100	Unknown		
	310	77			
	202	65			
	200	43			
	204	40			
	312	28			
15	230	100	Unknown		
	228	68			
	232	47			

(a) No matching spectra were found in the Eight Peak Index of Mass Spectra (1970) or in the Cyphernetics computer search system for Peak No. 6 or Peak No. 10 which constitute 0.2 and 0.5%, respectively, of the major peak. An attempt was made to assign the major fragments in the mass spectra of these compounds by comparison of the isotope ratios with those calculated by computer.

**Table F7. Isotope Ratios — Residue From Inhalation Studies**

Peak	Mass	Relative Intensity	Tentative Assignment	Computer Mass	Calculation Relative Intensity	
6	106	100	C <sub>2</sub> H <sub>3</sub> Br	106	100	
	108	93		108	98	
	185	47	C <sub>3</sub> BrCl <sub>2</sub>	185	61	
	187	100		187	100	
	189	38		189	45	
	266	100	C <sub>3</sub> Br <sub>2</sub> Cl <sub>2</sub>	266	100	
	268	67		268	90	
	10	106	100	C <sub>2</sub> H <sub>3</sub> Br	106	100
		108	100		108	98
		93	100	CH <sub>2</sub> Br	93	100
95		95	95		98	
121		97	C <sub>3</sub> H <sub>6</sub> Br	121	100	
123		100		123	98	

B. SAMPLE STORED AT HAZLETON LABORATORIES

Table F8. Vapor-Phase Chromatography Data -- Sample Stored at Hazleton Laboratories (a)

Peak	Retention Time (min)	Retention Time (Relative to 1,2-Dibromoethane)	Corresponding Peak in Table F2 (Tentative)
1	2.3	0.2	1
2	2.8	0.2	2
3	3.7	0.3	3
4	10.1	0.8	not detected
5	10.8	0.8	not detected
6	12.9	1.0	4
7	15.8	1.2	5
8	16.5	1.3	6
9	17.5	1.4	7
10	18.7	1.4	8
11	20.4	1.6	9

(a) Results: Major peak and 10 impurities

Table F9. Mass Spectrometry Data -- Sample Stored at Hazleton Laboratories

Peak	Mass	Percent of Base Peak	Possible Identity	Literature	
				Mass	Percent of Base Peak
1	64	100	Unknown		
	80	95			
	82	86			
	55	86			
	48	53			
	57	48			
	79	47			
	56	44			
2	27	215	Vinyl bromide	27	100 ( <u>Eight Peak Index, 1970</u> )
	106	100		100	74
	108	97		108	70
	26	63		26	7
	25	23		25	5
	79	5		79	4
	81	6		81	4
	107	5		107	4
	3	108		100	Bromo-ethane
110		100	110	97	
29		100	29	62	
29		100	27	51	
28		100	28	35	
26		58	26	14	
93		11	93	6	
81		6	81	5	
4	105	100	Unknown		
	107	97			
	186	56			
	188	33			
	184	33			
	81	14			
	79	10			
	104	8			
5	63	100	Unknown		
	65	33			
	57	15			
	80	10			
	64	9			
	56	7			
	81	6			
	55	6			

Table F9. Mass Spectrometry Data -- Sample Stored at Hazleton Laboratories

Continued

Peak	Mass	Percent of Base Peak	Possible Identity	Literature	
				Mass	Percent of Base Peak
6	107	100	1,2-Dibromo-ethane	107	100 ( <u>Eight Peak Index, 1970</u> )
	109	100		109	
	27	100		27	
	28	100		28	
	26	50		26	
	93	9		93	
6	188	4		188	5
	95	7		95	4
7	57	100	Unknown		
	69	82			
	55	73			
	56	64			
	84	36			
	70	30			
	83	21			
	71	15			
8	187	100	Unknown		
	185	49			
	108	45			
	106	44			
	189	41			
	84	28			
	266	4			
	268	3			
9	157	100	1,2-Dibromo-3-chloro-propane	157	100 ( <u>Eight Peak Index, 1970</u> )
	155	65		155	
	75	92		75	
	159	19		159	
	39	79		39	
	77	29		77	
	49	20		49	
	93	12		93	
10	137	100	Bis (2-Bromoethyl) ether	137	100
	139	99		139	
	27	101		27	
	107	95		107	
	109	96		109	
	28	102		28	
	138	4		138	
	18	102		18	

**Table F9. Mass Spectrometry Data -- Sample Stored at Hazleton Laboratories**

Continued

Peak	Mass	Percent of Base Peak	Possible Identity	Literature	
				Mass	Percent of Base Peak
11	109	100	Unknown		
	107	96			
	55	58			
	80	36			
	82	35			
	57	23			
	121	9			
	123	7			

**APPENDIX G**  
**ANALYSIS OF CHAMBER CONCENTRATION OF**  
**1,2-DIBROMOETHANE**





## Appendix G

### Analysis of Chamber Concentrations of 1,2-Dibromoethane

Concentrations of 1,2-dibromoethane in the chambers were determined by gas chromatography using a Varian 600-D gas chromatograph equipped with an electron capture detector. The chromatograph was calibrated each day using newly prepared standards of 1,2-dibromoethane.

Samples were obtained for analysis from a closed-loop system sample line which was allowed a 1-hour equilibration period prior to sampling. Samples were pulled from a septum in the sample line using Tomac syringes with lock tip and 20 gauge stainless steel needles. The gas samples were discharged into sealed, evacuated, 15-ml test tubes containing 1.0-ml of isopropanol (IPA). The tube contents were then mixed using a Vortex<sup>®</sup> mixer for at least 1 minute. Measured aliquots of the IPA solutions from each tube were then injected directly into the gas chromatograph for analysis. A 6-inch X 1/8 -inch O.D. stainless steel column packed with 6% FFAP on Porapak<sup>®</sup> Q, 80/100 mesh, was used with an isothermal column and detector temperature of 165°C. Nitrogen was the carrier gas.

Chamber concentrations (reported as ppm) were determined by injecting measured aliquots of prepared sample, determining the peak-height response, and determining the equivalent weight from the appropriate standard curve. The weight thus found (ng) was divided by the equivalent volume of gas injected to yield the chamber concentration (mg/cc) of 1,2-dibromoethane. This value, divided by the appropriate 1,2-dibromoethane constant factor (7.66 ng/cc) gives the reported chamber concentrations in parts per million (ppm).





