MRI REPORT

EVALUATION OF THE ENVIRONMENTAL TOXICANTS VINYL CHLORIDE (VC) AND VINYLIDENE CHLORIDE (VDC)

FINAL REPORT
July 1975 through June 1977

Contract No. NO1-ES-2-2084
(Continuation of NIH-NIEHS-72-2-2084)

MRI Project No. 3612-B

For

National Institute of Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, NC 27709

Attn: Dr. James S. Woods

SL 083811

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By

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PREFACE

This report was prepared at Midwest Research Institute, 425 Volker Boulevard, Kansas City, Missouri 64110, under Contract No. NO1-ES-2-2084 (Continuation of NIH-NIEHS-72-2084) with the National Institutes of Health, Department of Health, Education and Welfare, MRI Project No. 3612-B, "Research Capability for Environmental Health Sciences, Research Triangle Park, North Carolina 27709. Dr. James S. Woods is the Project Officer.

This work was conducted in the Biological Sciences Division, under the direction of Dr. William B. House, between July 1975 and June 1977. Dr. Cheng-Chun Lee, Assistant Director, Biological Sciences for Pharmacology and Toxicology, was the Principal Investigator, assisted by Dr. Joseph M. Winston, Associate Toxicologist. Dr. William B. House supervised the inhalation chamber operation, assisted by Dr. Paul J. Peters, Associate Biologist. Necropsy, gross and microscopic examination of tissues were performed by Dr. Jagdish C. Bhandari, Senior Pathologist, with the technical assistance of Mr. Ernesto Castillo and Miss Judith Shifrin. Dr. John R. Hodgson, Head, Biochemical and Development Pharmacology, supervised the cytogenetic analysis and collagen assays with the technical assistance of Mrs. Mary A. Kowalski and Mr. Don Van Goethem. Dr. Robert D. Short, Jr., Senior Toxicologist, performed the ^{14}C-thymidine incorporation studies and heme synthesis studies with the technical assistance of Miss Mary D. Sawyer. Mr. Jack H. Hagensen and Mrs. Karen J. Smith performed the analytical monitoring of chamber concentrations. Mr. Thomas W. Reddig, M.T. (ASCP certified) and Miss Judith D. Girvin, M.T. (ASCP certified) supervised the hematology and clinical laboratory tests with the technical assistance of Miss Ilonna S. Elwood, Mr. Duane R. Smith and Mrs. Bhanu S. Gosalia. Mrs. Ellen R. Ellis, Histologist, supervised the histology preparation with the technical assistance of Mrs. Janet L. Kliethermes.

Approved for:

MIDWEST RESEARCH INSTITUTE

W. B. House, Director
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ABSTRACT

This report summarizes the results of up to 12 months exosure to various levels of vinyl chloride (VC) and one level of vinylidene chloride (VDC), 6 hr/day, 5 days/week, in rats and mice. Exposure of rats of both sexes to 50, 250 or 1,000 ppm VC was without adverse effects through the first 7 months of exposure. Beginning with the 8th month, a number of rats died or were terminated before schedule. Hemangiosarcomas occurred in the liver and lung. Hepatic hemangiosarcomas were found in two males and 10 females exposed to 250 ppm VC and in six males and 15 females exposed to 1,000 ppm VC. Most of the rats with hemangiosarcomas in the liver also had hemangiosarcomas in the lung. Hemangiosarcomas of the lung were found in three females exposed to 250 ppm VC and four males and nine females exposued to 1,000 ppm VC. The occurrence of hemangiosarcomas in the liver and lung was both dose and time related. Additional hemangiosarcomas were found in other tissues including skin, omentum, mesentery, and mesenteric lymph nodes.

Exposure of rats to 55 ppm VDC produced few adverse effects. The weight gain of both male and female rats was less than controls during the final 3 months of exposure. Hemangiosarcomas occurred in the mesenteric lymph nodes of one male and in the skin of another male. In addition, lesions including fatty changes and nodular or disseminated vacuolization in the liver were found in VDC-exposed rats.

Exposure of mice of both sexes to 50, 250 or 1,000 ppm VC resulted in a large number of deaths and unscheduled terminations beginning with the 6th month of exposure. At the end of 12 months, only a few mice exposed to 50 ppm VC survived. Bronchiolo-alveolar adenomas, first appeared during the second month, occurred in eight males and four females exposed to 250 ppm, and 22 males and 26 females exposed to 1,000 ppm. Hepatic-hemangiosarcomas first appeared during the 6th month, occurred in three males exposed to 50 ppm, seven males and 16 females exposed to 250 ppm, and 13 males and 18 females exposed to 1,000 ppm. Hemangiosarcomas also occurred in other tissues including mammary gland, heart, skeletal muscle, gastrointestinal tract, kidney, pancreas, mesenteric lymph nodes, epididymus, testes, and mesentery. The occurrence of the hemangiosarcomas was dose and time related. Mammary gland tumors consisting of ductular adenocarcinoma, squamous and/or anaplastic cell carcinoma with metastasis to the lung, also first appeared during the 6th month, occurred in female mice exposed to all levels of VC. The incidence of these tumors was greatest in the mice exposed to the highest level and for the longest period of time. Malignant lymphomas involving various organs were found in a few mice exposed to all levels of VC.

A few tumors including bronchiolo-alevolar adenomas, hepatic hemangiosarcomas and hepatomas were found in mice exposed to VDC. Hepatic-hemangiosarcomas occurred in two males and one female. The relationship of the bronchiolo-aleveolar adenomas and hepatomas to the VDC exposure is questionable. In addition, there were a number of lesions, including microfoci of mononuclear cells, focal degeneration and necrosis, intranuclear inclusions and/or large, basophilic nuclei, in the liver.

Exposure of mice to 1,000 ppm VC or 55 ppm VDC also caused some acute deaths between the 3rd and 13th days. There was toxic hepatitis and marked tubular necrosis of the renal cortex.

I. INTRODUCTION

Under Contract No. NO1-ES-2-2084 (NIH-NIEHS-72-2084) on "Research Capability for Environmental Toxicants," we have performed various studies on the toxic effects of the two commercially available dithiocarbamates, ferbam and thiram.[1] Following completion of these studies, the inhalation toxicity of various levels of vinyl chloride (VC) was chosen for study. In addition, one level of vinylidene chloride (VDC) was also included.

Vinyl chloride was first prepared more than a century ago and its fire and explosion hazard are well known. Acute toxicity of VC was first reported in guinea pigs.[2] As a possible anesthetic agent in dogs, VC was found to cause incoordinated muscular activity of the extremities, cardiac arrhythmias[3] and sensitization of the myocardium.[4] Relatively high concentrations of VC (20-40% in air) for 30 min produced narcosis and/or death in mice, rats, and guinea pigs.[5] The guinea pigs were found to be more resistant. The main lesions were congestion of the lung, with pulmonary edema and hemorrhages, in some animals, and congestion of the liver and kidneys. Blood coagulation was also impaired. Various laboratory animals were exposed to 50, 100, 200 or 500 ppm of VC, 7 hr/day and 5 days/week, for up to 6 months.[6] A threshold limit value of 100 ppm, below which no detectable changes occurred, was suggested. A recent study indicated that rats (Ar/IRE) exposed to high concentration of VC (3% V/V in air, equal to 30,000 ppm), 4 hr/day, 5 days/week for 12 months, developed tumors of the skin, lungs, and bones.[7] Furthermore, zymbal gland carcinomas, nephroblastoma, hepatic and extrahepatic angiosarcomas were observed in rats, and pulmonary tumors, mammary carcinomas and liver angiosarcomas were observed in mice exposed to as low as 250 ppm of VC, 4 hr/day and 5 days/week for 12 months.[8] The growing suspicion that exposure to VC has caused a number of deaths of workers from a rare form of liver cancer, angiosarcoma, has alarmed the OSHA to set an emergency rule on April 5, 1974, that lowered the permissible worker exposure level to 50 ppm from the previous level of 500 ppm.

This report summarizes the final results of up to 12 months exposure to VC or VDC.

II. MATERIAL AND METHODS

A. Methods of Exposure

1. Chamber design: Five stainless steel cubical type exposure chambers of 3.5 m^3 (123 ft^3) volume were used (Figure 1). Contaminant entered the air stream and was then mixed in a plenum at the top of each chamber. Each chamber contained a diffusion plate and two small squirrel-cage fans (100 cfm, 2.85 m^3/min) mounted on opposite sides of the top cone above the diffusion plate to ensure complete mixture of the gas with air.

2. Chamber air supply and flow rates: The air supply to the chambers was drawn from a stack on the roof of the building. Chamber air passed through a coarse filter and then over coils for heating, cooling, and dehumidifying. The air then passed through an absolute filter (99.97-99.99% retention of 0.3 μ particles) into the plenum of the chamber.

Initially, air flow rates were measured at the inlet side of the chamber with a pitot tube connected to a magnahelix gauge. Subsequently, critical orifice plates were installed on the chamber outlet exhaust syst Air flow rates were then measured with an air flow transducer (Autotronics 100-SSX). The readings obtained with the critical orifice plates were greater than those obtained with the pitot tube. The correct air flow rate is 26.4 ft^3/min (0.75 m^3/min) or approximately 13 air changes per hour.

3. Generation of VC and VDC vapor: Vinyl chloride at a purity of 99.8% was obtained from Matheson Products. It is a gas at room temperature and was metered with rotameters into the chamber air supply. VDC with a purity of 99% was obtained from the Aldrich Company. Its boiling point is 32°C (89.6°F) and was heated to 37°C (98.6°F) to generate the gas. All gas lines and the rotameter were heated to 40°C (104°F) to prevent condensation.

4. Chamber atmosphere monitoring: Chamber concentrations were monitored using a gas chromatograph (Varian-2700) with a flame ionization detector. A 6 ft x 1/8 in. stainless steel column packed with 0.4% Carbowax 1500 on Carbopak A was used with a nitrogen carrier flow rate of 80 ml/min. The injection, column, and detector temperatures were 135°C, 65°C and 170°C, respectively.

5. Standards: VC standards at dilutions of 10, 50 and 100 ppm were obtained in lecture bottles from Supelco, Inc., Bellefonte, Pennsylvania. VC standard gas at a concentration of 1,000 ppm was obtained from Matheson Gas Products, Joliet, Illinois.

VDC standards were prepared by a serial dilution (weight/volume) of VDC in carbon tetrachloride. The desired final concentrations in a 4 μl injection were determined by the following procedure:

$$mg/\ell \ (\mu g/ml) = \frac{ppm \times mw}{24,450}$$

With a molecular weight for VDC of 96.94, the final concentrations of 10, 50 and 100 ppm, the amount of VDC in a 1-ml sample from the chamber would be 0.04, 0.20 or 0.40 μg, respectively. For 1 μl of standard, these same amounts would be obtained from solutions of 40, 200 and 400 mg/liter; but since 4 μl of standard were injected, the final dilutions of VDC in carbon tetrachloride were 10, 50 and 100 mg/liter.

All liquids were injected at a volume of 4 μl and all gases at 1 ml. Standards at each point on the calibration curve were injected in triplicate.

6. Chamber sampling: Each chamber was fitted with 10 sampling ports on two sides of the chamber. During preliminary studies, a series of distribution studies were made to determine the uniformity of the test material in the chamber. These tests were made with three sampling lines of polyethylene capillary tubing, of varying lengths, passed through each sampling port. It was determined that a valid measure of chamber contaminant distribution could be obtained by sampling periodically through three positions and occasionally through nine positions (Figure 2). Samples were withdrawn from the chamber with the same syringe used to introduce the sample to the gas chromatograph. Tests indicated that a valid sample could be withdrawn by pumping the syringe three times on the short sampling lines, and five times on the longest line.

All sampling was done in triplicate. During the first 3 months, distribution studies were compared with a reference point in the center of the chamber. The results showed that average chamber concentrations were ± 3% of the desired concentration; the reference point averages were 98.4% to 100.4% of these chamber averages.

At a later point in the study, the manual sampling system was replaced by an automatic sampling system. The sampling system consisted of 1/4 in. teflon lines that were placed at the reference point in the chambers (see Figure 2). The teflon lines, which were purged with chamber atmosphere continuously, then ran through a series of sampling valves. Samples were injected through twin 1-ml sampling loops which were allowed to reach equilibrium before the sample was injected. The sampling sequence was controlled by a Varian CDS-111® chromatography data system. The concentrations were determined by integration of peak areas by the CDS-111®. The CDS-111® was calibrated each morning with VC and VDC standards.

The average weekly concentrations and the range of all samples for VC are shown in Figure 3. The weekly variations for the average chamber concentration of VC did not vary more than ± 5% from the desired values. With a few exceptions, the range of individual samples did not vary more than ± 10% from the desired concentration.

At the beginning of testing with VDC, it was planned that the exposure level would be 50 ppm. Due to technical problems with the standards. the objective of 50 ppm was not achieved. These problems were associated with the use of chloroform as the solvent during the first 4 weeks, which was subsequently changed to carbon tetrachloride, and a nonlinear calibration curve during the 5th through the 10th week. By the 11th week, these problems had been solved and the slightly higher exposure level of 55 ppm was obtained.

The average weekly concentrations of VDC are shown in Figure 4, as well as the range of individual samples. Due to the problems discussed above, the analytical concentration during the first 10 weeks is not precisely known. Since air flow rates have been constant throughout, we can calculate the nominal concentration using the amount of VDC used each day. This has been done (Figure 4) for the 4th through the 10th week. However, the material balance was not recorded during the first 3 weeks. Therefore, we have estimated the average concentration during the first 3 weeks by replicating all magnahelic and rotameter settings, which were known, and measuring the chamber concentration. By this method, we estimate the average concentration during the first 3 weeks to be 30, 80 and 95 ppm. The average chamber concentrations from the 11th week on were generally within ± 5% of the desired 55 ppm VDC. Exceptions to this were weeks 27, 28, 44 and 45. The range of individual samples was within ± 15% of the desired 55 ppm VDC.

B. Safety

All chambers were operated with a slight negative pressure (0.1-0.2 in. water) to prevent escape of contaminant through leaks into the room. Before opening, chambers were flushed with clean air for a minimum of 30 min. Sampling from the chambers and from the doorway upon opening always showed less than 1 ppm of contaminant. In addition, after operating for 30 min without contaminant, on one occasion, the air supply and exhaust were shut off to the 1,000 ppm chamber for 10 min. Thus, the animals sat in a static environment and any off-gassing would be allowed to accumulate. Samples taken from the chamber after the 10-min period showed less than 1 ppm of VC in the air.

Additional samples from doorways and numerous other places in the area were collected on charcoal tubes and by grab sampling with a syringe. All samples showed less than 1 ppm of VC. Room monitoring for VC and VDC was performed on a routine basis by grab samples with a syringe and analysis with the gas chromatograph used for chamber monitoring.

During all initial work, personnel wore impervious coveralls, gloves, and a demand type face mask when the chambers were opened for transfer of animals to holding racks. This practice was discontinued only after extensive sampling had shown that exposure to more than 1 ppm did not occur.

All air from the chambers travels under negative pressure to an incinerator outside the building. Integrated bag samples of stack gas were collected on January 12 and 13, 1976. These samples were collected according to Method 106, "Determination of Vinyl Chloride from Stationary Sources," Federal Register, Vol. 40, No. 248, December 24, 1975. This method involves pulling a sample of stack gas into a leak proof Tedlar bag with a vacuum pump set at a flow rate of 500 cc/min for a 1-hr period. The sample site was determined by cutting a hole in the stack wall at two duct diameters downstream from the flame.

Two tests were conducted on January 12, while three chambers operated at a combined level of 1,300 ppm of VC; and one chamber was operated at 55 ppm of VDC. An additional three chambers operated with only clean air. Test one, analyzed at the inhalation facility, showed 39 to 40 ppm of VC. Test two showed 38.5 to 39 ppm of VC. To check these values, a sample was drawn by syringe directly from the stack. This sample contained 29 ppm of VC. VDC was never detected.

On January 13, a third test was conducted and showed 38 ppm of VC. Samples from the third test were taken to the Environmental Measurements Section at MRI. After setting overnight, the average of 6 peaks equalled 29 ppm of VC. This lower value could be due to loss of VC through absorption in the Tedlar bag, or due to loss through the used septum.

During all three tests, the burner of the incinerator operated at 1700 to 1800°F. Subsequent tests at higher or lower temperatures did not lower the VC.

C. Animals

1. Species and number: Albino CD® rats and albino Swiss mice (Charles River Breeding Laboratory), about 2 months old at the start, were used in these studies. They were acclimated in our holding quarters for 1 week before the experiment began. For each species, a total of 360 animals were divided into five groups, each consisting of 36 males and 36 females.

2. Animal housing: All animals lived in the same stainless steel cages during exposure and outside of the chambers. Rats were housed two per cage and mice six to eight per cage. Powdered or block laboratory chow (Wayne Manufacturing Company) was provided at all times except during the 6-hr period of exposure each day. Water was available ad libitum.

The temperature in the chamber and in the room averaged 24 ± 1.3°C (75 ± 5°F). The relative humidity in the chambers ranged from 25 to 60%; in the room it also ranged from 25 to 60%, but was regulated at 45 ± 5% after the 6th month. A 12-hr light cycle was maintained at all times.

When out of the chambers, the animals were placed in holding racks similar to those in Figure 1. A continuous supply of room air was drawn over the cages while in the holding racks. Provisions were made for covering the front of each compartment in the holding rack in the event of significant off-gassing from the animals. This was found not to be necessary with VC or VDC.

3. Animal hygiene: All cages and feeders were washed and sanitized each week. The floors of the room, the holding racks, and the interior of the chambers were frequently washed with disinfectant. Animal caretakers wore gloves and surgical masks when handling animals.

It was found that when the cages were loaded into the chambers without drop-pans (so not to impair air flow) the animals on the bottom shelves were frequently drenched with urine and water. In order to alleviate this problem, the cages were loaded into the chambers with clean drop pans in place. Sampling studies showed that the vapor distribution was actually improved slightly. Thus, from the 6th month on, drop pans were washed daily and a clean drop pan without bedding was inserted into each cage before loading into the chamber.

D. Experimental Protocol

1. Experimental design: A total of five chambers were used. Each chamber held one group of 72 rats and one group of 72 mice. Animals in the chambers were exposed at 6 hr/day and 5 days/week to the following:

Chamber 1: Uncontaminated air
Chamber 2: 50 ppm of VC
Chamber 3: 250 ppm of VC
Chamber 4: 1,000 ppm of VC
Chamber 5: 55 ppm of VDC

Four animals of each species, sex and exposure level, were terminated for various studies, necropsy, and histopathology at the end of 1, 2, 3, 6 and 9 months. At the conclusion of 12 months exposure, all remaining animals were terminated. Moribund animals were terminated as required. All terminated animals were replaced in the respective chambers at periodic intervals. The replacement animals are exposed for 1, 3 and 6 months for mice and 1, 3, 6 and 10 months for rats. At the conclusion of the exposure periods, the animals are removed from the chambers and held for 1 year for observation. At the end of 1 year, all animals will be terminated for necropsy and histopathology.

2. Observations and studies:

a. General observations and weight gain: All animals were observed throughout the study for behavioral changes and any unusual or toxic signs. Food consumption was recorded weekly and body weights biweekly at a uniform time of the day. Any unusual changes in weight were investigated. An attempt was made to determine the cause when any unscheduled death occurred.

b. Hematology and clinical blood chemistry: Aortic blood from males and females of each group of each species was collected under anesthesia (sodium pentobarbital for rats and ether for mice) at each termination period. Hematology (various blood counts, hematocrit, hemoglobin, methemoglobin and Heinz bodies) and clinical blood chemistry (fasting blood glucose, SGOT, SGPT, alkaline phosphatase, BUN, creatinine and/or LDH) were performed on all samples. The procedures for these tests and the normal values for rats are given in Appendix I. In addition, the following tests were also performed for rats.

(1) Prothrombin time: The prothrombin time was measured by the one-step method of Quick[9] using the Fibro System (BBL) with activated thromboplastin (Dade). Standardized Normal Plasma (Dade) was used as the control for each assay.

(2) Bilirubin: Total and direct bilirubin was measured using the Billi-Strate Kit (General Diagnostics) which is based on a modified Jendrassik-Grof method.[10] Moni-Trol I, Versatol (General Diagnostics), and Calibrate I (General Diagnostics) was used as the reference for each assay.

c. Serum immunoglobins: Serum immunoglobins were measured in four male and four female rats from the control, 1,000 ppm of VC, or 55 ppm of VDC groups. The radial immunodiffusion technique of Mancini et al.,[11] was used to assay immunoglobin groups IgA, IgG, subgroups A and B, and IgM.

A replicate serum sample from each rat was placed in wells in an immunodiffusion chamber along with a standard, and held until the precipitin ring reached equilibrium. The square root of the diameter of the precipitan ring is directly proportional to the concentration of antibody.

d. Serum protein:

(1) Total protein: Total protein was measured by the biuret method of Kingsley.[12] Standard Human Protein (Dade) was used as the standard for each assay.

(2) Albumin: Albumin was measured by the Albu-Strate Kit (General Diagnostics) which is based on the bromcresol green method of Doumas et al.,[13] Lab-Trol (Dade) and Calibrate I was used as the reference for each assay.

(3) Globulin: Globulin was calculated by the difference of total protein and albumin.

e. Pulmonary macrophages: Four males and four females of each species from the control, 1,000 ppm of VC, or 55 ppm of VDC groups were used for the pulmonary macrophage count.

At the time of necropsy, the left lung was removed at the bifurcation of the trachea; a small needle was inserted into the bronchus; and 5 ml of the sterile saline was gently flushed into the lungs of rats and 0.5 ml in the lungs of mice. The fluid was withdrawn and flushed again several times. This fluid was then transferred from the syringe to a glass tube and stained. The number of cells in the preparation was counted under a microscope with a differentiation made between macrophages and leukocytes. If changes were observed in lungs from animals exposed to 1,000 ppm of VC, then animals from the groups exposed to 250 or 50 ppm were also examined.

f. Cytogenetic analysis: Bone marrow samples were collected from four males and four females of each species from the control, 1,000 ppm of VC, or 55 ppm of VDC groups. Short-term bone marrow cultures were made according to the methods of Tjio and Wang.[14] After allowing approximately 5 hr for sufficient members of cells to be arrested in metaphase, the cells were collected, swollen in hypotonic saline, and processed for spreading on glass slides according to the method of Moorhead and Norwell.[15] Slides were then stained with giesma and scanned under low power optics. Those slides showing a minimum scattering of cells in metaphase were selected for chromosomal analysis using oil immersion optics. Estimation of cell polyploidy was obtained by rough chromosomal estimates of at least 200 cells. Exact chromosomal counts and chromosomal aberration estimates were determined for at least 50 metaphase spreads. Special attention was given to chromosomal damage such as breaks, gaps, and translocations.

g. Examination of bones: At the time of scheduled necropsies, the hind limbs from both species were excised and fixed in formalin. After fixation, the limbs were wrapped in plastic and frozen for storage. Following the 12 months terminations, limbs were examined for evidence of osteolysis or other changes.

The limbs were examined using a senograph X-ray machine set at 10 mA, 0.4 sec and 22 KVP with a large mammographic cone and focal film distance of 37 cm. The specimens were radiographed with Kodak MIN-R film. The radiographs were then viewed as unknowns and evaluated for any radiographically discernable differences between groups. They were examined for the presence of any bone tumors, any changes in bone density, cortical thickness or striations within the bone cortex, any loss of bone cortex in terms of total width and/or subperiosteal or endosteal erosion, or any unusually widened, narrowed or distorted trabecular pattern of the bone.

h. Necropsy and histopathology: When moribund or at the end of each termination period, males and females from all groups were euthanized for necropsy after the collection of blood. Gross examination of all tissues, especially for any appearance of abnormal growth or other lesions, were carefully performed. The brain, liver, kidney, spleen and gonads were removed and weighed. Portions of these and other tissues were fixed, processed, sectioned and stained for microscopic examination. The procedures are given in Appendix I.

3. Statistical analysis: The results of the various parameters were compared with the control groups at the respective time intervals, whenever applicable, according to the Dunnett's Multiple Comparison Procedures.[16]

4. Special studies:

a. Thymidine incorporation into DNA: Male mice were exposed to 50 ppm VC for 43 to 45 weeks as previously described. On the day following the last exposure, mice were injected with 100 μCi/kg of thymidine [2-^{14}C] from New England Nuclear (Boston, Massachusetts). One hour following the injection of ^{14}C-thymidine, mice were sacrificed by cervical dislocation and the liver was removed and weighed. A portion of the liver (2-300 mg) was saved for histopathological examination while the remaining portion (>1.3 g) was homogenized in 5 ml of cold water. Macro-molecules were precipitated by the addition of 5 ml of 1 N perchloric acid (PCA). The resulting precipitate was washed with successive 5 ml portions of 0.2 N PCA, 0.2 N PCA, 95% ethanol saturated with sodium acetate, ethanol:ether (3:1). The precipitate was dissolved in 4 ml of 0.3 N sodium hydroxide and heated for 1 hr at 37°C. The mixture was acidified by the addition of 1.8 ml of 50% trichloroacetic acid (TCA). The precipitate was washed twice with 5 ml of 5% TCA and heated at 90°C for 20 min in 5 ml of

5% TCA. The supernatant was saved and the precipitate was heated again in 5% TCA. This supernatant was saved and combined with the previous supernatant. Aliquots of the hot acid extract were used for liquid scintillation counting and DNA determination.[17] The results were expressed as DPM/mg DNA and mg DNA/g liver.

b. δ-Aminolevulinic acid synthetase (ALAS) and urinary aminolevulinic acid (ALA) assays: Rats were exposed to various concentrations of VC for 6 hr a day, 5 days a week for 12 months. The ALAS assay described by Woods[18] was used in this study. Basically the method involves the preparation of a mitochondrial fraction from homogenates of rat liver and the incubation of 0.5 ml of this fraction with 50 mM Tris-HCl buffer (pH-8.5), 10 mM $MgCl_2$, 100 mM glycine, 10 mM sodium succinate, 0.2 mM pyridoxal phosphate, 1 mM β-mercaptoethanol, 250 mM sodium chloride, 0.1 mM GTP, 5 mM EDTA, 60 μM coenzyme A, 3 mM ATP and 0.2 units of succinyl thiokinase (one unit converts 1 mole of succinate to succinyl-Co A per minute at pH 7.4 at 30°C) for a final volume of 2.5 ml. All reactions were conducted at 37°C for 1 hr in room air. Reactions were terminated with 0.5 ml of 10% TCA. ALA was converted to the pyrole derivative and quantified with modified Ehrlich's Reagent using a molar extinction coefficient of 5.3×10^4 as previously described.[18] Proteins in the mitochondrial fraction were quantified by the method of Lowry et al.[19]

The Bio-Rad Urinary ALA Test Units (Bio-Rad Laboratories, Richmond, California) were used in this study. The assay is based on the method described by Davis.[20] Basically, the method involves separating ALA from porphobilinogen on ion-exchange columns, eluting the ALA from the column, and producing a pyrole derivative of ALA which is detected with Ehrlich's Reagent. Urine was collected overnight from rats housed in metabolism cages with free access to feed and water.

c. Alpha-fetoprotein assay: Serum samples from selected rats and mice were retained for assay of alpha-fetoprotein levels.[21] The assays of alpha-fetoprotein were performed by Dr. Stewart Sell, Department of Pathology, School of Medicine, University of California at San Diego, LaJolla, California.

d. Dominant lethal study: Groups of male rats that were in the 11th and 12th week of exposure to VC or VDC were used in this study. In the evenings following exposure, each male was housed overnight with two nonexposed virgin female CD® rats. This procedure was followed for seven successive evenings or until a male mated with two females. All females were examined in the morning for evidence of mating. On gestational day 13, females were sacrificed and the number of corpora lutea and implants (viable and dead) determined.

III. RESULTS

A. Rats

1. General observations and weight gain: Rats were exposed to VC or VDC, 6 hr/day, 5 days/week, for periods of 1, 2, 3, 6, 9 or 12 months. During these periods, these rats were exposed for a total of 22, 41, 61, 131, 196 or 259 days, respectively. All groups of rats gained weight and appeared to be in good health until the final 1 to 2 months of exposure. The body weights of the control rats and rats exposed to 1,000 ppm VC or 55 ppm VDC are shown in Figure 5. During most of the exposure, the body weights of the control rats and rats exposed to VC or VDC were comparable. However, the body weights of the males and females exposed to 1,000 ppm VC decreased as compared to controls after 43 weeks of exposure in the females and after 49 weeks of exposure in the males. The body weights of the males and females exposed to 55 ppm VDC were less than those of controls during the final 3 months of exposure. Although not shown in Figure 5, the body weights of the male and female rats exposed to 50 or 250 ppm VC were comparable to controls. The final 1 to 2 months of exposure to VC was marked by a substantial number of terminations, due to ill health and deaths. These terminations and deaths occurred primarily in the 250 and 1,000 ppm VC exposed groups.

2. Laboratory data: The results of hematology, clinical blood chemistry, serum immunoglobins, serum proteins, and macrophage counts in the lungs of male and female rats after exposure to VC or VDC for 1, 2, 3, 6, 9 or 12 months are summarized in Tables 1 through 12. At each of the periods of observation, the peripheral blood elements and clinical chemistry values were within normal ranges for rats observed in our laboratory as shown in Appendix I. When compared with control rats, there were a number of occasional differences at each observation period. However, these differences do not appear to be related to the VC or VDC exposures.

At the end of 1 month, in the male rats (Table 1) the SGOT level was lower and the alkaline phosphatase level was higher in the group exposed to 50 ppm VC, and the direct bilirubin concentration was higher in the group exposed to 250 ppm VC or 55 ppm VDC. In the female rats (Table 2), the leukocyte counts, creatinine concentration and total protein were higher in the group exposed to 55 ppm VDC.

At the end of 2 months, in the male rats (Table 3), the leukocyte count was higher in the group exposed to 50 ppm VC, the B factor of immunoglobin G was lower in the group exposed to 1,000 ppm VC, and the reticulocyte count was higher and the hematocrit was lower in the group exposed to 55 ppm VDC. SGOT levels were lower in all groups exposed to VC as well as VDC. SGPT levels were lower in the groups exposed to 250 ppm VC or 55 ppm

VDC. The lactic dehydrogenase (LDH) and alpha-hydroxybutyrate dehydrogenase (alpha-HBDH) levels were lower in all groups exposed to VC. In the female rats (Table 4), the percentage of reticulocytes was higher in the group exposed to 250 ppm VC.

At the end of 3 months, the prothrombin time in male rats exposed to 1,000 ppm VC and immunoglobin A and the A factor of immunoglobin G in males exposed to 55 ppm VDC were lower than controls (Table 5). In the female rats (Table 6), the pulmonary macrophage counts of the group exposed to 1,000 ppm VC or 55 ppm VDC, the hemoglobin, mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCHb) indices, and the immunoglobin A of the group exposed to 55 ppm VDC were lower than the respective controls.

At the end of 6 months, the prothrombin time of the male rats exposed to 250 ppm VC and the serum immunoglobin M level of the males exposed to 55 ppm VDC were lower, and the creatinine level of the males exposed to 1,000 ppm VC was higher than controls (Table 7). In the female rats (Table 8), the MCHbC index and the serum albumin level was higher in the group exposed to 50 ppm VC; the MCHb index was higher in the group exposed to 1,000 ppm VC, the hemoglobin and the immunoglobin M levels were lower and the immunoglobin A level was higher in the group exposed to 55 ppm VDC than the respective controls.

At the end of 9 months, the LDH and α-HBDH levels of male rats exposed to all levels of VC were lower than controls (Table 9). In addition, the percentage of monocytes were lower and the SGOT level was higher in males exposed to 50 ppm VC or 55 ppm VDC; the erythrocyte count and serum immunoglobin M level were lower, and the MCV and MCHb indices were higher in males exposed to 55 ppm VDC than in controls. There were no significant changes in female rats exposed to VC or VDC for 9 months (Table 10).

At the end of 12 months, the LDH and/or α-HBDH levels was lower in male rats exposed to 50 or 250 ppm VC (Table 11). The serum immunoglobin A and/or M was lower in males exposed to 1,000 ppm VC or 55 ppm VDC. In the female rats (Table 12), increases in percentage of reticulocytes, leukocyte count, SGOT, SGPT, alkaline phosphatase levels and pulmonary macrophage count occurred in the group exposed to 1,000 ppm VC. However, the measurements were performed in only two females and the increases were due to the extremely high values found in one of these rats (No. 275).

3. Cytogenetic analysis: Bone marrow cultures were prepared from both sexes of control rats and rats exposed to 1,000 ppm VC or 55 ppm VDC at each termination period. The results of these studies are presented in Tables 13 and 14. The bone marrow preparations from rats exposed to 1,000 ppm VC or 55 ppm VDC, for each of the exposure periods studied, showed no changes in chromosome frequency, distribution or number of tetraploids, or any changes in the frequency of chromatid breaks, gaps or translocations.

4. Examination of bones: X-ray examination of the hind limbs of rats terminated after 12 months exposure to VC or VDC showed no evidence of osteolysis or other abnormalities. The bones from rats terminated at earlier periods were removed, fixed and/or frozen and stored, but not examined.

5. Collagen content in liver and lung: The collagen content in the liver and lungs of control rats and rats exposed to 1,000 ppm VC or 55 ppm VDC for 6, 9 or 12 months is summarized in Tables 15 to 17. No significant changes in collagen content were found in the livers or lungs of rats exposed to 1,000 ppm VC or 55 ppm VDC for 6, 9 or 12 months.

6. Organ weights: The organ weights of male and female rats exposed to VC or VDC for 1, 2, 3, 6, 9 or 12 months are summarized in Tables 18 to 29. At 2 months, the absolute brain weight of female rats exposed to 55 ppm VDC was statistically smaller than that of the controls although this difference was small (Table 21). At 6 months, the absolute spleen weights of male rats exposed to 1,000 ppm VC or 55 ppm VDC were smaller than controls (Table 24). Based on brain weight, however, the difference was not significant. The absolute brain weight of females exposed to 55 ppm VDC for 6 months was smaller than control values (Table 25). At 12 months, the absolute liver weight and liver weight relative to brain weight were both significantly higher in female rats exposed to 1,000 ppm VC (Table 29). However, there were only two rats in this group and the increase was due to one of the rats (No. 275) which had a hepatic hemangiosarcoma. With the exception of the changes just noted, there were no other differences in organ weights at any of the observation times.

7. Gross and microscopic examination of tissues:

a. Gross changes: Gross examination of rats exposed to VC or VDC for 1, 2, 3 or 6 months revealed no remarkable lesions or tumors. Beginning about the end of the 8th month, a number of rats died or were terminated before scheduled because of ill health. The number of deaths and early terminations increased sharply during the final 3 months of exposure. Gross examination of rats exposed to VC terminated after 9 or 12 months or terminated before scheduled showed a number of lesions. The livers from these rats appeared mottled, with spots ranging from pin-head size to several millimeters in diameter or had small white, tan or red nodules in the liver. Lungs obtained from numerous rats also had a red mottled appearance. In addition, some subcutaneous tumors ranging in size from 2 to 5.5 cm and greyish white to dark in color were noted.

b. Tumors in rats exposed to VC or VDC: Microscopic examination of tissues showed a number of tumors. The tumor occurrence in rats exposed 7 to 9 months and 10 to 12 months are summarized in Tables 30 to 32. The cumulative incidence of all tumors is summarized in Table 33. The only tumor found in control rats was a ductular adenocarcinoma in the mammary gland in one female control.

The most prevalent tumors found in rats exposed to VC were hepatic and pulmonary hemangiosarcoma. Hepatic hemangiosarcoma occurred in two females exposed to 250 ppm VC and four females exposed to 1,000 ppm VC during the 35th through 39th weeks (Table 30). An additional two males and eight females exposed to 250 ppm and six males and 11 females exposed to 1,000 ppm developed hemangiosarcoma during the 40th through 52nd weeks (Tables 31 and 32). Most of these rats also developed hemangiosarcoma in the lung. Pulmonary hemangiosarcoma occurred in one female exposed to 250 ppm and one female exposed to 1,000 ppm during the 39th week (Table 30). An additional two females exposed to 250 ppm and four males and eight females exposed to 1,000 ppm developed pulmonary hemangiosarcoma during the 43rd through 52nd weeks (Tables 31 and 32). No hemangiosarcoma was found in the liver or lung of rats exposed to 50 ppm VC or 55 ppm VDC. Hemangiosarcoma occurred occasionally in other tissues also (Tables 30-32). These included one rat (subcutaneous) exposed to 50 ppm VC, two rats (omentum or mesentery) exposed to 250 ppm, five rats (omentum or mesentery) exposed to 1,000 ppm, and two rats (subcutaneous or mesenteric lymph nodes) exposed to 55 ppm VDC.

Malignant lymphoma occurred in one female exposed to 250 ppm VC for 52 weeks, one male exposed to 1,000 ppm VC for 52 weeks and in two females exposed to 1,000 ppm VC for 47 to 49 weeks. The malignant lymphoma in the male (No. 242, Table 32) exposed to 1,000 ppm VC was widely disseminated being found in adrenal, heart, lung, liver, mesenteric lymph nodes, spleen, kidney, intestine, prostate and pancreas. The malignant lymphomas found in the other rats appeared to be confined to the spleen. Other tumors which occurred in one or several rats were bronchiolar adenoma and squamous cell carcinoma of the lung; reticuloendothelial cell carcinoma and hepatoma in the liver; ductular adenocarcinoma and fibroadenoma in the mammary gland; renal adenoma; hemangioma of the adrenal gland; squamous cell carcinoma, keratocanthoma or fibroma in the skin; adenocarcinoma in the sebaceous gland; and chromophobe cell adenoma in the pituitary (Table 33). These occasional tumors were not related to VC or VDC.

c. Other lesions: There were a number of spontaneous or incidental lesions in various tissues of control rats and rats exposed to VC or VDC for various lengths of time (Tables 34-39). These lesions were not related to VC or VDC. However, there were a few lesions in the livers of rats exposed to 55 ppm VDC. These lesions included fatty changes in the liver after exposure for 6 and 9 months (Tables 37 and 38) and nodular or disseminated vacuolization after exposure for 12 months (Table 39). Generally, these lesions were more severe and the incidence was greater than in control rats.

The myeloid/erythroid (M/E) ratios of the rib bone marrow smears of control rats and rats exposed to VC or VDC were within normal limits at all time periods examined (Tables 34-39).

B. Mice

1. General observations and weight gain: The mice were exposed to VC or VDC, 6 hr/day, 5 days/week, for periods of 1, 2, 3, 6, 9 or 12 months. During these periods, these mice were exposed for a total of 19, 39, 59, 128, 193 or 256 days, respectively. There were five early deaths, apparently due to the acute effect of the test compounds. Two male and one female mice exposed to the highest level of VC were found dead between the 3rd and 9th days of exposure; two males exposed to VDC died on the 13th day. They were replaced with healthy mice from the same shipment for the remainder of the experiment. Thereafter, all mice appeared in good health.

During the 6th month of exposure, the health of a few mice exposed to various levels of VC deteriorated. The clinical signs included rough hair coat, lethargy, anorexia and rapid weight loss. They died or were terminated before their imminent death. During the 7th through the 9th months, the general health of the mice worsened. Additional clinical signs were abdominal distention and/or the appearance of external tumor masses, especially mammary tumors in the females. There were a large number of deaths or unscheduled terminations, proportional to exposure VC levels. By the end of the 9th month, all males and females in the group exposed to 1,000 ppm and all females exposed to 250 ppm died or were terminated. By the end of 12 months, only the controls and a few mice exposed to 50 ppm VC had survived. In contrast, only a few deaths or early terminations occurred in the VDC exposed group. The number of deaths and early terminations during the final 6 months of exposure is shown in Table 40.

The average weight gains of the mice exposed to 1,000 ppm VC or 55 ppm VDC are shown in Figure 6. The weight gains of these mice were comparable to controls through the 35th week of exposure. The weight gain of the male mice exposed to 1,000 ppm VC began to decline at week 36 and remained less than controls through week 39. The body weights of the females exposed to 1,000 ppm VC followed this same pattern although the weight loss during weeks 37 and 38 was exaggerated since only one or two animals remained in the group. The body weights of the mice exposed to 55 ppm VDC remained similar to those of controls although during the period of weeks 46 through 51 the weights were less than the controls. The body weights of the mice exposed to 50 and 250 ppm VC, although not shown in Figure 6, were similar to that of the controls throughout the exposure period.

2. Laboratory data: The results of hematology, clinical blood chemistry, and pulmonary macrophage counts in male and female mice exposed to VC or VDC for 1, 2, 3, 6, 9 or 12 months are summarized in Tables 41 to 52. At each of the observation periods, the peripheral blood elements and clinical blood chemistry values were within normal ranges. When compared with control mice, there were some occasional differences at the respective observation period. However, these differences were small and not seen consistently.

At the end of 1 month, the MCV index of male mice exposed to 50 ppm VC, the MCHb index of male mice exposed to 250 ppm VC, and the SGPT level of male mice exposed to 55 ppm VDC were higher than controls (Table 41). At the end of 2 months, the percentage of eosinophils of male mice exposed to 50 ppm VC, the reticulocyte count and BUN levels of female mice exposed to 55 ppm VDC were higher, and the BUN levels of male mice at all levels of VC were lower than controls (Tables 43 and 44). At the end of 3 months, statistical difference was not found between any values of the control and the exposed mice (Tables 45 and 46). At the end of 6 months, the male mice exposed to 1,000 ppm VC had lower hematocrit and hemoglobin concentration; the percentage of neutrophils of these mice was higher with a corresponding lower percentage of lymphocytes (Table 47). At the end of 6 months, the pulmonary macrophage counts of male and female mice exposed to 1,000 ppm VC, were higher than controls (Tables 47 and 48). At the end of 9 months, the pulmonary macrophage count of male mice exposed to 1,000 ppm VC was higher than controls (Table 49). In female mice exposed to 2 or 1,000 ppm VC (Table 50), there were several differences as compared to the controls. However, only one animal was examined in each group and no statistical comparison was made. At the end of 12 months, the SGPT and BUN levels of male mice exposed to 55 ppm VDC were higher than controls (Table 51). In female mice exposed to 55 ppm VDC (Table 52), the percentage of reticulocytes and BUN level were higher than controls and the percentag of monocytes was lower than controls.

3. Cytogenetic analysis: Bone marrow cultures were prepared from both sexes of control mice and mice exposed to 1,000 ppm VC or 55 ppm VDC at each termination period. The results of these studies are summarized in Tables 53 and 54. The bone marrow preparations from mice exposed to 1,000 ppm VC or 55 ppm VDC showed no changes in chromosome frequency, distribution or number of tetraploids, or any changes in the frequency of chromatid breaks, gaps or translocations.

4. Examination of bones: X-ray examination of the hind limbs from mice exposed to VC or VDC for 12 months or from those terminated before schedule showed no evidence of osteolysis or other abnormalities. The hind limbs of mice exposed to VC or VDC for 9 months or less were removed, fixed and/or frozen and stored, but not examined.

5. Organ weights: The organ weights of mice exposed to VC or VDC for 1, 2, 3, 6, 9 or 12 months are summarized in Tables 55 to 66. At 1 month, the absolute brain weight in male mice exposed to all levels of VC and VDC and the absolute spleen weight in male mice exposed to 55 ppm VDC were significantly lower than controls (Table 55). The relative spleen to brain weight in female mice exposed to 250 ppm VC for 2 months (Table 58) and the relative spleen and testes weight in male mice exposed to 50 ppm VC for 3 months (Table 59) were statistically larger than controls. At 9 months, the brain weights of male mice exposed to 50 ppm VC or 55 ppm VDC and the testes weights of male mice exposed to 50 or 1,000 ppm VC were smaller than the respective controls (Table 63). No significant changes in organ weights were seen in female mice at 9 months. However, the one female survivor at 9 months exposed to 250 ppm VC had a greatly enlarged liver and spleen (Table 64). Histopathologic examination showed that this mouse had a hepatic hemangiosarcoma and lymphoid hyperplasia of the spleen. At 12 months, the absolute kidney weight and the kidney weight relative to brain weight in male mice exposed to 55 ppm VDC were significantly smaller than controls (Table 65). In female mice exposed to 55 ppm VDC for 12 months, the absolute liver weight and liver and spleen weights relative to brain weight were significantly larger than the respective controls (Table 66). No significant change was seen in any mice exposed to 50 ppm VC and no mice exposed to 250 or 1,000 ppm VC survived for 12 months.

6. Gross and microscopic examination of tissues:

a. Early deaths: Microscopic examination revealed a number of lesions in the five unscheduled deaths (two males and one female exposed to 1,000 VC for 3 to 9 days, and two males exposed to 55 ppm VDC for 13 days). These lesions included acute toxic hepatitis, characterized by focal to marked congestion, and marked diffuse coagulation type necrosis of hepatocytes beginning in the centrilobular region of the liver. Marked tubular necrosis characterized by pyknosis and eosinophilic granulation of the cytoplasm in the renal cortex was also observed. One mouse had R-E cells and lymphoid hyperplasia and a number of megakaryocytes in the spleen.

b. Gross changes in later deaths and unscheduled terminations: Mice that died or were terminated before schedule were generally in poor nutritional condition with little or no fat deposits. A number of lesions were noted in these mice as well as those terminated as scheduled. These lesions included small, raised tan to grey nodules varying from pinhead size to 0.5 cm in diameter, and small dark hemorrhagic spots from petechiae to 1 cm in diameter in the lung. Small, dark nodular masses in the liver as well as internal hemorrhage into the abdominal cavity were observed in some of the mice. Most of the livers were moderately to severely mottled in appearance. The mammary tumors found were of varying size and were greyish white to dark red in color.

c. Tumors in mice exposed to VC: Microscopic examination of the mice that died or were terminated, both scheduled and unscheduled, revealed a variety of tumors. The tumor occurrence during 1 to 3 months, 4 to 6 months, 7 to 9 months, and 10 to 12 months are summarized in Tables 67 to 72. The cumulative incidence of all tumors is summarized in Table 73.

Bronchiolo-alveolar adenomas in mice first occurred during the 2nd month of exposure (Table 67). At this time, one male and two females exposed to 1,000 ppm and one male exposed to 250 ppm were found to have bronchiolo-alveolar adenomas. After 3 months exposure, one male at 50 ppm, one male at 250 ppm, and two males and one female at 1,000 ppm were found to have bronchiolo-alveolar adenomas. Between 4 and 6 months, two males at 50 ppm, one male and four females at 250 ppm, and six males and four females at 1,000 ppm had bronchiolo-alveolar adenomas (Table 68). Between 7 and 9 months, two males and four females at 50 ppm, five males and eight females at 250 ppm, and 13 males and 19 females at 1,000 ppm developed this tumor (Tables 69-71). During the final 3 months of exposure, three males at 50 ppm and two males at 250 ppm were found to have bronchiolo-alveolar adenomas (Table 72). The bronchiolo-alveolar adenoma was characterized by papillary proliferation of alveolar epithelium forming small and well-demarcated, but not encapsulated, round nodules. The severity of this tumor was in direct proportion to the level of VC and length of exposure. In the more severe lesions, there was an increase in number and size of the nodules by expansion and coalescing to cause consolidation of the affected lobes of some animals. These bronchiolo-alveolar adenomas occurred in a total of eight males and four females exposed to 50 ppm, 10 males and 12 females exposed to 250 ppm, and 22 males and 26 females exposed to 1,000 ppm (Table 73). Only one control male mouse was found to have a bronchiolo-alveolar adenoma during the 9th month.

Hemangiosarcoma of the liver was first seen in mice during exposure for 4 to 6 months. Two females exposed to 250 ppm and two males and three females exposed to 1,000 ppm had hemangiosarcomas of the liver during this period (Table 68). Between 7 and 9 months, one male at 50 ppm, five males and 14 females at 250 ppm, and 11 males and 15 females at 1,000 ppm were found to have hepatic hemangiosarcomas (Tables 69-71). Between 10 and 12 months, additional hemangiosarcomas of the liver were found in two males at 50 ppm and two males at 250 ppm (Table 72). These hemangiosarcomas were characterized by mild to severe proliferation of endothelial cells lining the sinusoids, dilation of the sinusoids, focal hemorrhage forming small to large cavernous blood spaces, invasion of the hepatic parenchyma with neoplastic tissue and mild to severe necrosis. Hepatic hemangiosarcomas occurred in a total of three males exposed to 50 ppm, seven males and 16 females exposed to 250 ppm, and 13 males and 18 females exposed to 1,000 ppm (Table 73). This tumor was not found in any control mice. A few hemangiosarcomas were also found in tissues other than liver. These

tissues included the mammary gland, heart, skeletal muscle, gastrointestinal tract, kidney, pancreas, mesenteric lymph nodes, epididymus, testes, and mesentery (Table 73). The severity of hemangiosarcoma in the liver and the overall incidence in other tissues were related to the level of VC and the length of exposure.

The third major type of tumors was found in the mammary gland of the female mice exposed to VC. These tumors were composed of ductular adenocarcinoma, squamous cell carcinoma, and/or anaplastic carcinoma. Between 4 and 6 months, one and three females exposed to 250 or 1,000 ppm, respectively, had mammary gland tumors (Table 68). Between 7 and 9 months, seven, two and 10 females exposed to 50, 250 or 1,000 ppm, respectively, developed these tumors (Tables 69, 70 and 71). Between 10 and 12 months, mammary gland tumors occurred in two females exposed to 50 ppm (Table 72). No females exposed to 250 or 1,000 ppm survived during this period. The adenocarcinoma was characterized by proliferation of ductular epithelium with marked anaplastic and squamous cell metaplasia; the squamous cell carcinoma was characterized by marked proliferation of stratified squamous epithelium, marked keratinization, marked purulent inflammation and necrosis; and anaplastic carcinoma was characterized by marked proliferation of undifferentiated cells in large sheets, irregular cords and packets. These mammary gland tumors occurred in nine, three and 13 female mice exposed to 50, 250 or 1,000 ppm, respectively. Most of these mice had more than one of these different tumors in the mammary gland. These tumors were more severe in the mice exposed to higher levels of VC and in the mice that died or were terminated at a later date. In addition, the squamous and/or anaplastic cell carcinomas metastasized to the lung of a number of mice. This type of tumor was not seen in control female mice (Table 73).

Malignant lymphoma was seen in one female mouse exposed to 50 ppm during the 6th month and was characterized by marked disseminated or diffused infiltration of lympho-reticular cells in the epicardium and myocardium, perivascular and interstitial areas of the lung, liver, spleen and kidney. There was loss of splenic architecture. In addition, one male exposed to 1,000 ppm had a malignant lymphoma characterized by a large mass of lympho-reticular cells and necrotic debris, infiltrating the cervical tissue surrounding the trachea, blood vessels and esophagus. During the 9th month, two females exposed to 250 ppm and one male and three females exposed to 1,000 ppm had malignant lymphomas involving spleen, liver, lung, heart, subcutaneous tissue in the cervical area, and/or mammary gland. Malignant lymphoma was not found in any control mice or mice exposed to 55 ppm of VDC at any time. There was hemangioma, renal adenoma or skin keratocanthoma in one mouse each exposed to VC (Table 73).

d. Tumors in mice exposed to VDC: In mice exposed to 55 ppm VDC, a few small nodules of bronchiolo-alveolar adenoma occurred in one male during the 6th month, two males during the 9th month, and three males during the 12th month. Hemangiosarcoma occurred in the liver of one male during the 9th month, and one male and one female during the 12th month. One male had a hepatoma when terminated during the 9th month, one female developed a hepatoma during the 12th month. The hepatomas were characterized by a marked proliferation of hepatocytes with a loss of the lobular pattern in the liver, except for the male terminated during the 12th month. This mouse had only a tiny focus of the neoplastic cells. Hepatoma was not found in any control mice or mice exposed to any level of VC. Hepatic cell carcinoma or renal adenoma occurred in one male each exposed to VDC during the 12th month. Mammary gland tumors were not found in any mice exposed to VDC. The cumulative incidence of tumors in mice exposed to VDC is summarized in Table 73.

e. Other lesions: As seen in rats, there were a number of spontaneous or incidental lesions in various tissues of the control mice and mice exposed to VC or VDC for various lengths of time (Tables 74-79). These lesions were not related to VC or VDC. However, there were a few lesions in the liver of mice that appeared to be related to VDC. The livers of mice exposed to 55 ppm VDC for 9 or 12 months had microfoci of mononuclear cells, focal degeneration and necrosis, intranuclear inclusions and/or large basophilic nuclei (Tables 78 and 79). While these lesions also appeared in some controls, the incidence and/or severity was greater in the mice exposed to VDC. In addition, there was an increased incidence of amyloidosis in the kidney of mice exposed to VDC (Table 79).

The myeloid/erythroid (M/E) ratios of the bone marrow smears of control mice and mice exposed to VC or VDC were within normal limits at all time periods examined (Tables 74-79).

C. Special Studies

1. ^{14}C-Thymidine incorporation into DNA in mice: Histopathologic examination had revealed a moderate number of mitotic figures in the livers of some mice exposed to VC during the 9th month. The DNA synthesis was undertaken to determine if this observation could be confirmed at the biochemical level. DNA synthesis, as measured by ^{14}C-thymidine incorporation into DNA, was significantly increased in the livers of male mice exposed to 50 ppm VC for 11 months (Table 80). However, the DNA concentration, expressed as mg DNA/g of liver, was not significantly affected. Histopathologic examination of these livers used in this study did not reveal an increase in the number of mitotic figures or any evidence of neo- or preneoplastic lesions.

2. Heme synthesis in rats: A number of chemicals are known to produce porphyria in both man and animals by disrupting porphyrin metabolism.[22] To determine whether VC affects porphyrin metabolism some aspects of the heme biosynthetic pathway were studied in rats exposed to VC for 12 months. Hepatic levels of ALAS were determined since it is the rate limiting step in heme biosynthesis and the activity of ALAS is increased in drug-induced porphyria. Urinary levels of ALA were also determined because epoxides of VC may combine with essential sulhydryl groups on ALA dehydrogenase in a manner similar to lead. Inactivating this enzyme may result in an increased excretion of ALA. In addition, urinary ALA excretion, which is used to detect lead poisoning, might also be used as a monitoring system for detection of VC intoxication if heme synthesis was affected by VC.

The studies of ALAS activity in liver of rats exposed to 50 or 250 ppm VC for 12 months showed no significant effect of VC (Table 81). The ALAS activity observed in this study was about 50% of the activity previously reported by Woods.[18]

Although there was some contamination of urine samples with drinking water, the general pattern of results suggest that VC exposure does not alter the urinary excretion of ALA. The results of this study were expressed on an arbitrary scale since the low level of ALA prevented an accurate determination of ALA concentration (Table 82). After the addition of Ehrlich's Reagent, all samples produced a faint yellow to pink color while none of the samples had a distinct red color.

3. Dominant lethal studies in rats: The purpose of this study was to determine if repeated exposures to VC or VDC, for nearly 3 months, produced germinal mutations, of the dominant lethal type, in male rats. VC exposure did not significantly reduce the ratio of fertile to tested males. However, there was a reduced number of males exposed to 1,000 ppm VC that mated with two females (Table 83). In addition, there was a reduced ratio of pregnant to mated females in the groups mated with males exposed to 250 or 1,000 ppm VC or 55 ppm VDC. The mating period ranged from 7 days for the control group to 8 to 9 days for the treated groups.

Pregnancies that resulted from the mating of exposed males with unexposed females were normal in terms of corpora lutea and implants (Table 84). In these females, there was no evidence of preimplantation loss, as measured by the ratio of implants to corpora lutea, or postimplantation loss, as measured by the ratio of viable implants to total implants.

4. Alpha-fetoprotein: The appearance of an embryo-specific globulin (α-fetoprotein) in serum has been reported in adult animals and humans with primary hepatomas.[23] In order to determine whether α-fetoprotein could serve as an early indicator of hepatic hemangiosarcoma, serum or plasma

from rats and mice were assayed for α-fetoprotein levels. The serum or plasma was obtained from animals terminated at various periods as well as from a number of unscheduled terminations. Levels of α-fetoprotein from rats exposed to VC for 9 months showed no differences from controls (Table 85). In mice exposed to VC or VDC, occasional high levels of α-fetoprotein occurred (Table 86). Two (Nos. 177 and 240) of the mice with elevated α-fetoprotein levels had hepatic hemangiosarcomas and the third mouse (No. 324) had a hepatoma. However, the α-fetoprotein level of several other mice that had hepatic hemangiosarcoma was not elevated.

IV. DISCUSSION AND CONCLUSIONS

A. Rats

1. Vinyl chloride: Exposure of rats of both sexes to 50, 250 or 1,000 ppm VC was without adverse effects through 7 months of exposure. Beginning with the 8th month, a number of rats died or were terminated before schedule. These deaths and early terminations occurred primarily in the 250 and 1,000 ppm VC exposed groups.

The body weights of the male and female rats exposed to VC were comparable to controls until after 43 weeks of exposure. At this time, the weight gains of both males and females exposed to 1,000 ppm VC were less than controls. The exposure to VC did not result in any persistent changes in hematology, clinical blood chemistry, cytogenetic parameters, collagen content in liver or lung, pulmonary macrophage count or the bones of the extremities.

Histopathologic examination of rats exposed to VC for up to 12 months showed a number of tumors. The tumors found with the greatest frequency were hemangiosarcomas of the liver and lung. Hemangiosarcoma of the liver started to appear during the 9th month. It occurred in two males and 10 females exposed to 250 ppm VC and in six males and 15 females exposed to 1,000 ppm. Most rats with hepatic hemangiosarcoma also developed hemangiosarcoma in the lung. Hemangiosarcoma of the lung was found in three females exposed to 250 ppm and four males and nine females exposed to 1,000 ppm. The occurrence of these tumors is dose and time related; the occurrence in females was greater than in males. Hemangiosarcomas were also found in other tissues including skin, omentum, mesentery, and mesenteric lymph nodes.

Malignant lymphoma was found in one female rat exposed to 250 ppm VC and one male and two females exposed to 1,000 ppm VC. The occurrence of the malignant lymphomas may be related to the VC exposure. A number of spontaneous or incidental tumors were found in various tissues. These tumors occurred in one or a few rats and were not related to the exposure to VC.

2. Vinylidene chloride: Exposure of rats to 55 ppm VDC for up to 12 months had very few adverse effects. The weight gain of both males and females were less than controls during the final 3 months of exposure. No consistent changes in hematology, clinical blood chemistry, cytogenetic analysis, collagen content of liver or lung, pulmonary macrophage counts or in the bones of the extremities were found.

One male rat exposed to 55 ppm VDC was found to have a hemangiosarcoma of the mesenteric lymph nodes and another male had a hemangiosarcoma of the skin. These tumors may be related to the VDC exposure.

A few lesions occurred in the livers of rats exposed to 55 ppm VDC. Fatty changes of the liver appeared during the 9th month; nodular or disseminated vacuolization occurred during the 12th month. These lesions were more severe and the incidence was greater in rats exposed to VDC. It appears that these lesions were related to VDC.

B. Mice

1. Vinyl chloride:

a. Acute effect and general observation: Exposure to VC caused deaths of two males and one female exposed to 1,000 ppm VC between the 3rd and 9th days. Histopathology revealed acute toxic hepatitis and marked tubular necrosis of the renal cotex. Thereafter, the mice appeared to be in good health. During the 6th month, the general health of a few mice began to deteriorate. They died or were terminated. During the 7th month, the health of these mice worsened. By the end of the 9th month, all males and females exposed to 1,000 ppm VC and all females exposed to 250 ppm VC had died or were terminated before scheduled. At the conclusion of 12 months, only the controls and a few mice exposed to 50 ppm VC had survived. The clinical signs included rough hair coat, lethargy, sudden weight loss, and the development of external tumor masses and/or abdominal distensions. Nearly all of the mice that died or were terminated ahead of schedule and many of the mice terminated at the scheduled times had one or more types of tumors.

b. Bronchiolo-alveolar adenoma: Bronchiolo-alveolar adenoma was first noted in mice exposed to 250 or 1,000 ppm VC for 2 months and in mice exposed to 50 ppm VC after 3 months exposure. In the period between 3 and 12 months of exposure to VC, bronchiolo-alveolar adenomas were found in 37% of the mice exposed to 50 ppm VC, in 51% of the mice exposed to 250 ppm VC, and in 89% of the mice exposed to 1,000 ppm VC. The overall incidence and severity of the tumor was directly related to the level and length of exposure. Only one bronchiolo-alveolar adenoma was found in the control mice and this occurred in one male during the 9th month of exposure.

Bronchiolo-alveolar adenoma, bronchiolar adenoma, or pulmonary adenomatosis, in mice have been reported to occur spontaneously in aging mice, mostly over 1 year of age.[24-26] However, in our study, large numbers of mice exposed to various levels of VC developed this tumor. In addition, the tumor started to occur at a very early age and had a dose and time relationship as regard to the incidence and severity. On the other hand,

only a few small nodules of this tumor occurred in several mice treated with VDC. In addition, they occurred relatively at a later time. Its significance in these mice is questionable.

c. Hemangiosarcoma: Hemangiosarcoma of the liver first occurred in mice exposed to 250 or 1,000 ppm VC for 5 to 6 months. After the 6th month, approximately 75% of the mice examined in the 250 and 1,000 ppm VC exposed groups had hepatic hemangiosarcomas. The occurrence of the hepatic hemangiosarcoma appeared to be greater in the female mice than in the males. In the mice exposed to 50 ppm VC, three male mice were found to have hepatic hemangiosarcomas. In addition, hemangiosarcomas were occasionally found in other tissue including mammary gland, heart, skeletal muscle, gastrointestinal tract, kidney, pancreas, mesenteric lymph nodes, epididymis, testes and mesentery. The incidence and severity of the hemangiosarcoma in the liver and the overall incidence of hemangiosarcoma in other tissues were related to the exposure level of VC and the length of exposure. No hemangiosarcomas were found in any tissues of control mice.

d. Mammary tumors: Mammary tumors were found in females exposed to all levels of VC. The tumors consisted of ductular adenocarcinoma, squamous and anaplastic cell carcinomas. The mammary gland tumors were first found after 6 to 7 months. The incidence and severity of the tumors appeared to be greater in mice exposed to higher levels of VC and in those mice exposed for the longest periods of time. This may explain the higher incidence of mammary tumors in the group exposed to 50 ppm as compared to the group exposed to 250 ppm. All females exposed to 250 ppm had died by the end of 9 months, while many females exposed to 50 ppm survived beyond this time. This increased exposure time may thus account for the greater number of mammary tumors. As mentioned above, a number of hemangiosarcomas were found in the mammary gland. In addition, the squamous and/or anaplastic cell carcinomas of the mammary gland also metastasized to the lung. No mammary gland tumors were found in control mice or in male mice.

The pathogenesis of the mammary tumor was of a complex type. Observations of various stages and sizes of the mammary tumors suggest that the tumor originated as ductular adenocarcinoma and then in a very early stage underwent an anaplastic and squamous cell metaplasia. At this point, the tumor was quite malignant and invasive. In many cases, there was metastasis of squamous and/or anaplastic cell carcinoma to the lung. In addition, the ductular or alveolar involvement or pattern in the mammary gland, characteristic of spontaneously occurring mammary tumors in mice, was minimal except in the early stages of some small tumors. This provides further evidence that the mammary tumors are related to the VC exposure.

e. Malignant lymphoma: Malignant lymphoma was found in one female exposed to 50 ppm VC, two females exposed to 250 ppm VC, and in two males and three males exposed to 1,000 ppm VC. Generally, the lymphomas appeared to be disseminated, affecting a number of various tissues. No malignant lymphomas were found in control mice.

f. Other tumors: There were other tumors occasionally found in mice but these tumors were considered to be spontaneous and unrelated to the VC exposure.

Other observations: No consistent changes were found in mice exposed to VC when compared to controls in hematology, clinical blood chemistry, cytogenetic analysis of bone marrow cultures, or X-ray examination of bones from the extremities. The pulmonary macrophages count was elevated in mice exposed to 250 or 1,000 ppm. The mice with elevated macrophage counts also had bronchiolo-alveolar adenoma. However, not all mice with bronchiolo-alveolar adenomas had the elevation of macrophage count. The significance of this observation is not clear.

2. Vinylidene chloride: Mice exposed to 55 ppm VDC for up to 12 months were found to have some tumors including bronchiolo-alveolar adenoma, hepatic hemangiosarcoma and hepatomas. The bronchiolo-alveolar adenomas were found in six male mice. Bronchiolo-alveolar adenoma, bronchiolar adenoma or pulmonary adenomatosis has been reported to occur spontaneously in aging mice, mostly over 1 year of age.[24-26] Since most of the bronchiolo-alveolar adenomas in VDC exposed mice occurred in the late stages of exposure, the relationship of these tumors and the VDC exposure is questionable.

Hemangiosarcoma of the liver was found in two males and one female exposed to 55 ppm VDC, and is probably related to the VDC exposure. In addition, one male and one female mouse exposed to VDC developed hepatomas. The significance of this tumor and its relationship to VDC exposure is questionable. Hepatomas have been reported to occur spontaneously in small numbers in mice approximately 1 year of age.[27-29] Therefore, it is possible that the hepatomas found in this study are of a spontaneous nature since they occurred later in the study. There were no hepatomas found in control mice.

A number of other lesions also occurred in the liver of mice exposed to 55 ppm VDC. These lesions included enlarged and basophilic hepatocytes, enlarged nuclei with eosinophilic inclusions, mitotic figures or polyploidy, microfoci of mononuclear cells, focal degeneration and necrosis. It may be that these lesions are "preneoplastic" and may be related to the occurrence of hemangiosarcoma or other liver tumors. Since only a few mice developed liver tumors compared to the large number with the "preneoplastic" lesions, further study of VDC in mice utilizing additional exposure levels is needed to establish any definite relationship between the VDC exposure, the "preneoplastic" lesions, and subsequent development of neoplastic lesions in the liver.

C. Special Studies

1. ^{14}C-Thymidine incorporation into DNA in mice: An increased incorporation of ^{14}C-thymidine into liver DNA was found in male mice exposed to 50 ppm VC for approximately 11 months. Disregarding pool size considerations, this suggests that there was an increased population of dividing cells in the livers of these mice. An increased population of dividing cells could be due to either regenerative or carcinogenic processes. Due to the low incidence of hepatic tumors at 50 ppm VC, it would seem most likely that the increased thymidine incorporation into DNA is the result of regenerative processes. However, further study would be needed to confirm this observation.

As previously mentioned, the study of the thymidine incorporation into DNA was undertaken in response to the observation of the increased numbers of mitotic figures in the livers of mice exposed to VC. While increased incorporation of ^{14}C-thymidine into DNA was observed in the present study, histopathologic examination did not reveal an increased number of mitotic figures in the liver of these mice. This would indicate that biochemical changes may provide a more sensitive monitor for VC related effects than do morphological changes.

2. Heme synthesis in rats: Studies of hepatic ALAS activity in the liver and urinary levels of ALA did not show any effects related to the VC exposure. These results would indicate that VC, under the conditions of this study, does not have an effect on the heme biosynthetic pathway. However, the possibility that long-term exposure to VC may result in an adaptation to an acute effect of VC on the heme pathway should be considered.

3. Dominant lethal studies in rats: Neither preimplantation nor postimplantation losses were observed in pregnancies that resulted from the mating of VC or VDC exposed male rats. However, the occurrence of a preimplantation loss was suggested by the increased number of nonpregnant females in the groups mated with males exposed to 250 or 1,000 ppm VC and 55 ppm VDC. The relevance of this observation to the detection of a dominant lethal effect is of questionable significance for two reasons. First, there was no indication of a preimplantation loss in pregnant rats. Secondly, a postimplantation loss is more indicative of dominant lethality than a preimplantation loss. Since neither preimplantation nor postimplantation losses were observed in pregnant rats, it is concluded that the VC and VDC exposures utilized in this study did not produce dominant lethal mutations in the germinal cells of male rats.

4. Alpha-fetoprotein levels in rats and mice: The assay of α-fetoprotein levels in the serum or plasma of rats and mice does not appear to serve as a useful indicator of VC or VDC induced hepatic hemangiosarcoma. Only three mice were found to have elevated α-fetoprotein levels. Two of these mice had hepatic hemangiosarcomas and the third mouse had a hepatoma. However, an additional 10 mice with hepatic hemangiosarcoma did not have elevated α-fetoprotein levels.

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TABLE 1

LABORATORY DATA OF MALE RATS AFTER EXPOSURE TO VC OR VDC FOR 1 MONTH

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
ERYTHROCYTES ($X10^6$ /MM^3)	8.80 ± .54 (3)	7.09 ± .13	7.46 ± .04	6.04 ± .46	7.01 ± .08
RETICULOCYTES, %	.95 ± .25 (3)	1.36 ± .52	1.46 ± .07	2.30 ± 1.14	1.17 ± .10
HEMATOCRIT, VOL. %	44.0 ± .6 (3)	44.3 ± .6	45.0 ± .4	42.5 ± .9	44.3 ± .9
HEMOGLOBIN, GM. %	15.1 ± .2 (3)	15.0 ± .2	15.2 ± .1	14.4 ± .3	14.3 ± .2
MCV, CUBIC MICRONS	65.5 ± 4.9 (3)	62.4 ± 1.0	60.3 ± .7	71.7 ± 6.2	60.3 ± .9
MCHB, MICRO MICROGMS.	22.4 ± 1.6 (3)	21.2 ± .2	20.4 ± .3	24.2 ± 1.9	20.4 ± .3
MCHBC, GM %	34.2 ± .0 (3)	33.9 ± .2	33.8 ± .2	33.9 ± .4	33.8 ± .1
PLATELETS ($X10^5$ /MM^3)	7.4 ± .7 (3)	6.2 ± .8	8.2 ± .8	8.7 ± 1.1	5.2 ± .6
LEUKOCYTES ($X10^3$ /MM^3)	8.7 ± .4 (3)	11.6 ± 1.5	9.0 ± .5	11.3 ± 1.1	9.8 ± .6
NEUTROPHILS, %	14.3 ± 1.8	14.3 ± 3.2	9.5 ± 1.6	18.3 ± 5.4	14.0 ± 2.7
LYMPHOCYTES, %	83.5 ± 2.6	83.0 ± 4.4	89.8 ± 1.8	80.3 ± 5.7	83.3 ± 2.4
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	.5 ± .3	1.8 ± 1.2	.5 ± .3	1.0 ± .6	1.0 ± 0.0
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	1.8 ± .8	1.0 ± .7	.3 ± .3	.5 ± .3	1.8 ± .3
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
PROTHROMBIN TIME, SEC.	12.2 ± .3	11.6 ± .6	11.8 ± .1	12.1 ± .5	12.1 ± [illegible]
SGOT, IU/L	83.3 ± 9.3	65.0 ± 3.5	69.5 ± 2.9	66.5 ± 1.9	85.8 ± [illegible]
SGPT, IU/L	39.3 ± 1.4	32.5 ± 1.5 a/	33.3 ± 1.4	34.0 ± 1.2	38.5 ± 1.4
ALK. PHOS., IU/L	93 ± 8	129 ± 8 a/	95 ± 9	102 ± 5	103 ± 6
BILIRUBIN, TOTAL MG %	.1 ± .1	.3 ± .1	.3 ± .1	.3 ± .1	.3 ± .1
BILIRUBIN, DIRECT MG %	0.0 ± 0.0	.1 ± .0	.2 ± .1 a/	.1 ± .0	.2 ± .1 a/
BUN, MG %	16.8 ± 1.1	17.8 ± .9	15.8 ± .9	15.3 ± .8	14.8 ± 1.1
CREATININE, MG %	.7 ± .1	.6 ± 0.0	.6 ± 0.0	.6 ± 0.0	.7 ± .1
LDH, IU/L	513 ± 307	235 ± 104	397 ± 149	302 ± 108	308 ± 198
IMMUNOGLOBULINS					
A, IU/ML	6.2 ± .4			5.5 ± .1	
B, A FACTOR, IU/ML	393 ± 42			340 ± 20	
B, B FACTOR, IU/ML	75 ± 22			107 ± 24	
M, IU/ML	47 ± 2			50 ± 1	
TOTAL PROTEIN, GM %	5.3 ± .3	5.4 ± .2	5.6 ± .1	5.6 ± .1	5.9 ± .1
ALBUMIN, GM %	3.3 ± .2	3.5 ± .1	3.7 ± .2	3.3 ± .3	3.5 ± .1
GLOBULIN, GM %	1.9 ± .2	1.6 ± .2	2.0 ± .1	2.4 ± .3	2.5 ± .1
MACROPHAGES (NO./MM^3)	188 ± 63			438 ± 85	293 ± 156

Entries are mean ± S.E. of 4 rats except as noted in parentheses.
a/ Significantly different from the Control group, $p < 0.05$, Dunnett's multiple comparison procedure.

TABLE 2

LABORATORY DATA OF FEMALE RATS AFTER EXPOSURE TO VC OR VDC FOR 1 MONTH

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 35 ppm
ERYTHROCYTES ($X10^6$ /MM^3)	6.19 ± .30	6.65 ± .21	6.22 ± .19	5.87 ± .51	6.73 ± .18
RETICULOCYTES, %	1.57 ± .67	1.34 ± .53	1.17 ± .35	1.76 ± .77	.94 ± .11
HEMATOCRIT, VOL. %	41.5 ± .5	43.0 ± 0.0	41.8 ± .4	40.0 ± .4	40.0 ± .7
HEMOGLOBIN, GM. %	14.5 ± .2	14.7 ± .2	14.2 ± .3	14.1 ± .1	14.3 ± .2
MCV, CUBIC MICRONS	67.8 ± 4.7	64.8 ± 2.0	67.2 ± 1.3	70.0 ± 7.4	59.5 ± .8
MCHB, MICRO MICROGMS.	23.7 ± 1.7	22.2 ± .8	22.9 ± .2	24.6 ± 2.4	20.8 ± .2
MCHBC, GM %	34.9 ± .1	34.2 ± .4	34.1 ± .3	35.2 ± .3	34.9 ± .2
PLATELETS ($X10^5$ /MM^3)	6.5 ± .5	5.5 ± .4	7.5 ± .6	7.9 ± .8	5.5 ± .6
LEUKOCYTES ($X10^3$ /MM^3)	7.3 ± .6	7.3 ± .9	7.7 ± .5	5.9 ± .5	11.9 ± 1.3 [a]
NEUTROPHILS, %	17.3 ± 3.1	10.0 ± 2.8	13.5 ± 4.6	16.3 ± 3.3	12.8 ± 3.3
LYMPHOCYTES, %	81.8 ± 3.1	88.5 ± 3.3	85.3 ± 4.1	83.0 ± 3.4	86.0 ± 2.7
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	.8 ± .5	1.0 ± .4	.8 ± .5	.3 ± .3	.8 ± .7
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	.3 ± .3	.5 ± .3	.5 ± .3	.5 ± .3	.5 ± .7
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
PROTHROMBIN TIME, SEC.	12.1 ± .3 (2)	11.5 ± .2	11.6 ± .2	11.7 ± .6	11.2 ± .1 (3)
SGOT, IU/L	74.3 ± 9.8	65.8 ± 10.7	71.3 ± 8.6	81.0 ± 2.0	73.3 ± 8.3 (3)
SGPT, IU/L	35.5 ± 2.9	27.0 ± 2.1	27.8 ± 1.4	29.3 ± 2.1	34.0 ± 1.7 (3)
ALK. PHOS., IU/L	74 ± 7	65 ± 8	77 ± 10	80 ± 2	80 ± 5 (3)
BILIRUBIN, TOTAL MG %	.1 ± .1	.2 ± .1	.2 ± .1	.2 ± .1	.3 ± .1 (3)
BILIRUBIN, DIRECT MG %	.1 ± .1	.1 ± .1	.1 ± .1	.0 ± .0	.2 ± .1 (3)
BUN, MG %	15.5 ± 1.6	15.0 ± 1.2	16.0 ± .7	15.0 ± .9	17.3 ± 1.2 (3)
CREATININE, MG %	.6 ± 0.0	.6 ± 0.0	.7 ± .1	.8 ± 0.0	1.0 ± .1 (3) [a]
LDH, IU/L	391 ± 216	404 ± 234	464 ± 187	72 ± 8	325 ± 186 (3)
IMMUNOGLOBULINS					
A, IU/ML	7.3 ± .8			7.1 ± .6	
G, A FACTOR, IU/ML	393 ± 34			389 ± 41	
G, B FACTOR, IU/ML	71 ± 12			80 ± 13	
M, IU/ML	49 ± 3			46 ± 2	
TOTAL PROTEIN, GM %	5.5 ± .1	5.7 ± .1	5.6 ± .2	5.7 ± .1	6.2 ± .2 (3) [a]
ALBUMIN, GM %	3.4 ± .1	3.7 ± .2	3.6 ± .2	3.5 ± .2	3.9 ± .3 (3)
GLOBULIN, GM %	2.1 ± .1	2.0 ± .1	2.0 ± .1	2.2 ± .2	2.4 ± .3 (3)
MACROPHAGES (NO./MM^3)	288 ± 72			263 ± 63	269 ± 45

Entries are mean ± S.E. of 4 rats except as noted in parentheses.

a/ Significantly different from the Control group, $p < 0.05$, Dunnett's multiple comparison procedure.

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TABLE 3

LABORATORY DATA OF MALE RATS AFTER EXPOSURE TO VC OR VDC AFTER 2 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
ERYTHROCYTES ($X10^6/MM^3$)	6.94 ± .10	7.03 ± .12	6.92 ± .12	6.83 ± .02	6.57 ± .20
RETICULOCYTES, %	1.01 ± .12	1.52 ± .08	1.30 ± .18	1.32 ± .18	1.59 ± .03 [a]
HEMATOCRIT, VOL. %	44.5 ± .3	43.8 ± .9	43.0 ± .7	42.8 ± .3	42.3 ± .5 [a]
HEMOGLOBIN, GM. %	14.8 ± .2	14.9 ± .0	14.7 ± .2	14.1 ± .2	14.6 ± .4
MCV, CUBIC MICRONS	64.1 ± .6	62.3 ± 1.7	62.2 ± 1.5	62.6 ± .5	64.5 ± 1.9
MCHB, MICRO MICROGMS.	21.3 ± .3	21.2 ± .3	21.2 ± .6	20.6 ± .2	22.2 ± .4
MCHMC, GM %	33.3 ± .4	34.1 ± .6	34.1 ± .4	32.9 ± .4	34.5 ± .6
PLATELETS ($X10^5/MM^3$)	5.7 ± .6	5.8 ± .3	6.7 ± .7	5.9 ± .5	5.7 ± .2
LEUKOCYTES ($X10^3/MM^3$)	9.4 ± .6	12.4 ± .7 [a]	8.5 ± 1.1	9.2 ± .7	8.5 ± .5
NEUTROPHILS, %	12.0 ± 1.2	19.0 ± 6.1	14.0 ± 2.7	9.0 ± 1.1	11.3 ± 1.3
LYMPHOCYTES, %	86.3 ± 2.1	79.3 ± 6.8	82.8 ± 2.8	90.3 ± .9	87.8 ± 1.8
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	1.8 ± 1.4	.5 ± .3	.5 ± .5	.3 ± .3	1.0 ± .7
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	0.0 ± 0.0	1.3 ± .6	.3 ± .3	.5 ± .3	0.0 ± 0.0
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
PROTHROMBIN TIME, SEC.	11.4 ± .0 (3)	10.8 ± .1	10.4 ± .4	10.6 ± .3	11.3 ± .2
SGOT, IU/L	100 ± 7	74 ± 4 [a]	64 ± 6 [a]	70 ± 3 [a]	74 ± 8 [a]
SGPT, IU/L	43.8 ± 3.5	34.0 ± 2.4	32.5 ± 2.9 [a]	34.8 ± 1.4	28.5 ± 1.4
ALK. PHOS., IU/L	73 ± 5	68 ± 4	73 ± 5	68 ± 2	59 ± 5
BILIRUBIN, TOTAL MG %	.0 ± .0	.1 ± .1	.1 ± .1	.1 ± .0	.2 ± .1
BILIRUBIN, DIRECT MG %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	.1 ± .1
BUN, MG %	13.8 ± .5	16.3 ± .6	14.5 ± 1.0	13.8 ± .3	15.5 ± .6
CREATININE, MG %	.6 ± 0.0	.6 ± 0.0	.6 ± 0.0	.6 ± 0.0	.6 ± 0.0
LDH, IU/L	1024 ± 143	540 ± 54 [a]	311 ± 73 [a]	501 ± 44 [a]	849 ± 163
ALPHA-HBDH, IU/L	436 ± 64	227 ± 23 [a]	128 ± 28 [a]	207 ± 20 [a]	362 ± 67
IMMUNOGLOBULINS A, IU/ML	10.3 ± 2.1			10.2 ± 2.4	12.2 ± 1.6
G, A FACTOR, IU/ML	325 ± 19			298 ± 34	310 ± 12
G, B FACTOR, IU/ML	69 ± 5			47 ± 8 [a]	74 ± 5
M, IU/ML	75 ± 20			67 ± 17	103 ± 24
TOTAL PROTEIN, GM %	5.7 ± .1	5.7 ± .1	5.6 ± .1	5.5 ± .2	6.0 ± .2
ALBUMIN, GM %	3.3 ± .1	3.4 ± .1	3.5 ± .0	3.5 ± .0	3.5 ± .1
GLOBULIN, GM %	2.4 ± .2	2.3 ± .2	2.1 ± .1	2.0 ± .2	2.4 ± .1
MACROPHAGES ($NO./MM^3$)	206 ± 48			294 ± 136	288 ± 46

Entries are mean ± S.E. of 4 rats except as noted in parentheses.

[a] Significantly different from the Control group, $p < 0.05$, Dunnett's multiple comparison procedure.

TABLE 4

LABORATORY DATA OF FEMALE RATS AFTER EXPOSURE TO VC OR VDC FOR 2 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
ERYTHROCYTES ($X10^6/MM^3$)	6.59 ± .13	6.61 ± .23	6.19 ± .21	6.70 ± .20	6.35 ± .20
RETICULOCYTES, %	1.06 ± .13	1.48 ± .23	1.89 ± .21 a/	1.45 ± .15	1.28 ± .24
HEMATOCRIT, VOL. %	42.3 ± .5	41.8 ± .9	41.8 ± .8	42.3 ± .6	40.5 ± .6
HEMOGLOBIN, GM. %	14.5 ± .2	14.2 ± .2	14.1 ± .2	14.1 ± .1	13.9 ± .2
MCV, CUBIC MICRONS	64.2 ± 1.6	63.3 ± 2.1	67.7 ± 2.4	63.1 ± 1.5	63.9 ± 1.2
MCHR, MICRO MICROGMS.	22.0 ± .4	21.6 ± .6	22.8 ± .7	21.1 ± .5	22.0 ± .4
MCHBC, GM %	34.3 ± .4	34.1 ± .4	33.7 ± .2	33.4 ± .3	34.5 ± .5
PLATELETS ($X10^5/MM^3$)	6.0 ± .4	6.3 ± .5	5.4 ± .7	6.1 ± .3	7.2 ± .7
LEUKOCYTES ($X10^3/MM^3$)	7.8 ± .4	7.5 ± .5	8.1 ± 1.1	7.2 ± .3	6.0 ± .6
NEUTROPHILS, %	11.0 ± 3.1	11.5 ± 2.8	14.3 ± 5.0	16.5 ± 7.5	16.3 ± 2.8
LYMPHOCYTES, %	87.5 ± 3.3	87.0 ± 2.9	84.5 ± 5.4	82.5 ± 7.2	81.5 ± 2.1
BANDS, %	.3 ± .3	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	1.3 ± .5	1.0 ± 0.0	1.3 ± .5	.8 ± .5	2.0 ± 1.1
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	0.0 ± 0.0	.5 ± .5	0.0 ± 0.0	.3 ± .3	.3 ± .3
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
PROTHROMBIN TIME, SEC.	10.6 ± .1	10.6 ± .3	10.5 ± .2	10.8 ± .2	10.2 ± .5
SGOT, IU/L	75.0 ± 10.3	68.8 ± 9.2	67.0 ± 6.1	84.0 ± 7.7	73.3 ± 4.3
SGPT, IU/L	32.5 ± 2.6	35.3 ± 4.7	33.0 ± 3.1	39.3 ± 4.1	22.8 ± 2.1
ALK, PHOS., IU/L	50 ± 3	58 ± 10	43 ± 6	60 ± 8	38 ± 2
BILIRUBIN, TOTAL MG %	.0 ± .0	.1 ± .1	.1 ± .0	.1 ± .1	.1 ± .1
BILIRUBIN, DIRECT MG %	0.0 ± 0.0	.0 ± .0	0.0 ± 0.0	.0 ± .0	.0 ± .0
BUN, MG %	15.0 ± .4	16.8 ± 1.3	14.0 ± .9	15.5 ± .8	17.0 ± 1.2
CREATININE, MG %	.8 ± .1	.9 ± .1	.7 ± .1	.9 ± .1	.8 ± 0.0
LDH, IU/L	178 ± 94	228 ± 98	280 ± 115	521 ± 71	568 ± 93
ALPHA-HBDH, IU/L	166 ± 42	98 ± 39	121 ± 47	204 ± 16	245 ± 32
IMMUNOGLOBULINS A, IU/ML	11.8 ± 3.5			11.1 ± 2.9	11.7 ± 1.7
G, A FACTOR, IU/ML	458 ± 15			458 ± 35	363 ± 44
G, B FACTOR, IU/ML	79 ± 16			83 ± 12	43 ± 8
M, IU/ML	51 ± 15			53 ± 15	24 ± 3
TOTAL PROTEIN, GM %	6.0 ± .2	6.2 ± .1	6.0 ± .2	6.1 ± .2	6.0 ± .2
ALBUMIN, GM %	3.3 ± .2	3.4 ± .0	3.6 ± .1	3.5 ± .1	3.6 ± .0
GLOBULIN, GM %	2.6 ± .2	2.8 ± .1	2.4 ± .2	2.5 ± .1	2.3 ± .2
MACROPHAGES ($NO./MM^3$)	200 ± 43			150 ± 18	125 ± 10

Entries are mean ± S.E. of 4 rats except as noted in parentheses.

a/ Significantly different from the Control group, $p < 0.05$, Dunnett's multiple comparison procedure.

SL 083850

TABLE 5

LABORATORY DATA OF MALE RATS AFTER EXPOSURE TO VC OR VDC FOR 3 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
ERYTHROCYTES ($X10^6$ /MM^3)	6.93 ± .35	6.73 ± .07	6.65 ± .07	6.97 ± .14	7.32 ± .11 (2)
RETICULOCYTES, %	1.35 ± .08	1.31 ± .19	1.43 ± .31	1.01 ± .23	1.09 ± .02 (2)
HEMATOCRIT, VOL. %	42.8 ± 1.3	43.0 ± .7	41.3 ± .3	44.0 ± .4	42.0 ± 1.0 (2)
HEMOGLOBIN, GM. %	14.6 ± .4	14.7 ± .3	14.2 ± .3	15.0 ± .3	14.6 ± .3 (2)
MCV, CUBIC MICRONS	61.9 ± 1.4	63.9 ± .7	62.0 ± .6	63.2 ± 1.1	57.3 ± .5 (2)
MCHB, MICRO MICROGMS.	21.2 ± .6	21.9 ± .4	21.3 ± .4	21.6 ± .4	20.0 ± .1 (2)
MCHHC, GM %	34.3 ± .2	34.2 ± .3	34.4 ± .4	34.2 ± .3	34.9 ± .2 (2)
PLATELETS ($X10^5$ /MM^3)	5.4 ± .5	6.0 ± .4	7.7 ± .7	6.5 ± .8	5.2 ± .3 (2)
LEUKOCYTES ($X10^3$ /MM^3)	9.3 ± 1.1	8.9 ± .7	9.9 ± 1.2	10.9 ± 2.8	8.9 ± 1.7 (2)
NEUTROPHILS, %	11.5 ± 4.9	15.3 ± 3.1	11.3 ± 2.4	22.0 ± 6.9	10.5 ± .5 (2)
LYMPHOCYTES, %	85.3 ± 5.1	82.8 ± 3.4	87.3 ± 2.1	77.5 ± 6.8	88.5 ± 1.5 (2)
BANDS, %	.3 ± .3	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0 (2)
EOSINOPHILS, %	2.3 ± .6	1.5 ± .9	1.3 ± .6	0.0 ± 0.0	.3 ± .3 (2)
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0 (2)
MONOCYTES, %	.8 ± .5	.5 ± .3	.3 ± .3	.5 ± .5	.3 ± .3 (2)
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0 (2)
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0 (2)
PROTHROMBIN TIME, SEC.	11.8 ± .2	11.4 ± .0	11.3 ± .2	11.0 ± .3 a/	
SGOT, IU/L	112 ± 21	70 ± 7	74 ± 9	82 ± 9	103 ± 10 (3)
SGPT, IU/L	54.8 ± 15.5	31.0 ± 1.2	34.0 ± 1.7	33.8 ± 3.5	40.0 ± 0.0 (3)
ALK. PHOS., IU/L	67 ± 8	74 ± 8	40 ± 4	71 ± 7	51 ± 6 (3)
BILIRUBIN, TOTAL MG %	.0 ± .0	.1 ± .0	.1 ± .0	.1 ± .0	.1 ± .1 (2)
BILIRUBIN, DIRECT MG %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0 (2)
BUN, MG %	15.0 ± 1.1	13.3 ± .5	12.5 ± .3	14.5 ± .9	15.0 ± .6 (3)
CREATININE, MG %	.6 ± 0.0	.5 ± .1	.4 ± .1	.5 ± .1	.6 ± 0.0 (3)
LDH, IU/L	899 ± 222	596 ± 186	503 ± 137	777 ± 156	942 ± 183 (3)
ALPHA-HBDH, IU/L	378 ± 91	263 ± 81	232 ± 94	335 ± 70	432 ± 64 (3)
IMMUNOGLOBULINS					
A, IU/ML	9.0 ± .3			9.5 ± .5	5.1 ± 0.0 (3) a/
G, A FACTOR, IU/ML	418 ± 15			413 ± 6	244 ± 87 (3) a/
G, B FACTOR, IU/ML	82 ± 9			89 ± 22	90 ± 24 (3)
M, IU/ML	103 ± 5			89 ± 7	124 ± 9 (3)
TOTAL PROTEIN, GM %	5.8 ± .1	5.6 ± .1	5.7 ± .1	5.6 ± .3	6.0 ± .2 (3)
ALBUMIN, GM %	3.3 ± .0	3.2 ± .0	3.1 ± .1	3.1 ± .2	3.3 ± .2 (3)
GLOBULIN, GM %	2.6 ± .1	2.4 ± .0	2.6 ± .1	2.5 ± .2	2.7 ± .1 (3)
MACROPHAGES ($NO./MM^3$)	180 ± 99			246 ± 59	296 ± 133

Entries are mean ± S.E. of 4 rats except as noted in parentheses.

a/ Significantly different from the Control group, $p < 0.05$, Dunnett's multiple comparison procedure.

SL 083851

TABLE 6

LABORATORY DATA OF FEMALE RATS AFTER EXPOSURE TO VC OR VDC FOR 3 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
ERYTHROCYTES ($\times 10^6$ /MM^3)	6.37 ± .16	6.56 ± .15	6.45 ± .17	6.53 ± .15	6.51 ± .14
RETICULOCYTES, %	1.29 ± .24	1.26 ± .26	1.49 ± .16	1.74 ± .06	.89 ± .07
HEMATOCRIT, VOL. %	42.0 ± .8	41.3 ± 1.3	42.3 ± .5	41.5 ± .6	39.3 ± .6
HEMOGLOBIN, GM. %	14.5 ± .2	14.2 ± .2	14.6 ± .1	14.3 ± .3	13.5 ± .2 a/
MCV, CUBIC MICRONS	66.0 ± 1.5	62.8 ± 1.4	65.5 ± .9	63.6 ± .8	60.3 ± 1.2 a/
MCHA, MICRO MICROGMS.	22.8 ± .4	21.7 ± .3	22.7 ± .3	21.9 ± .2	20.7 ± .6 a/
MCHMC, GM %	34.6 ± .2	34.5 ± .5	34.7 ± .2	34.4 ± .4	34.3 ± .3
PLATELETS ($\times 10^5$ /MM^3)	6.2 ± .5	5.7 ± .1	5.9 ± .4	6.2 ± .5	5.5 ± .3
LEUKOCYTES ($\times 10^3$ /MM^3)	5.8 ± .3	6.8 ± .8	6.5 ± .7	6.1 ± .6	5.0 ± .5
NEUTROPHILS, %	14.3 ± 3.4	19.5 ± 6.8	9.8 ± 1.9	14.3 ± 2.9	12.8 ± 2.4
LYMPHOCYTES, %	84.3 ± 3.8	79.5 ± 6.7	89.5 ± 1.7	83.5 ± 2.7	87.0 ± 2.7
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	1.3 ± .6	.5 ± .5	.5 ± .3	1.8 ± .5	.3 ± .3
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	.3 ± .3	.5 ± .3	.3 ± .3	.5 ± .3	0.0 ± 0.0
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
PROTHROMBIN TIME, SEC.	11.0 ± .2	10.7 ± .2	11.0 ± .3	11.1 ± .1	11.0 ± .4 (3)
SGOT, IU/L	40.3 ± 4.1	93.3 ± 9.4	41.0 ± 5.1	84.5 ± 10.5	40.3 ± 4.9
SGPT, IU/L	34.5 ± 5.1	36.3 ± 1.9	33.0 ± 3.5	32.3 ± 4.9	31.0 ± 1.2
ALK. PHOS., IU/L	39 ± 4	34 ± 3	50 ± 6	49 ± 7	21 ± 1
BILIRUBIN, TOTAL MG %	.1 ± .0	.1 ± .1	.1 ± .0	.1 ± .0	.1 ± .1
BILIRUBIN, DIRECT MG %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
BUN, MG %	13.3 ± .6	14.3 ± .6	15.0 ± .7	15.0 ± .9	14.3 ± .8
CREATININE, MG %	.6 ± 0.0	.6 ± 0.0	.6 ± 0.0	.5 ± .1	.6 ± 0.0
LDH, IU/L	600 ± 75	709 ± 190	621 ± 59	449 ± 144	493 ± 112
ALPHA-HBDH, IU/L	262 ± 33	318 ± 82	275 ± 19	308 ± 44	229 ± 49
IMMUNOGLOBULINS					
A, IU/ML	10.6 ± .6			9.2 ± .4	5.2 ± .0 a/
G, A FACTOR, IU/ML	626 ± 47			453 ± 106	385 ± 22
G, B FACTOR, IU/ML	79 ± 5			98 ± 28	84 ± 10
M, IU/ML	79 ± 10			80 ± 14	108 ± 10
TOTAL PROTEIN, GM %	6.3 ± .1	6.1 ± .1	5.9 ± .1	5.8 ± .3	6.4 ± .1
ALBUMIN, GM %	3.6 ± .0	3.6 ± .1	3.3 ± .1	3.4 ± .0	3.4 ± .1
GLOBULIN, GM %	2.7 ± .0	2.5 ± .1	2.7 ± .0	2.4 ± .3	3.0 ± .1
MACROPHAGES (NO./MM^3)	125 ± 13			84 ± 7 a/	41 ± 6 a/

Entries are mean ± S.E. of 4 rats except as noted in parentheses.

a/ Significantly different from the Control group, $p < 0.05$, Dunnett's multiple comparison procedure.

SL 083852

TABLE 7

LABORATORY DATA OF MALE RATS EXPOSED TO VC OR VDC FOR 6 MONTHS

DOSE: PPM	CONTROL	50 PPM VC	250 PPM VC	1,000 PPM VC	55 PPM VDC
ERYTHROCYTES ($\times 10^6$ /MM^3)	6.23 ± .30 (2)	6.81 ± .33	6.89 ± .16 (3)	6.74 ± .22 (3)	7.24 ± .13
RETICULOCYTES, %	1.43 ± .34 (3)	.89 ± .12	1.30 ± .13	1.00 ± .17 (3)	.79 ± .14
HEMATOCRIT, VOL. %	43.5 ± .5 (2)	44.8 ± .5	41.7 ± .7 (3)	44.0 ± 1.0 (3)	45.0 ± .7
HEMOGLOBIN, GM. %	15.1 ± .1 (2)	15.9 ± .5	14.9 ± .1 (3)	15.4 ± .3 (3)	15.3 ± .2
MCV, CUBIC MICRONS	69.9 ± 2.4 (2)	66.2 ± 3.4	60.6 ± 1.9 (3)	65.3 ± 1.7 (3)	62.2 ± .4
MCH, MICRO MICROGMS.	24.3 ± .7 (2)	23.6 ± 1.5	21.7 ± .6 (3)	22.9 ± .8 (3)	21.2 ± .1
MCHC, GM %	34.7 ± .3 (2)	35.6 ± .7	35.9 ± .6 (3)	35.1 ± .4 (3)	34.1 ± .3
PLATELETS ($\times 10^5$ /MM^3)	4.3 ± .1 (2)	4.7 ± .3	4.3 ± .6 (3)	4.8 ± .6 (3)	3.9 ± .2
LEUKOCYTES ($\times 10^3$ /MM^3)	9.8 ± .6 (2)	10.2 ± 1.0	9.6 ± 1.4 (3)	10.8 ± 1.2 (3)	8.8 ± .5
NEUTROPHILS, %	14.0 ± .6 (3)	16.3 ± 2.3	20.5 ± 4.2	19.0 ± 3.7	12.8 ± 2.4
LYMPHOCYTES, %	84.7 ± .9 (3)	81.0 ± 3.5	77.3 ± 6.0	79.5 ± 3.8	84.5 ± 2.0
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	1.0 ± .6	1.5 ± .9	2.0 ± .7	1.3 ± .3	2.8 ± .6
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	0.0 ± 0.0	1.3 ± .6	.3 ± .3	.3 ± .3	0.0 ± 0.0
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
PROTHROMBIN TIME, SEC.	12.3 ± .1 (2)	11.8 ± .3	10.8 ± .3 (3)[a/]	11.2 ± .1	12.6 ±
SGOT, IU/L	69.3 ± 7.5	71.0 ± 2.1	69.3 ± 6.3	76.5 ± 8.0	71.0 ±
SGPT, IU/L	34.0 ± 1.7	37.8 ± 5.0	29.0 ± 1.1	31.8 ± 1.4	31.5 ±
ALK. PHOS., IU/L	40 ± 2	49 ± 8	43 ± 1	40 ± 4	40 ± 5
BILIRUBIN, TOTAL MG %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
BILIRUBIN, DIRECT MG%	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
BUN, MG %	13.0 ± .6	11.3 ± .5	12.0 ± .6	12.3 ± .5	12.5 ± .5
CREATININE, MG %	.6 ± .1	.5 ± .1	.6 ± .1	.8 ± .1[a/]	.6 ± .1
LDH, IU/L	731 ± 142	441 ± 158	416 ± 101	748 ± 218	439 ± 102
ALPHA-HBDH, IU/L	437 ± 74	258 ± 80	245 ± 58	440 ± 117	262 ± 57
IMMUNOGLOBINS					
A, IU/ML	8.1 ± .5			7.9 ± .6	9.8 ± 1.2
G, A FACTOR, IU/ML	509 ± 36			490 ± 30	425 ± 26
G, B FACTOR, IU/ML	106 ± 13			80 ± 20	92 ± 8
M, IU/ML	120 ± 5			120 ± 5	46 ± 3[a/]
TOTAL PROTEIN, GM %	6.0 ± .1	6.2 ± .1	6.1 ± .0	6.0 ± 0.0	6.1 ± .2
ALBUMIN, GM %	3.4 ± .1	3.3 ± .1	3.5 ± .0	3.4 ± .0	3.4 ± .1
GLOBULIN, GM %	2.6 ± .2	2.9 ± .0	2.6 ± .0	2.6 ± .0	2.7 ± .1
MACROPHAGES (NO./MM^3)	144 ± 104			244 ± 41	220 ± 101

ENTRIES ARE MEAN ± STANDARD ERROR OF 4 RATS EXCEPT AS NOTED IN PARENTHESES.

a/ Significantly different from the Control group, $p < 0.05$, Dunnett's multiple comparison procedure.

TABLE 8

LABORATORY DATA OF FEMALE RATS EXPOSED TO VC OR VDC FOR 6 MONTHS

DOSE: PPM	CONTROL	50 PPM VC	250 PPM VC	1,300 PPM VC	55 PPM VDC
ERYTHROCYTES ($\times 10^6$ /MM^3)	6.92 ± .21	6.96 ± .09	6.69 ± .23	6.48 ± .23 (3)	6.84 ± .04
RETICULOCYTES, %	.97 ± .10	.65 ± .24	.79 ± .25	.95 ± .16 (3)	.89 ± .07
HEMATOCRIT, VOL. %	42.3 ± 1.1	41.5 ± .9	42.0 ± .7	42.7 ± .7 (3)	39.5 ± .5
HEMOGLOBIN, GM. %	14.9 ± .2	15.2 ± .3	15.0 ± .2	15.2 ± .3 (3)	13.8 ± .2[a/]
MCV, CUBIC MICRONS	61.1 ± 1.1	59.7 ± 1.0	63.0 ± 2.5	66.0 ± 2.0 (3)	59.5 ± .4
MCHM, MICRO MICROGMS.	21.6 ± .4	21.9 ± .3	22.4 ± .7	23.5 ± .5 (3)[a/]	20.9 ± .3
MCHMC, GM %	35.3 ± .4	36.8 ± .1[a/]	35.7 ± .4	36.7 ± .3 (3)	35.1 ± .2
PLATELETS ($\times 10^5$ /MM^3)	6.3 ± .8	6.7 ± .3	6.1 ± .6	5.2 ± .6 (3)	6.4 ± .3
LEUKOCYTES ($\times 10^3$ /MM^3)	8.6 ± .6	8.2 ± 1.0	6.9 ± 1.0	5.7 ± 1.6 (3)	5.5 ± .7
NEUTROPHILS, %	12.3 ± .3	18.5 ± 6.6	20.0 ± 3.6	28.3 ± 4.9 (3)	20.5 ± 3.6
LYMPHOCYTES, %	85.8 ± .9	79.8 ± 6.3	77.8 ± 3.6	72.3 ± 5.5 (3)	78.8 ± 3.7
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	1.8 ± .8	1.5 ± .3	2.3 ± .9	1.0 ± .6	.8 ± .5
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	.3 ± .3	.3 ± .3	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
PROTHROMBIN TIME, SEC.	11.4 ± .2	11.4 ± .3	11.4 ± .2 (3)	10.9 ± .0 (3)	11.4 ± .1
SGOT, IU/L	81.0 ± 10.9	89.5 ± 6.7	79.8 ± 8.9	87.3 ± 2.5	73.3 ± 4.3
SGPT, IU/L	37.0 ± 9.6	29.5 ± 2.5	28.8 ± 1.7	35.5 ± 1.9	25.3 ± 2.8
ALK. PHOS., IU/L	22 ± 3	18 ± 2	10 ± 7	26 ± 4	17 ± 3
BILIRUBIN, TOTAL MG %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
BILIRUBIN, DIRECT MG%	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
BUN, MG %	13.3 ± .8	12.5 ± .6	13.5 ± 1.9	12.3 ± 1.1	13.5 ± 1.0
CREATININE, MG %	.6 ± .0	.6 ± .1	.5 ± .1	.7 ± .1	.6 ± .1
LDH, IU/L	552 ± 71	447 ± 154	321 ± 66	443 ± 96	257 ± 97
ALPHA-HBDH, IU/L	328 ± 44	245 ± 45	230 ± 44	381 ± 58	180 ± 44
IMMUNOGLOBINS					
A, IU/ML	7.7 ± .2			8.3 ± .4	10.4 ± .7[a/]
G, A FACTOR, IU/ML	565 ± 33			519 ± 41	665 ± 45
G, B FACTOR, IU/ML	79 ± 14			76 ± 18	102 ± 12
M, IU/ML	107 ± 3			115 ± 9	97 ± 3 [a/]
TOTAL PROTEIN, GM %	6.3 ± .1	7.0 ± .1	6.0 ± .3	6.2 ± .2	6.5 ± .2
ALBUMIN, GM %	3.6 ± .1	4.2 ± .1[a/]	3.4 ± .2	3.5 ± .1	3.8 ± .1
GLOBULIN, GM %	2.7 ± .1	2.8 ± .0	2.6 ± .2	2.7 ± .2	2.7 ± .1
MACROPHAGES (NO./MM^3)	93 ± 7			105 ± 18	101 ± 34

ENTRIES ARE MEAN ± STANDARD ERROR OF - RATS EXCEPT AS NOTED IN PARENTHESES

a/ Significantly different from the Control group, $p < 0.05$, Dunnett's multiple comparison procedure.

SL 083854

BLE 9

LABORATORY DATA OF MALE RATS POSED TO VC OR VDC FOR 9 MONTHS

DOSE: PPM	Control	50 ppm VC	250 ppm VC	1000 ppm VC	55 ppm VDC
ERYTHROCYTES ($X10^6$ /MM^3)	7.75 ± .26	7.74 ± .27	7.58 ± .14	7.12 ± .41	6.53 ± .15 a/
RETICULOCYTES, %	1.26 ± .37	.99 ± .16	1.08 ± .12	1.14 ± .12	1.39 ± .36
HEMATOCRIT, VOL. %	45.8 ± 1.3	46.0 ± .8	44.5 ± 1.0	42.3 ± 1.7	42.5 ± .9
HEMOGLOBIN, GM. %	15.4 ± .5	15.5 ± .3	14.8 ± .4	14.2 ± .8	14.3 ± .3
MCV, CUBIC MICRONS	59.1 ± 1.3	59.6 ± 1.3	59.4 ± 2.0	59.6 ± 1.4	65.1 ± 1.1 a/
MCH, MICRO MICROGMS.	19.9 ± .4	20.1 ± .3	19.8 ± .8	20.0 ± .4	21.9 ± .4 a/
MCHC, GM %	33.7 ± .2	33.8 ± .2	33.4 ± .2	33.7 ± .7	33.6 ± .2
PLATELETS ($X10^5$ /MM^3)	4.1 ± .1	4.0 ± .5	4.0 ± .4	4.8 ± 1.3	4.9 ± .5
LEUKOCYTES ($X10^3$ /MM^3)	10.4 ± .9	10.6 ± 1.2	10.9 ± .9	11.5 ± .9	9.5 ± .5
NEUTROPHILS, %	18.5 ± 1.2	11.3 ± 4.3	21.8 ± 4.2	24.3 ± 5.6	26.3 ± 6.7
LYMPHOCYTES, %	78.3 ± 1.3	86.3 ± 4.0	74.8 ± 3.6	73.5 ± 6.2	72.0 ± 6.4
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	.3 ± .3	0.0 ± 0.0
EOSINOPHILS, %	1.3 ± .3	2.0 ± 1.1	2.5 ± .7	1.3 ± .9	1.5 ± 1.0
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	2.0 ± .4	.5 ± .3 a/	1.0 ± .4	.8 ± .3	.3 ± .3 a/
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ±
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0
PROTHROMBIN TIME, SEC.	11.4 ± .4	10.5 ± .4	11.1 ± .1	11.4 ± .3	12.0 ±
SGOT, IU/L	103 ± 9	68 ± 11 a/	76 ± 2	81 ± 11	57 ± 2 (3) a/
SGPT, IU/L	35.5 ± 3.6	31.5 ± 4.1	37.8 ± 2.8	43.3 ± 9.8	21.3 ± 3.3 (3)
ALK. PHOS., IU/L	± 4	44 ± 4	55 ± 8	57 ± 5	37 ± 7 (3)
BILIRUBIN, TOTAL MG %	± 0.0	0.0 ± 0.0	.1 ± .0	0.0 ± 0.0	0.0 ± 0.0
BILIRUBIN, DIRECT MG%	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
BUN, MG %	14.5 ± 1.3	15.0 ± .4	16.0 ± .4	15.5 ± .3	12.0 ± 1.2 (3)
CREATININE, MG %	.7 ± .0	.6 ± .1	.7 ± .0	.8 ± .1	.7 ± .0 (3
LDH, IU/L	1014 ± 180	323 ± 179 a/	359 ± 81 a/	414 ± 93 a/	
ALPHA-HBDH, IU/L	624 ± 107	198 ± 103 a/	246 ± 65 a/	248 ± 52 a/	
IMMUNOGLOBINS A, IU/ML	6.2 ± .5			5.8 ± .3	5.7
G, A FACTOR, IU/ML	466 ± 105			478 ± 112	218 ±
G, B FACTOR, IU/ML	113 ± 29			123 ± 39	66 ± 2 (3)
M, IU/ML	103 ± 4			84 ± 17	51 ± 7 (3) a/
TOTAL PROTEIN, GM %	6.1 ± .2	5.6 ± .5	6.1 ± 0.0	6.0 ± .1	6.0 ± .1 (3)
ALBUMIN, GM %	3.5 ± .1	3.4 ± .1	3.5 ± .0	3.4 ± .1	3.4 ± 0.0 (3)
GLOBULIN, GM %	2.4 ± .2	2.1 ± .5	2.6 ± .0	2.6 ± .2	2.6 ± .1 (3)
MACROPHAGES (NO./MM^3)	33 ± 10			69 ± 28	80 ± 19

ENTRIES ARE MEAN ± STANDARD ION OF FOUR RATS EXCEPT AS NOTED IN PARENTHESES

a/ Significantly different from the control group, $P < 0.05$, Dunnett's multiple comparison procedure.

SL 083855

TABLE 10

LABORATORY DATA OF FEMALE RATS EXPOSED TO VC OR VDC FOR 9 MONTHS

DOSE: PPM	Control	50 ppm VC	250 ppm VC	1000 ppm VC	55 ppm VDC
ERYTHROCYTES ($X10^6$ /MM^3)	6.82 ± .16 (3)	6.27 ± .41	6.76 ± .97 (3)	6.40 ± .34 (3)	6.43 ± .31
RETICULOCYTES, %	1.06 ± .34	1.07 ± .18	1.60 ± .27 (3)	.94 ± .19 (3)	1.14 ± .07
HEMATOCRIT, VOL. %	41.7 ± .7 (3)	40.0 ± .4	40.0 ± 1.7 (3)	40.7 ± 1.2 (3)	39.5 ± 1.0
HEMOGLOBIN, GM. %	14.1 ± .1 (3)	13.3 ± .3	13.6 ± .6 (3)	14.1 ± .4 (3)	13.4 ± .3
MCV, CUBIC MICRONS	61.1 ± .8 (3)	64.6 ± 4.2	59.6 ± 2.7 (3)	59.9 ± 1.3 (3)	61.6 ± 1.1
MCHB, MICRO MICROGMS.	20.7 ± .4 (3)	21.5 ± 1.2	20.3 ± 1.0 (3)	20.8 ± .4 (3)	20.9 ± .5
MCHBC, GM %	33.9 ± .3 (3)	33.4 ± .5	34.1 ± .3 (3)	34.8 ± .1 (3)	34.0 ± .2
PLATELETS ($X10^5$ /MM^3)	3.8 ± .3 (3)	3.4 ± .5	4.0 ± .3 (3)	3.3 ± .5 (3)	5.3 ± .4
LEUKOCYTES ($X10^3$ /MM^3)	5.2 ± .1 (3)	5.3 ± .7	5.6 ± .8 (3)	5.8 ± 1.1 (3)	4.4 ± .4
NEUTROPHILS, %	15.0 ± 1.9	27.5 ± 5.7	20.3 ± 5.9 (3)	28.3 ± 4.1 (3)	17.8 ± 2.1
LYMPHOCYTES, %	82.8 ± 2.0	70.3 ± 5.8	76.7 ± 5.6 (3)	70.3 ± 4.8 (3)	80.0 ± 2.9
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	1.5 ± .6	.3 ± .3	1.3 ± .8	.5 ± .5	1.5 ± .5
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	.8 ± .5	2.0 ± .7	1.0 ± .8	.5 ± .3	.8 ± .5
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
PROTHROMBIN TIME, SEC.	11.0 ± .4 (3)	11.1 ± .2	11.0 ± .2 (3)	11.1 ± .1 (3)	11.4 ± .2
SGOT, IU/L	74.8 ± 3.8	80.3 ± 4.3	74.3 ± 14.9	93.3 ± 11.9 (3)	72.8 ± 7.8
SGPT, IU/L	30.3 ± 2.3	34.5 ± 5.5	29.8 ± 4.5	42.0 ± 4.4 (3)	24.3 ± 1.4
ALK. PHOS., IU/L	26 ± 3	27 ± 5	22 ± 0	26 ± 2 (3)	17 ± 2
BILIRUBIN, TOTAL MG %	.0 ± .0	0.0 ± 0.0	.1 ± .1	0.0 ± 0.0	0.0 ± 0.0
BILIRUBIN, DIRECT MG%	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
BUN, MG %	17.0 ± 1.6	14.3 ± .8	16.0 ± 1.7	19.7 ± 2.9 (3)	14.0 ± .7
CREATININE, MG %	.7 ± .0	.7 ± .0	.7 ± .0	.8 ± .1 (3)	.7 ± .1
LDH, IU/L	602 ± 102	489 ± 48	352 ± 131	494 ± 165 (3)	644 ± 214
ALPHA-HBDH, IU/L	375 ± 62	295 ± 27	228 ± 85	312 ± 97 (3)	420 ± 133
IMMUNOGLOBINS					
A, IU/ML	6.3 ± 1.2			5.4 ± .0 (3)	5.9 ± .5
G, A FACTOR, IU/ML	590 ± 150			378 ± 129	450 ± 47
G, B FACTOR, IU/ML	84 ± 12			89 ± 16 (3)	95 ± 18
M, IU/ML	89 ± 24			89 ± 14 (3)	61 ± 2
TOTAL PROTEIN, GM %	6.4 ± .2	6.1 ± .3	6.2 ± .2	6.0 ± .2 (3)	6.4 ± .4
ALBUMIN, GM %	3.7 ± .1	3.6 ± .3	4.0 ± .2	3.8 ± .1 (3)	4.1 ± .3
GLOBULIN, GM %	2.7 ± .1	2.4 ± .3	2.5 ± .1	2.2 ± .2 (3)	2.3 ± .4
MACROPHAGES (NO./MM^3)	58 ± 4			44 ± 26	51 ± 13

ENTRIES ARE MEAN ± STANDARD ERROR OF FOUR RATS EXCEPT AS NOTED IN PARENTHESES.

SL 083856

TABLE 11

LABORATORY DATA OF MALE RATS EXPOSED TO VC OR VDC FOR 12 MONTHS

DOSE: ppm	Control	50 ppm VC	250 ppm VC	1,000 ppm VC	55 ppm VDC
ERYTHROCYTES ($X10^6$ /MM^3)	8.96 ± .20	6.50 ± .19	7.52 ± .24	6.32 ± .49	7.72 ± .
RETICULOCYTES, %	1.03 ± .11	1.49 ± .46	.78 ± .08	1.48 ± .46	.83 ± .1
HEMATOCRIT, VOL. %	45.0 ± .8	42.9 ± 1.6	44.1 ± .8	41.5 ± 2.0	44.8 ± .4
HEMOGLOBIN, GM. %	14.8 ± .2	14.2 ± .6	14.8 ± .3	13.7 ± .6	14.6 ± .2
MCV, CUBIC MICRONS	64.8 ± 1.1	66.0 ± 2.3	58.9 ± 1.2	67.2 ± 3.0	58.1 ± .8
MCHa, MICRO MICROGMS.	21.4 ± .5	21.8 ± .8	19.8 ± .4	22.2 ± 1.2	19.0 ± .2
MCHbC, GM %	33.0 ± .4	33.1 ± .6	33.7 ± .2	33.0 ± .5	32.7 ± .2
PLATELETS ($X10^5$ /MM^3)	6.2 ± .6	5.4 ± .4	5.7 ± .6	5.7 ± .4	5.0 ± .2
LEUKOCYTES ($X10^3$ /MM^3)	10.2 ± .6	11.4 ± .5	8.9 ± .6	24.5 ± 16.5	8.9 ± .4
NEUTROPHILS, %	27.0 ± 2.6	22.1 ± 4.7	21.8 ± 3.9	28.5 ± 3.3	15.3 ± 2.1
LYMPHOCYTES, %	70.6 ± 2.4	76.3 ± 5.0	77.0 ± 3.8	62.3 ± 8.8	82.6 ± 2.2
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	9.4 ± 9.4	0.0 ± 0.0
EOSINOPHILS, %	1.5 ± .5	.9 ± .3	.6 ± .2	.9 ± .2	1.8 ± .6
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	.9 ± .4	.8 ± .4	.6 ± .4	.4 ± .2	.4 ± .2
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	.5 ± .5	0.0 ± 0.0
PROTHROMBIN TIME, SEC.	11.2 ± .1	10.5 ± .4 (7)	10.9 ± .3	10.8 ± .4	11.3 ± .2
SGOT, IU/L	68 ± 12	45 ± 3	55 ± 3	164 ± 94	59 ± 3
SGPT, IU/L	34.4 ± 1.7	26.9 ± 2.7	26.4 ± 1.4	45.3 ± 21.5	35.1 .3
ALK. PHOS., IU/L	51 ± 4	44 ± 4	39 ± 3	81 ± 37	46 1
BILIRUBIN, TOTAL MG %	0.0 ± 0.0	.0 ± .0	.0 ± .0	.0 ± .0	0.0 ± 0.0
BILIRUBIN, DIRECT MG%	0.0 ± 0.0	0.0 ± 0.0	.0 ± .0	0.0 ± 0.0	0.0 ± 0.0
BUN, MG %	15.4 ± 1.0	15.4 ± .8	15.6 ± .5	14.0 ± 1.1	13.4 ± .7
CREATININE, MG %	.6 ± .0	.4 ± .0	.6 ± .1	.5 ± .1	.6 ± .1
LDH, IU/L	508 ± 108	138 ± 31[a/]	224 ± 60[a/]	363 ± 64	366 ± 74
ALPHA-HBDH, IU/L	302 ± 61	97 ± 17[a/]	148 ± 38	218 ± 38	230 ± 43
IMMUNOGLOBINS					
A, IU/ML	7.2 ± .4			3.7 ± .3[a/]	4.5 ± .4
G, A FACTOR, IU/ML	331 ± 17			266 ± 64	441 ± 40
G, B FACTOR, IU/ML	101 ± 4			92 ± 4	98 ±
M, IU/ML	106 ± 21			85 ± 20	36 ±
TOTAL PROTEIN, GM %	5.9 ± .1	5.8 ± .1	6.1 ± .2	5.7 ± .1	6.0 ± .1
ALBUMIN, GM %	3.6 ± .1	3.5 ± .1	3.7 ± .2	3.4 ± .1	3.9 ± .1
GLOBULIN, GM %	2.2 ± .1	2.3 ± .1	2.3 ± .2	2.3 ± .1	2.2 ± .1
MACROPHAGES (NO./MM^3)	64 ± 30			93 ± 44	50 ± 25

ENTRIES ARE MEAN ± STANDARD ERROR OF EIGHT RATS UNLESS OTHERWISE INDICATED IN PARENTHESES.
a/ Significantly different from the control group, $P \leq 0.05$, Dunnett's multiple comparison procedure.

TABLE 12

LABORATORY DATA OF FEMALE RATS

DOSE: PPM	Control	50 ppm VC	250 ppm VC	1,000 ppm VC	55 ppm VDC
ERYTHROCYTES ($X10^6$ /MM^3)	5.26 ± .41 (7)	6.99 ± .18	5.50 ± .91 (7)	4.53 ± 2.23	6.90 ± .05
RETICULOCYTES, %	1.56 ± .19	1.16 ± .14	6.56 ± 4.27 (7)	17.00 ± 16.33[a/]	1.13 ± .15
HEMATOCRIT, VOL. %	42.3 ± 1.0 (7)	43.6 ± .9	35.1 ± 4.6 (7)	32.5 ± 9.5	42.4 ± .3
HEMOGLOBIN, GM. %	13.9 ± .4 (7)	14.3 ± .3	11.7 ± 1.6 (7)	10.4 ± 3.6	13.9 ± .1
MCV, CUBIC MICRONS	83.7 ± 7.4 (7)	62.6 ± 1.3	69.1 ± 6.0 (7)	81.1 ± 18.9	61.4 ± .5
MCHB, MICRO MICROGMS.	27.5 ± 2.4 (7)	20.6 ± .4	22.6 ± 1.5 (7)	25.1 ± 4.4	20.1 ± .2
MCHBC, GM %	32.8 ± .3 (7)	32.9 ± .2	32.9 ± .6 (7)	31.4 ± 1.9	32.7 ± .1
PLATELETS ($X10^5$ /MM^3)	5.8 ± .6 (7)	5.0 ± .5	4.8 ± .7 (6)	6.3 ± .7	4.3 ± .2
LEUKOCYTES ($X10^3$ /MM^3)	6.9 ± 1.0 (7)	5.8 ± .5	10.6 ± 4.0 (7)	20.3 ± 11.7[a/]	4.1 ± .3
NEUTROPHILS, %	27.3 ± 3.8	20.6 ± 4.4	35.9 ± 6.5 (7)	42.0 ± 16.0	21.0 ± 2.7
LYMPHOCYTES, %	70.0 ± 3.6	78.0 ± 4.4	63.3 ± 6.4 (7)	55.0 ± 15.0	78.0 ± 2.7
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	.1 ± .1	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	1.9 ± .6	.6 ± .2	.5 ± .2	2.0 ± 2.0	.6 ± .3
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	1.0 ± .3	.8 ± .4	.1 ± .1	1.0 ± 1.0	.4 ± .2
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
PROTHROMBIN TIME, SEC.	10.9 ± .2	10.6 ± .2	11.5 ± .8 (7)	12.0 ± 1.2	10.5 ± .3 (
SGOT, IU/L	53 ± 5	61 ± 3	71 ± 22	447 ± 430[a/]	61 ± 6
SGPT, IU/L	24.5 ± 2.0	24.4 ± 1.8	35.6 ± 10.2	81.5 ± 60.5[a/]	28.9 ± 2.3
ALK. PHOS., IU/L	24 ± 3	18 ± 3	26 ± 7	70 ± 49[a/]	24 ± 3
BILIRUBIN, TOTAL MG %	.1 ± .0	.0 ± .0	.2 ± .2	.1 ± .0	.0 ± .0
BILIRUBIN, DIRECT MG%	0.0 ± 0.0	0.0 ± 0.0	.1 ± .1	0.0 ± 0.0	0.0 ± 0.0
BUN, MG %	16.9 ± 2.2	16.8 ± 1.1	20.6 ± 5.0	15.5 ± .5	14.5 ± .8
CREATININE, MG %	.7 ± .0	.6 ± .0	.7 ± .0	.7 ± 0.0	.6 ± .1
LDH, IU/L	414 ± 102	473 ± 96	791 ± 255	1099 ± 913	351 ± 124
ALPHA-HBDH, IU/L	245 ± 53	294 ± 46	480 ± 160	730 ± 616	218 ± 73
IMMUNOGLOBINS					
A, IU/ML	6.3 ± .6			5.8 ± .5	4.4 ± .4[a/]
G, A FACTOR, IU/ML	439 ± 30			302 ± 226	304 ± 82
G, B FACTOR, IU/ML	86 ± 3			56 ± 28	68 ± 13 (
M, IU/ML	91 ± 17			70 ± 24	54 ± 12
TOTAL PROTEIN, GM %	6.6 ± .2	6.4 ± .2	6.4 ± .2	6.4 ± .4	6.5 ± .1
ALBUMIN, GM %	4.0 ± .1	4.0 ± .1	3.9 ± .2	3.7 ± .2	4.2 ± .1
GLOBULIN, GM %	2.7 ± .1	2.4 ± .2	2.4 ± .2	2.7 ± .2	2.3 ± .1
MACROPHAGES (NO./MM^3)	31 ± 17			403 ± 183[a/]	24 ± 10

ENTRIES ARE MEAN ± STANDARD ERROR OF EIGHT RATS UNLESS OTHERWISE INDICATED IN PARENTHESES. THE VALUES FOR THE 1,000 PPM VC GROUP ARE THE MEAN ± S.E. OF TWO RATS.

a/ Significantly different from the control group, $P \leq 0.05$, Dunnett's multiple comparison procedure.

TABLE 13

NUMBERICAL DISTRIBUTION OF CHROMOSOMES IN BONE MARROW OF RATS EXPOSED TO VC OR VDC

Treatment	No. of Rats	Chromosome Frequency ≤ 40	41	42	43	≥ 44	Tetraploids (4N) per 100 cells
After One Month							
Control	6	3[a]	4	42	1	0	0.25 ± 0.11[b]
VC (1,000 ppm)	6	4	4	41	1	0	0.33 ± 0.17
VDC (55 ppm)	6	3	3	43	1	0	0.42 ± 0.08
After Three Months							
Control	5	6	7	34	2	1	0.0 ± 0.0
VC (1,000 ppm)	5	9	7	30	3	1	0.0 ± 0.0
VDC (55 ppm)	3	5	5	39	1	0	0.0 ± 0.0
After Six Months							
Control	5	5	6	36	2	1	0.2 ± 0.2
VC (1,000 ppm)	5	8	6	35	1	0	0.2 ± 0.2
VDC (55 ppm)	6	6	5	36	1	0	0.33 ± 0.21
After Nine Months							
Control	5	7	3	36	1	1	0.4 ± 0.25
VC (1,000 ppm)	6	6	5	37	1	1	0.5 ± 0.22
VDC (55 ppm)	6	4	6	38	2	0	0.5 ± 0.22
After Twelve Months							
VC (1,000 ppm)	4	3	3	41	2	1	0.25 ± 0.31
VDC (55 ppm)	2	6[c]	6	38	2	0	0.5 ± 0.86

a/ Mean

b/ Mean ± S.E.

c/ Chromosome frequency based on numerical counts of 25 metaphase spreads.

TABLE 14

MORPHOLOGICAL ABERRATIONS OF CHROMOSOMES IN BONE MARROW OF RATS EXPOSED TO VC OR VDC

Treatment	No. of Mice	Chromatid Gaps per 50 Cells	Chromatid Breaks per 50 Cells	Translocations per 50 Cells	Total Aberrations per 50 Cells
		After One Month			
Control	6	0.67 ± 0.21[a/]	0.33 ± 0.33	0.33 ± 0.21	1.33 ± 0.21
VC (1,000 ppm)	6	0.83 ± 0.31	0.50 ± 0.22	0.33 ± 0.21	1.67 ± 0.56
VDC (55 ppm)	6	0.33 ± 0.21	0.87 ± 0.48	0.17 ± 0.17	1.37 ± 0.61
		After Three Months			
Control	5	0.80 ± 0.40	0.0 ± 0.0	0.25 ± 0.25	0.05 ± 0.32
VC (1,000 ppm)	5	0.14 ± 0.14	0.0 ± 0.0	0.20 ± 0.20	0.34 ± 0.21
VDC (55 ppm)	3	0.33 ± 0.33	0.53 ± 0.53	0.0 ± 0.0	0.86 ± 0.47
		After Six Months			
Control	5	0.66 ± 0.27	0.26 ± 0.26	0.20 ± 0.20	0.12 ± 0.52
VC (1,000 ppm)	5	0.20 ± 0.20	0.0 ± 0.0	0.0 ± 0.0	0.20 ± 0.20
VDC (55 ppm)	6	0.60 ± 0.28	0.33 ± 0.21	0.0 ± 0.0	0.93 ± 0.33

(Continued to next page)

TABLE 14 (Concluded)

Treatment	No. of Mice	Chromatid Gaps per 50 Cells	Chromatid Breaks per 50 Cells	Translocations per 50 Cells	Total Aberrations per 50 Cells
			After Nine Months		
Control	5	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
VC (1,000 ppm)	6	0.33 ± 0.21	0.17 ± 0.17	0.17 ± 0.17	0.67 ± 0.33
VDC (55 ppm)	6	0.33 ± 0.21	0.0 ± 0.0	0.0 ± 0.0	0.33 ± 0.21
			After Twelve Months		
VC (1,000 ppm)	4	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
VDC (55 ppm)	2	0.0 ± 0.0 b/	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0

a/ Mean ± S.E.

b/ Chromosomal aberrations based on analysis of 25 metaphase spreads.

TABLE 15

COLLAGEN CONTENT IN LIVER AND LUNG OF RATS EXPOSED TO VC OR VDC FOR 6 MONTHS

	Collagen Content (µg/gm)	
	Males	Females
Liver		
Controls	188.9 ± 25.4[a/]	226.0 ± 72.2
Vinyl Chloride (1,000 ppm)	259.8 ± 42.1	213.0 ± 16.6
Vinylidene Chloride (55 ppm)	254.7 ± 44.0	213.0 ± 16.6
Lung		
Controls	329.8 ± 111.3	363.6 ± 166.2
Vinyl Chloride (1,000 ppm)	545.9 ± 97.9	364.2 ± 26.5
Vinylidene Chloride (55 ppm)	612.3 ± 165.6	425.6 ± 74.0

a/ Mean ± S.E. of four rats.

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TABLE 16

COLLAGEN CONTENT IN LIVER AND LUNG OF RATS EXPOSED TO VC OR VDC FOR 9 MONTHS

	Collagen Content (μg/gm)	
	Males	Females
Liver		
Controls	283.8±145.6[a/]	206.2±81.1
Vinyl Chloride (1,000 ppm)	264.0±30.2	256.7±56.4
Vinylidene Chloride (55 ppm)	330.7±87.8	349.2±143.7
Lung		
Controls	151.3±35.3	188.4±31.0
Vinyl Chloride (1,000 ppm)	225.9±26.9	178.0±29.3
Vinylidene Chloride (55 ppm)	298.6±47.5	273.0±107.9

a/ Mean ± S.E. of four rats.

TABLE 17

COLLAGEN CONTENT IN LIVER AND LUNG OF RATS EXPOSED TO VC OR VDC FOR 12 MONTHS

	Collagen Content (µg/gm)	
	Males	Females
Liver		
Controls	425.6 ± 42.6[a]	388.4 ± 106.2
Vinyl Chloride (1,000 ppm)	335.0 ± 73.4[b]	293.0 ± 45.4[c]
Vinylidene Chloride (55 ppm)	465.6 ± 128.6	331.6 ± 52.6
Lung		
Controls	256.7 ± 32.5	266.2 ± 139.7
Vinyl Chloride (1,000 ppm)	151.6 ± 57.9[b]	303.2 ± 117.4[c]
Vinylidene Chloride (55 ppm)	320.2 ± 136.2	294.4 ± 55.1

a/ Mean ± S.E. of four rats.
b/ Mean ± S.E. of three rats.
c/ Mean ± S.E. of two rats.

TABLE 18

ORGAN WEIGHTS OF MALE RATS AFTER EXPOSURE TO VC OR VDC FOR 1 MONTH

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
			Absolute Weight (gm)		
Terminal Body Weight	350 ± 45[a/]	371 ± 27	367 ± 11	384 ± 26	363 ± 3
Brain	2.11 ± 0.03	1.82 ± 0.25	1.98 ± 0.02	2.04 ± 0.04	1.87 ± 0.04
	10.4 ± 0.9	11.4 ± 0.9	11.2 ± 0.5	12.4 ± 0.7	11.0 ± 0.5
Kidney	2.91 ± 0.13	3.36 ± 0.40	2.87 ± 0.08	3.20 ± 0.13	2.98 ± 0.03
Spleen	0.75 ± 0.06	0.73 ± 0.05	0.64 ± 0.02	0.80 ± 0.02	0.64 ± 0.04
Testes	3.35 ± 0.05	2.98 ± 0.14	3.07 ± 0.00	3.18 ± 0.11	3.12 ± 0.10
			Relative to Brain Weight (gm/gm)		
Liver	4.9 ± 0.4	6.6 ± 1.0	5.7 ± 0.3	6.1 ± 0.2	5.9 ± 0.3
Kidney	1.4 ± 0.1	2.1 ± 0.7	1.5 ± 0.1	1.6 ± 0.0	1.6 ± 0.0
Spleen	0.36 ± 0.03	0.43 ± 0.08	0.33 ± 0.01	0.39 ± 0.00	0.34 ± 0.02
Testes	1.59 ± 0.02	1.77 ± 0.34	1.55 ± 0.02	1.56 ± 0.05	1.66 ± 0.03

a/ Mean ± S.E. of four rats.

TABLE 19

ORGAN WEIGHTS OF FEMALE RATS AFTER EXPOSURE TO VC OR VDC FOR 1 MONTH

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
			Absolute Weight (gm)		
Terminal Body Weight	235 ± 15[a/]	235 ± 8	230 ± 8	210 ± 8	230 ± 7
Brain	1.91 ± 0.06	1.95 ± 0.04	1.88 ± 0.04	1.81 ± 0.07	1.74 ± 0.05
Liver	6.9 ± 0.2	7.3 ± 0.2	7.5 ± 0.2	7.5 ± 0.3	7.0 ± 0.2
Kidney	1.82 ± 0.09	1.92 ± 0.06	1.88 ± 0.02	1.77 ± 0.10	1.55 ± 0.23
Spleen	0.46 ± 0.02	0.51 ± 0.03	0.48 ± 0.02	0.48 ± 0.04	0.50 ± 0.04
Ovaries	0.22 ± 0.06	0.13 ± 0.01	0.14 ± 0.01	0.17 ± 0.03	0.12 ± 0.02
			Relative to Brain Weight (gm/gm)		
Liver	3.63 ± 0.05	3.72 ± 0.09	4.01 ± 0.15	4.19 ± 0.28	4.05 ± 0.22
Kidney	0.96 ± 0.06	0.98 ± 0.02	1.00 ± 0.03	0.98 ± 0.06	0.90 ± 0.14
Spleen	0.24 ± 0.01	0.26 ± 0.02	0.26 ± 0.01	0.27 ± 0.02	0.29 ± 0.03
Ovaries	0.12 ± 0.04	0.07 ± 0.01	0.07 ± 0.01	0.09 ± 0.02	0.07 ± 0.01

a/ Mean ± S.E. of four rats.

TABLE 20

ORGAN WEIGHTS OF MALE RATS AFTER EXPOSURE TO VC OR VDC FOR 2 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
			Absolute Weight (gm)		
Terminal Body Weight	477 ± 9[a/]	475 ± 11	451 ± 16	488 ± 15	479 ± 11
Brain	2.14 ± 0.05	2.09 ± 0.04	2.19 ± 0.02	2.21 ± 0.01	1.70 ± 0.28
	12.1 ± 0.4	12.4 ± 0.7	13.0 ± 0.8	14.6 ± 0.7	12.7 ± 0.6
Kidney	3.32 ± 0.17	3.25 ± 0.08	3.30 ± 0.08	3.65 ± 0.13	3.13 ± 0.11
Spleen	0.81 ± 0.05	0.74 ± 0.05	0.76 ± 0.08	0.83 ± 0.08	0.79 ± 0.05
Testes	2.83 ± 0.27	3.27 ± 0.16	3.53 ± 0.17	3.32 ± 0.10	3.08 ± 0.06
			Relative to Brain Weight (gm/gm)		
Liver	5.7 ± 0.3	6.0 ± 0.4	6.0 ± 0.4	6.6 ± 0.3	8.4 ± 1.9
Kidney	1.55 ± 0.09	1.55 ± 0.03	1.51 ± 0.03	1.65 ± 0.06	2.07 ± 0.46
Spleen	0.38 ± 0.02	0.35 ± 0.03	0.35 ± 0.03	0.38 ± 0.01	0.51 ± 0.09
Testes	1.3 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	1.5 ± 0.1	2.0 ± 0.5

a/ Mean ± S.E. of four rats.

TABLE 21

ORGAN WEIGHTS OF FEMALE RATS AFTER EXPOSURE TO VC OR VDC FOR 2 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
			Absolute Weight (gm)		
Terminal Body Weight	271 ± 8[a/]	274 ± 9	273 ± 12	265 ± 3	270 ± 11
Brain	2.08 ± 0.04	2.16 ± 0.09	2.03 ± 0.03	1.98 ± 0.05	1.84 ± 0.03[b/]
Liver	7.4 ± 0.3	8.0 ± 0.8	8.1 ± 0.2	7.9 ± 0.1	6.9 ± 0.3
Kidney	1.97 ± 0.06	2.13 ± 0.07	2.02 ± 0.03	1.95 ± 0.05	1.59 ± 0.18
Spleen	0.59 ± 0.05	0.54 ± 0.05	0.58 ± 0.04	0.50 ± 0.02	0.48 ± 0.01
Ovaries	0.14 ± 0.02	0.18 ± 0.02	0.15 ± 0.00	0.13 ± 0.01	0.11 ± 0.00
			Relative to Brain Weight (gm/gm)		
Liver	3.57 ± 0.16	3.66 ± 0.20	4.02 ± 0.09	3.98 ± 0.06	3.75 ± 0.20
Kidney	0.95 ± 0.01	0.99 ± 0.03	1.00 ± 0.02	0.99 ± 0.04	0.86 ± 0.11
Spleen	0.28 ± 0.03	0.25 ± 0.03	0.29 ± 0.02	0.25 ± 0.01	0.26 ± 0.01
Ovaries	0.07 ± 0.01	0.08 ± 0.01	0.07 ± 0.00	0.06 ± 0.00	0.06 ± 0.00

a/ Mean ± S.E. of four rats.

b/ Significantly different from control, $p < 0.05$, Dunnett's Multiple Comparison procedure.

TABLE 22

ORGAN WEIGHTS OF MALE RATS AFTER EXPOSURE TO VC OR VDC FOR 3 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
			Absolute Weight (gm)		
Terminal Body Weight	554 ± 21[a/]	519 ± 35	516 ± 37	500 ± 12	520 ± 17
Brain	2.22 ± 0.05	2.18 ± 0.05	2.22 ± 0.07	2.23 ± 0.04	2.36 ± 0.22
Liver	15.0 ± 0.4	13.8 ± 0.5	12.8 ± 1.3(3)	14.2 ± 0.6	13.9 ± 0.3
Kidney	3.65 ± 0.19	3.28 ± 0.18	3.42 ± 0.10(3)	3.30 ± 0.21	3.43 ± 0.33
Spleen	0.76 ± 0.03	0.80 ± 0.12	0.78 ± 0.07(3)	0.83 ± 0.07	0.77 ± 0.07
Testes	3.4 ± 0.1	3.5 ± 0.1	3.4 ± 0.0	2.9 ± 0.5	3.4 ± 0.2
			Relative to Brain Weight (gm/gm)		
Liver	6.8 ± 0.3	6.3 ± 0.1	5.6 ± 0.6 (3)	6.4 ± 0.3	6.0 ± 0.4
Kidney	1.65 ± 0.12	1.50 ± 0.06	1.49 ± 0.03(3)	1.48 ± 0.10	1.51 ± 0.24
Spleen	0.34 ± 0.02	0.36 ± 0.05	0.34 ± 0.03(3)	0.38 ± 0.03	0.33 ± 0.02
Testes	1.53 ± 0.06	1.61 ± 0.04	1.54 ± 0.06	1.29 ± 0.21	1.50 ± 0.17

a/ Mean ± S.E. of four rats except as noted in parentheses.

TABLE 23

ORGAN WEIGHTS OF FEMALE RATS AFTER EXPOSURE TO VC OR VDC FOR 3 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
			Absolute Weight (gm)		
Terminal Body Weight	322 ± 10[a/]	309 ± 6	284 ± 2[b/]	305 ± 10	278 ± 9[b/]
Brain	2.06 ± 0.08	2.13 ± 0.03	2.05 ± 0.01	2.02 ± 0.02	1.91 ± 0.03
Liver	8.6 ± 0.4	8.4 ± 0.2	8.4 ± 0.3	8.7 ± 0.5	7.1 ± 0.3
Kidney	2.08 ± 0.06	2.26 ± 0.05	2.22 ± 0.07	2.13 ± 0.08	1.98 ± 0.04
Spleen	0.55 ± 0.04	0.63 ± 0.06	0.58 ± 0.03	0.57 ± 0.02	0.48 ± 0.02
Ovaries	0.14 ± 0.01	0.17 ± 0.02	0.16 ± 0.01	0.15 ± 0.01	0.17 ± 0.02
			Relative to Brain Weight (gm/gm)		
Liver	4.16 ± 0.16	3.97 ± 0.09	4.08 ± 0.16	4.29 ± 0.27	3.74 ± 0.18
Kidney	1.01 ± 0.03	1.06 ± 0.01	1.09 ± 0.04	1.06 ± 0.04	1.04 ± 0.02
Spleen	0.27 ± 0.02	0.29 ± 0.03	0.29 ± 0.02	0.28 ± 0.01	0.25 ± 0.02
Ovaries	0.07 ± 0.00	0.08 ± 0.01	0.08 ± 0.01	0.08 ± 0.01	0.09 ± 0.01

a/ Mean ± S.E. of four rats.

b/ Significantly different from control, $p < 0.05$, Dunnett's Multiple Comparison procedure.

TABLE 24

ORGAN WEIGHTS OF MALE RATS EXPOSED TO VC OR VDC FOR 6 MONTHS

Group	Control	50 ppm VC	250 ppm VC	1,000 ppm VC	55 ppm VDC
	Absolute Weight (gm)				
Terminal body weight	632 ± 30[a/]	660 ± 12	686 ± 20	607 ± 0.32	623 ± 15
Brain	2.82 ± 0.18	2.41 ± 0.11	2.17 ± 0.13	2.11 ± 0.08	2.17 ± 0.06
Liver	16.6 ± 1.9	16.4 ± 0.7	17.4 ± 0.6	16.4 ± 1.4	16.0 ± 1.0
Kidney	4.13 ± 0.33	4.09 ± 0.20	4.01 ± 0.19	3.74 ± 0.24	3.87 ± 0.20
Spleen	1.17 ± 0.05	1.10 ± 0.06	0.95 ± 0.11	0.86 ± 0.03[b/]	0.85 ± 0.03[b/]
Testes	3.29 ± 0.32	3.40 ± 0.14	3.59 ± 0.07	3.46 ± 0.20	3.49 ± 0.24
	Relative to Brain Weight (gm/gm)				
Liver	7.6 ± 1.6	6.8 ± 0.1	8.1 ± 0.8	7.4 ± 0.6	7.4 ± 0.4
Kidney	1.88 ± 0.30	1.70 ± 0.06	1.87 ± 0.15	1.69 ± 0.09	1.78 ± 0.10
Spleen	0.53 ± 0.06	0.46 ± 0.04	0.45 ± 0.07	0.39 ± 0.02	0.39 ± 0.01
Testes	1.50 ± 0.25	1.42 ± 0.10	1.67 ± 0.09	1.57 ± 0.12	1.61 ± 0.10

a/ Mean ± S.E. of four rats.
b/ Significantly different from Control group (Dunnett's multiple comparison procedure).

TABLE 25

ORGAN WEIGHTS OF FEMALE RATS EXPOSED TO VC OR VDC FOR 6 MONTHS

Group	Control	50 ppm VC	250 ppm VC	1,000 ppm VC	55 ppm VDC
	Absolute Weight (gm)				
Terminal body weight	360 ± 29[a/]	315 ± 34	329 ± 12	310 ± 11	347 ± 16
Brain	2.16 ± 0.03	2.08 ± 0.08	2.13 ± 0.06	2.06 ± 0.07	1.87 ± 0.06[b/]
Liver	8.7 ± 0.7	8.7 ± 0.3	8.8 ± 0.3	8.7 ± 0.3	8.4 ± 0.4
Kidney	2.16 ± 0.11	2.38 ± 0.17	2.31 ± 0.15	2.08 ± 0.14	2.14 ± 0.16
Spleen	0.61 ± 0.04	0.58 ± 0.06	0.69 ± 0.08	0.07 ± 0.06	0.53 ± 0.04
Ovaries	0.30 ± 0.13	0.13 ± 0.03	0.19 ± 0.02	0.21 ± 0.03	0.15 ± 0.02
	Relative to Brain Weight (gm/gm)				
Liver	4.05 ± 0.35	4.21 ± 0.02	4.16 ± 0.14	4.21 ± 0.22	4.48 ± 0.18
Kidney	1.00 ± 0.06	1.15 ± 0.08	1.09 ± 0.07	1.01 ± 0.07	1.14 ± 0.05
Spleen	0.28 ± 0.02	0.28 ± 0.02	0.32 ± 0.03	0.34 ± 0.04	0.28 ± 0.02
Ovaries	0.14 ± 0.06	0.06 ± 0.01	0.09 ± 0.01	0.10 ± 0.02	0.08 ± 0.01

a/ Mean ± S.E. of four rats.
b/ Significantly different from Control group (Dunnett's multiple comparison procedure).

TABLE 26

ORGAN WEIGHTS OF MALE RATS EXPOSED TO VC OR VDC FOR 9 MONTHS

	Control	50 PPM VC	250 PPM VC	1,000 PPM VC	55 PPM VDC
			Absolute Weight (gm)		
Terminal Body Weight	682 ± 40[a/]	669 ± 18	724 ± 22	658 ± 15	688 ± 27
Brain	2.37 ± 0.06	2.27 ± 0.11	2.38 ± 0.03	2.47 ± 0.08	2.13 ± 0.07
Liver	18.0 ± 0.9	16.7 ± 0.9	18.7 ± 0.5	17.9 ± 0.9	14.9 ± 0.9
Kidney	4.10 ± 0.12	4.11 ± 0.25	4.27 ± 0.11	3.90 ± 0.15	4.07 ± 0.19
Spleen	0.98 ± 0.03	0.93 ± 0.06	1.07 ± 0.05	0.92 ± 0.11	0.88 ± 0.06
Testes	4.43 ± 0.79	3.63 ± 0.14	3.82 ± 0.13	3.58 ± 0.29	3.37 ± 0.12
			Relative to Brain Weight (gm/gm)		
Liver	7.6 ± 0.4	7.4 ± 0.4	7.9 ± 0.3	7.2 ± 0.4	7.0 ± 0.4
Kidney	1.73 ± 0.05	1.81 ± 0.12	1.80 ± 0.05	1.58 ± 0.08	1.91 ± 0.08
Spleen	0.41 ± 0.01	0.41 ± 0.04	0.45 ± 0.02	0.37 ± 0.05	0.41 _ 0.03
Testes	1.86 ± 0.30	1.61 ± 0.12	1.61 ± 0.06	1.46 ± 0.14	1.59 ± 0.10

a/ Mean ± S.E. of four rats.

TABLE 27

ORGAN WEIGHTS OF FEMALE RATS EXPOSED TO VC OR VDC FOR 9 MONTHS

	Control	50 PPM VC	250 PPM VC	1,000 PPM VC	55 PPM VC
			Absolute Weight (gm)		
Terminal Body Weight	383 ± 37[a/]	307 ± 36(3)	347 ± 25	341 ± 15	404 ± 24
Brain	2.17 ± 0.06	2.14 ± 0.10(3)	2.21 ± 0.10	2.12 ± 0.08	1.97 ± 0.04
Liver	12.0 ± 2.0	7.9 ± 1.2(3)	10.9 ± 0.9	10.5 ± 0.3	10.2 ± 0.9
Kidney	2.36 ± 0.09	2.18 ± 0.31(3)	2.51 ± 0.16	2.46 ± 0.06	2.63 ± 0.12
Spleen	0.59 ± 0.04	0.55 ± 0.05(3)	0.61 ± 0.10	0.55 ± 0.09	0.51 ± 0.01
Ovaries	0.10 ± 0.03	0.14 ± 0.03(3)	0.14 ± 0.01	0.11 ± 0.03	0.15 ± 0.01
			Relative to Brain Weight (gm/gm)		
Liver	5.6 ± 1.0	3.7 ± 0.6(3)	5.0 ± 0.5	5.0 ± 0.2	5.2 ± 0.5
Kidney	1.09 ± 0.05	1.02 ± 0.16(3)	1.14 ± 0.07	1.16 ± 0.03	1.34 ± 0.06
Spleen	0.27 ± 0.01	0.26 ± 0.03(3)	0.28 ± 0.05	0.25 ± 0.04	0.26 ± 0.01
Ovaries	0.05 ± 0.02	0.07 ± 0.01(3)	0.06 ± 0.01	0.05 ± 0.01	0.08 ± 0.00

a/ Mean ± S.E. of four rats except as noted in parentheses.

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TABLE 28

ORGAN WEIGHTS OF MALE RATS EXPOSED TO VC OR VDC FOR 12 MONTHS

	Absolute Weight (gm)				
	Control	50 ppm VC	250 ppm VC	1,000 ppm VC	55 ppm VDC
Terminal Body Weight	815 ± 16[a/]	824 ± 24	792 ± 16	722 ± 40	769 ± 30
Brain	2.31 ± 0.04	2.33 ± 0.04	2.40 ± 0.04	2.33 ± 0.05	2.21 ± 0.05
Liver	18.9 ± 0.3	22.3 ± 1.4	19.6 ± 1.0	20.5 ± 1.5	17.3 ± 0.8
Kidney	4.43 ± 0.13	5.07 ± 0.29	4.48 ± 0.27	4.33 ± 0.19	4.40 ± 0.09
Spleen	0.9 ± 0.1	1.1 ± 0.0	1.0 ± 0.1	2.3 ± 1.3	1.0 ± 0.1
Testes	3.67 ± 0.16	3.57 ± 0.06	3.40 ± 0.13	3.52 ± 0.19	3.61 ± 0.09
	Relative to Brain Weight (gm/gm)				
Liver	8.2 ± 0.2	9.6 ± 0.5	8.2 ± 0.4	8.8 ± 0.7	7.9 ± 0.4
Kidney	1.92 ± 0.07	2.18 ± 0.12	1.87 ± 0.11	1.86 ± 0.09	1.99 ± 0.04
Spleen	0.4 ± 0.0	0.5 ± 0.0	0.4 ± 0.0	1.0 ± 0.6	0.4 ± 0.0
Testes	1.60 ± 0.08	1.54 ± 0.05	1.42 ± 0.05	1.52 ± 0.09	1.64 ± 0.06

a/ Mean ± S.E. of eight rats.

TABLE 29

ORGAN WEIGHTS OF FEMALE RATS EXPOSED TO VC OR VDC FOR 12 MONTHS

	Control	50 ppm VC	250 ppm VC	1,000 ppm VC		55 ppm VDC
			Absolute Weight (gm)			
Terminal Body Weight	473 ± 15[a/]	416 ± 15	391 ± 24[b/]	412 ± 62	(2)	428 ± 22
Brain	2.18 ± 0.04	2.14 ± 0.02	2.13 ± 0.02	2.15 ± 0.07	(2)	2.08 ± 0.05
Liver	11.2 ± 0.6	10.4 ± 0.4	14.2 ± 2.4	19.9 ± 7.6[b/]	(2)	10.6 ± 0.4
Kidney	2.85 ± 0.19	2.50 ± 0.10	2.51 ± 0.09	3.11 ± 0.00	(2)	2.70 ± 0.07
Spleen	0.7 ± 0.1	0.7 ± 0.0	1.2 ± 0.5	2.1 ± 1.1	(2)	0.6 ± 0.0
Ovary	0.12 ± 0.01	0.17 ± 0.02	0.17 ± 0.03	0.12 ± 0.03	(2)	0.17 ± 0.01
			Relative to Brain Weight (gm/gm)			
Liver	5.1 ± 0.3	4.9 ± 0.2	6.7 ± 1.1	9.2 ± 3.2[b/]	(2)	5.1 ± 0.2
Kidney	1.31 ± 0.09	1.17 ± 0.04	1.18 ± 0.05	1.45 ± 0.05	(2)	1.30 ± 0.02
Spleen	0.33 ± 0.03	0.33 ± 0.02	0.57 ± 0.21	0.94 ± 0.50	(2)	0.29 ± 0.02
Ovary	0.06 ± 0.01	0.08 ± 0.01	0.08 ± 0.01	0.06 ± 0.12	(2)	0.08 ± 0.01

a/ Mean ± S.E. of eight rats unless otherwise indicated in parentheses

b/ Significantly different from control group, $p < 0.05$; Dunnett's multiple comparison procedure.

TABLE 30

SUMMARY OF TUMORS THAT OCCURRED IN RATS DURING 7 TO 9 MONTHS EXPOSURE TO VC OR VDC[a/]

	250 PPM VC		1,000 PPM VC						55 PPM VDC	
Sex	Female		Male	Female					Male	Female
Rat No.	197	200	252[c/]	269	270	271	288[c/]	287[c/]	286[c/]	305	360[c/]
Tumor[b/] Week Terminated	39	39	39	39	39	39	33	35	38	39	39
Liver											
Hemangiosarcoma	3	3			1	1		3	3		
Lung											
Hemangiosarcoma		3						1			
Mammary Gland											
Duct adenocarcinoma		2									2
Skin (subcutaneous)											
Hemangiosarcoma										1	
Squamous cell carcinoma			3								
Adrenal Gland											
Hemangioma				1			3				
Sebaceous gland											
Adenocarcinoma							3				

a/ Includes only rats which were found to have tumors during 7 to 9 months exposure to VC or VDC.

b/ Severity of lesion: 1 - mild; 2 - moderate; 3 - marked; 4 - severe.

c/ Died or unscheduled termination. No tumors were found in control rats during this period.

TABLE 31

SUMMARY OF TUMORS THAT OCCURRED IN CONTROL RATS AND RATS EXPOSED 10 TO 12 MONTHS TO 50 OR 250 PPM VC[a/]

	Control	50 ppm VC			250 ppm VC														
Sex	Female	Male	Female		Male				Female										
Rat No.	63	94	144[c/]	143[c/]	165	166	167	179[c/]	201	202	203	205	207	208	213[c/]	212[c/]	211[c/]	210[c/]	209[c/]
Tumor[b/] Week Terminated	52	52	40	50	52	52	52	50	52	52	52	52	52	52	48	49	49	51	51
Lung																			
Hemangiosarcoma										2									3
Squamous cell carcinoma						3													
Liver																			
Hemangiosarcoma					3			1	2	3		1	3	3			3	3	3
Hepatoma		3																	
Mammary gland																			
Adenocarcinoma	2		2							2						2	3	2	
Fibroadenoma															2				
Spleen																			
Malignant lymphoma														2					
Omentum																			
Hemangiosarcoma							2												
Mesentery																			
Hemangiosarcoma								4											
Skin																			
Hemangiosarcoma				3															
Pituitary																			
Chromophobe cell adenoma											2								

a/ Includes only rats that were found to have tumors during 10 to 12 months exposure to VC.
b/ Severity of lesions; 1 - mild; 2 - moderate; 3 - marked; 4 - severe.
c/ Death or unscheduled termination.

TABLE 32

SUMMARY OF TUMORS THAT OCCURRED IN RATS DURING 10 TO 12 MONTHS EXPOSURE TO 1,000 PPM VC OR 55 PPM VDC[a/]

Tumor[b/]	Sex	1,000 ppm VC																				55 ppm VDC
		Male									Female											Male
	Rat No.	237	238	240	241	242	251[c/]	250[c/]	248[c/]	247[c/]	246[c/]	274	275	285[c/]	284[c/]	283[c/]	282[c/]	281[c/]	280[c/]	279[c/]	278[c/]	277[c/]	276[c/]	313
	Week Terminated	52	52	52	52	52	45	48	49	49	50	52	52	40	43	46	46	46	47	48	49	50	51	52
Lung																								
Hemangiosarcoma					2		3	3			4	4	1		2			2	3	1	3	3		
Bronchiolar adenoma			1																					
Liver																								
Hemangiosarcoma		3		3	3		3	2			4	3	3	3	3		3	2	4	4	4	4	4	
Reticuloendothelial cell carcinoma																						1		
Mammary gland																								
Fibroadenoma																				3				
Malignant lymphoma						3													3		1			
Kidney																								
Adenoma											1											2		
Omentum																								
Hemangiosarcoma											1											3		
Mesentery																								
Hemangiosarcoma												4						3				2		
Mesenteric lymph node																								
Hemangiosarcoma																								2
Skin																								
Keratoacanthoma										1						1								
Fibroma									1															

a/ Includes only rats that were found to have tumors during 10 to 12 months exposure to VC or VDC.

b/ Severity of lesions: 1 - mild; 2 - moderate; 3 - marked; 4 - severe; 1 - questionable.

c/ Death or unscheduled termination.

TABLE 33

CUMULATIVE TUMOR INCIDENCE IN RATS DURING 12 MONTHS EXPOSURE TO VC OR VDC

	Control		50 ppm VC		250 ppm VC		1,000 ppm VC		55 ppm VDC	
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Tumor										
Lung										
Hemangiosarcoma	0/35	0/35	0/36	0/36	0/36	3/34	4/34	9/36	0/36	0/35
Bronchiolar adenoma	0/35	0/35	0/36	0/36	0/36	0/34	1/34	0/36	0/36	0/35
Squamous cell carcinoma	0/35	0/35	0/36	0/36	1/36	0/34	0/34	0/36	0/36	0/35
Liver										
Hemangiosarcoma	0/35	0/35	0/36	0/36	2/36	10/34	6/34	15/36	0/36	0/35
Reticuloendothelial cell carcinoma	0/35	0/35	0/36	0/36	0/36	0/34	0/34	1/36	0/36	0/35
Hepatoma	0/35	0/35	1/36	0/36	1/36	0/34	0/34	0/36	0/36	0/35
Mammary gland										
Duct adenocarcinoma	0/35	1/35	0/36	0/36	0/36	5/34	0/34	0/36	0/36	1/35
Fibroadenoma	0/35	0/35	0/36	0/36	0/36	1/34	0/34	1/36	0/36	0/35
Malignant lymphoma	0/35	0/35	0/36	0/36	0/36	1/34	1/34	2/36	0/36	0/35
Kidney										
Adenoma	0/35	0/35	0/36	0/36	0/36	0/34	1/34	1/36	0/36	0/35
Hemangiosarcoma										
Omentum	0/35	0/35	0/36	0/36	1/36	0/34	1/34	1/36	0/36	0/35
Mesentery	0/35	0/35	0/36	0/36	1/36	0/34	0/34	3/36	0/36	0/35
Mesenteric lymph nodes	0/35	0/35	0/36	0/36	0/36	0/34	0/34	0/36	1/36	0/35
Skin	0/35	0/35	0/36	1/36	0/36	0/34	0/34	0/36	1/36	0/35
Adrenal										
Hemangioma	0/35	0/35	0/36	0/36	0/36	0/34	0/34	2/36	0/36	0/35

(continued to next page)

TABLE 33 (Concluded)

CUMULATIVE TUMOR INCIDENCE IN RATS DURING 12 MONTHS EXPOSURE TO VC OR VDC

	Control		50 ppm VC		250 ppm VC		1,000 ppm VC		55 ppm VDC	
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Skin										
Squamous cell carcinoma	0/35	0/35	0/36	0/36	0/36	0/34	1/34	0/36	0/36	0/35
Keratoacanthoma	0/35	0/35	0/36	0/36	0/36	0/34	1/34	1/36	0/36	0/35
Fibroma	0/35	0/35	0/36	0/36	0/36	0/34	1/34	0/36	0/36	0/35
Sebaceous gland										
Adenocarcinoma	0/35	0/35	0/36	0/36	0/36	0/34	0/34	1/36	0/36	0/35
Pituitary										
Chromophobe cell adenoma	0/35	0/35	0/36	0/36	0/36	1/34	0/34	0/36	0/36	0/35

a/ Number of rats with tumor/total number of rats that died or were terminated during 12 months exposure to VC or VDC.

TABLE 34

SUMMARY OF TISSUE LESIONS AND M/E RATIOS IN RATS AFTER EXPOSURE TO VC OR VDC FOR 1 MONTH

	Controls								VC (1,000 ppm)								VDC (55 ppm)							
Sex:	Males				Females				Males				Females				Males				Females			
Lesions / Rat No:	1	2	3	4	37	38	39	40	217	218	219	220	253	254	255	256	289	290	291	292	325	326	327	328
Trachea																								
Chronic tracheitis	1				1				1			1	1											
Lung																								
Perivasculitis	1	1	1	1	1	1	1	2	1	3	2	1	1	1	1	1	3	3	1	1	2	2	2	1
Peribronchiolitis	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1		1
Pneumonia			1	1	1		1	1	1	2		2		1		1	1	2	2		1	2		1
Liver																								
Microfoci of mononuclear cells	1	1	1	1	1	1	1	1			1	1	1		1	1	1		1	1	1	1	1	1
Vacuolization of hepatocytes		1	1	1		1		1					1		1		1	1	1	1	1	1	1	1
Kidney																								
Chronic interstitial nephritis	1	1	1		1	1		1			1	1	1										1	
Microcalculi	1			1		1	1																1	1
Heart																								
Myocarditis												1												
Bone Marrow																								
M/E ratio	1.4	1.3	1.5	1.5	1.4	1.6	1.6	1.5	1.3	1.4	1.4	N/A	1.3	1.5	1.3	1.4	1.4	1.3	1.2	1.2	1.2	1.4	1.3	1.3

a/ Severity of lesion: 1 - mild, 2 - moderate, 3 - marked, 4 - severe, ± - questionable, N/A - not available.

TABLE 35

SUMMARY OF TISSUES LESIONS AND M/E RATIOS IN RATS AFTER EXPOSURE TO VC OR VDC FOR 2 MONTHS

	Controls								VC (1,000 ppm)								VDC (55 ppm)							
Sex:	Males				Females				Males				Females				Males				Females			
Lesions[a/] Rat No:	5	6	7	8	41	42	43	44	221	222	223	224	257	258	259	260	293	294	295	296	329	330	331	332
Lung																								
Perivasculitis	1	1	1	1	1	1			2	1	1	1	1	1	1	1	2	2	1	1	1	1	1	1
Peribroncheolitis	1	1		1	1	1		1	1	1	1	1	1	1		1	1	1	1	1	1			1
Pneumonia		1		1					1		1						1	1		1	1	1		
Trachea																								
Tracheitis																		1						
Liver																								
Microfoci of mononuclear cells	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1		1	1	1	1	1	1	1
Vacuolization of hepatocytes	1	1	1					1		1	1	1			1			1	1	1	1	1	1	1
Kidney																								
Chronic interstitial nephritis											1							1	1					
Heart																								
Myocarditis		1	1	1							1													
Skeletal Muscle																								
Myositis																							1	
Cecum																								
Pinworms																			1					
Bone Marrow																								
M/E ratio	1.5	1.3	1.3	1.5	1.4	1.3	1.4	1.3	1.5	1.4	1.5	1.3	1.2	1.3	1.4	1.5	1.3	1.4	1.2	1.4	1.3	1.4	1.4	1.3

a/ Severity of lesion: 1 - mild, 2 - moderate, 3 - marked, 4 - severe, ± - questionable.

TABLE 36

SUMMARY OF TISSUE LESIONS AND M/E RATIOS IN RATS AFTER EXPOSURE TO VC OR VDC FOR 3 MONTHS

Lesions[a/]	Sex	Control								VC (1,000 ppm)								VDC (55 ppm)							
		Male				Female				Male				Female				Male				Female			
	Rat No.	9	10	11	12	45	46	47	48	225	226	227	228	261	262	263	264	297	298	299	300	333	334	335	336
Eye																									
Retinal rosettes				1																		1			
Heart																									
Focal, chronic myocarditis		1	1						1		1	1	1												
Lung																									
Focal, chronic murine pneumonia			1		1							1					1	1	1	1	1	1	1	1	1
Liver																									
Microfoci of mononuclear cells		1	1	2	1	1	1	1	1	1	1	1	1		1	1	1	1	1	1	1	1	1	1	1
Focal vacuolization																		2			1				
Focal necrosis			1																						
Cecum																									
Pinworms in lumen																								1	
Pancreas																									
Focal, chronic pancreatitis																			1		1				
Kidney																									
Focal, chronic interstitial nephritis				1	1			1						1		1	1				1	1	1		1
Dilation of the pelvis				1																					
Microcalculi														1				1					2		
Testis																									
Tubular degeneration													2												
Prostate																									
Focal, chronic prostatitis			1																						
Ovary																									
Cystic							1																		
Bone Marrow																									
M/E ratio		1.5	1.5	1.4	1.6	1.5	1.5	1.4	1.5	1.7	1.6	1.5	1.6	1.5	1.5	1.6	1.7	1.6	1.4	1.6	1.7	1.6	1.7	1.6	1.5

a/ Severity of lesions: 1 - mild, 2 - moderate, 3 - marked, 4 - severe, ± - questionable.

TABLE 37

SUMMARY OF TISSUE LESIONS AND M/E RATIOS IN RATS EXPOSED TO VC OR VDC FOR 6 MONTHS

	Controls								VC (1,000 ppm)								VDC (55 ppm)							
Sex:	Males				Females				Males				Females				Males				Females			
Lesions[a] / Rat No.:	13	14	15	16	49	50	51	52	229	230	231	232	265	266	267	268	301	302	303	304	337	338	339	340
Eye																								
Retinal folds and rosettes				1																				
Heart																								
Myocarditis	1	1	1	1		1	1	1	2	2	1	1	1		1			1						
Hemorrhage													1											
Lung																								
Chronic murine pneumonia	1		1	1	1	1	1	1	1	1	1	1	2	1				1	1	1		1		1
Emphysema					1																1	1		
Foam cell infiltration								1											1	1				1
A focus of papillary proliferation														±										
Liver																								
Microfoci of mononuclear cells	1	1	1	1	1	1	1	1	1	1	1	1		1	1		1	1	1	1	1	1	1	1
Portal inflammation	1		1	1	1	1			1	1		1	1	1		1		1					1	
Fatty change											1						1	1	1	3	1	1	1	1
Pancreas																								
Chronic interstitial pancreatitis		1															1							
Cecum																								
Pinworms	1		1																					1
Kidney																								
Chronic interstitial nephritis	1	1		1	1		1	1	1		1	1				1	1	1	1	1		1		1
Microcalculi					1								1		1						1	1	1	
Pyelitis													1			1								
Testis																								
Tubular degeneration & necrosis with mineralization & sperm granuloma				3																				
Brain																								
Hemorrhage											1					1								
Gliosis											1													
Bone Marrow																								
M/E Ratio	1.5	1.4	1.3	1.4	1.5	1.4	1.5	1.4	1.2	1.4	1.3	1.3	1.1	1.2	1.3	1.2	1.4	1.3	1.4	1.4	1.3	1.4	1.5	1.3

Tissues not listed were normal.

a/ Severity of lesions: 1 - mild, 2 - moderate, 3 - marked, 4 - severe ± = questionable.

TABLE 38

SUMMARY OF TISSUE LESIONS (OTHER THAN TUMORS) AND M/E RATIOS IN RATS EXPOSED TO VC OR VDC FOR 9 MONTHS[a/]

	Controls								VC (1,000 ppm)								VDC (55 ppm)							
	Males				Females				Males				Females				Males				Females			
Lesion[b/]	17	18	19	20	53	54	55	56	233	234	235	236	269	270	271	272	305	306	307	308	341	342	343	344
Eye (retina and/or lens)																								
Degeneration and/or atrophy				2	1		1	3	2		2		3	2	3	2								
Inflammation				2	1		1	1						2	1									
Heart																								
Focal myocarditis	1	1	1	1						1	1	1						1	1				1	
Lung																								
Chronic murine pneumonia		1	1	1	1				1	1	1	1	1	1		1	1	1	1	1	1	1	1	1
Papillary proliferation of bronchiolar epithelium																	1							
Liver																								
Portal inflammation																	1							
Microfoci of mononuclear cells	1		1	1	1	1	1	1	1	1	1		1				1	1	1					1
Fatty change					1	1		1	1							1		1	1	1	2	1	3	1
Pancreas																								
Subacute inflammation									1		1													
Cecum																								
Pinworms	1			1	1						1				1									
Kidney																								
Microcalculi														1										
Chronic interstitial nephritis	2		1	1	1		1	1	1	1	1	1	1	1	1	1	1	1	1	3			1	
Tubular dilation and casts	1											1						1	1	3				
Epididymis																								
Vacuolization of tubular epithelium									1			1												
Prostate																								
Subacute prostatitis		1																						
Pituitary																								
Focal hemorrhage																	1							
Adrenal																								
Hemorrhage and hemosiderosis																					1			1
Thyroid																								
Chronic inflammation	1																							
Mesenteric Lymph Node																								
Hemosiderosis					1																			
Bone Marrow Smear																								
M/E ratio	1.6	0.9	1.3	1.4	1.4	1.5	1.2	1.6	1.5	1.6	1.3	1.4	1.3	--	1.4	1.5	1.6	1.7	1.5	1.6	1.5	1.4	1.8	1.5

a/ Does not include deaths and unscheduled terminations that occurred during 7 to 9 months.

b/ Severity of lesions: 1 - mild; 2 - moderate; 3 - marked; 4 - severe; ± - questionable.

TABLE 39

SUMMARY OF TISSUE LESIONS (OTHER THAN TUMORS) AND M/E RATIOS IN RATS EXPOSED TO VC OR VDC FOR 12 MONTHS[a/]

	Controls																1,000 ppm (VC)										
	Males								Females								Males								Females		
Lesions[b/]	21	22	23	24	25	26	27	28	57	58	59	60	61	62	63	64	237	238	239	240	241	242	243	244	273	274	275
Eye																											
Retinal degeneration	1	1		2	1		1				1			2	1				1			1	1				1
Uveitis	1																										
Heart																											
Myocarditis	2	1	1	1	1			1								1	1		1		1		1	2			
Lung																											
Chronic murine pneumonia		1		1	1		1	1				1							1				1	1			
Liver																											
Distended sinusoids																		2	1					1	1		
Fibrosis																1		1	1								
Microfoci of mononuclear cells	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1		1					1	1	1		
Vacuolization (nodular or disseminated)	1		1							1		1		1		1		1	1				1	2	1		
Degeneration and/or necrosis				1																					1		
Cecum																											
Pigment in lumen		1			1			1		1	1	1	1			1		1	1								
Kidney																											
Microcalculi										1																	
Chronic interstitial nephritis	1	1			1		1		2	1				1					1		1				1		1
Tubular dilation and casts		2					1	1	2								2	1	1			1	1	2	1	2	
Pigment in tubules														1													
Pyelonephritis																											
Urinary Bladder																											
Inflammation														2													
Testis																											
Tubular degeneration and necrosis				1													2										
Adrenal																											
Hemorrhage															1												
Distended sinusoids	1								2	1		1	2		2			2				2			1		
Hemosiderosis															2										1		
Pancreas																											
Chronic pancreatitis																			1								
Spleen																											
Extramedullary hematopoiesis																										2	3
Lymphoid hyperplasia																										3	
Bone Marrow Smear																											
M/E Ratio	1.8	1.7	1.6	1.8	1.8	1.6	1.5	1.8	1.5	1.7	1.7	1.1	1.7	1.8	1.6	1.7	1.6	1.7	2.0	1.2	1.7	2.2	1.8	1.5	1.6	--	1.6

TABLE 39 (Concluded)

Lesions[b/]	55 ppm (VDC)															
	Males								Females							
	309	310	311	312	313	314	315	316	345	346	347	348	349	350	351	352
Heart																
Myocarditis	1		1				1									
Lung																
Chronic murine pneumonia					1	1										1
Liver																
Microfoci of mononuclear cells	1			1	1		1	1	1			1	1	1	1	1
Vacuolization (nodular or disseminated)	1	3	2	1	1	2	1	2		2			2	4	1	1
Degeneration and/or necrosis		1														
Parasitic infection (coccidiosis)											2					
Cecum																
Pinworms in lumen							1		1							
Kidney																
Chronic interstitial nephritis	1	1	1	2	1	2	1	2					1	1		
Tubular dilation and casts		1		2		2		2		1			1			
Pituitary																
Cyst							1									
Adrenal																
Distended sinusoids																3
Pancreas																
Chronic pancreatitis			1													
Bone Marrow Smear																
M/E Ratio	1.6	1.6	1.8	1.8	--	1.6	1.7	1.8	1.9	1.8	1.8	1.8	1.7	1.6	1.8	1.8

a/ Does not include unscheduled terminations that occurred during 10 to 12 months.

b/ Severity of lesions: 1 - minimal; 2 - moderate; 3 - severe; 4 - very severe; and ± - questionable.

TABLE 40

NUMBER OF DEATHS AND UNSCHEDULED TERMINATIONS OF MICE EXPOSED TO VC OR VDC

Treatment	Sex	During Exposure Month 6	7	8	9	10	11	12
Control	Male	-	-	1	1	-	-	-
	Female	-	-	-	-	-	-	-
VC-50 ppm	Male	1	1	1	1	1	-	1
	Female	1	2	4	4	-	2	1
VC-250 ppm	Male	-	1	4	2	1	-	1
	Female	3	4	10	-	-	-	-
VC-1,000 ppm	Male	2	3	5	3	-	-	-
	Female	2	9	6	4	-	-	-
VC-55 ppm	Male	-	-	-	2	-	-	-
	Female	-	-	-	-	-	-	1

TABLE 41

LABORATORY DATA OF MALE MICE AFTER EXPOSURE TO VC OR VDC FOR 1 MONTH

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
ERYTHROCYTES ($X10^6$ /MM^3)	8.17 ± .66	6.33 ± .80 (3)	6.99 ± .48	7.27 ± .43	6.83 ± .44
RETICULOCYTES, %	1.08 ± .09	1.08 ± .28 (3)	1.63 ± .28	.74 ± .23	1.27 ± .21
HEMATOCRIT, VOL. %	45.5 ± .6	44.3 ± 2.7 (3)	45.8 ± 2.8	47.3 ± 2.1	46.5 ± 1.2
HEMOGLOBIN, GM. %	13.4 ± .3	13.0 ± 1.2 (3)	15.1 ± .4	14.0 ± .6	14.0 ± .6
MCV, CUBIC MICRONS	56.8 ± 4.5	71.3 ± 4.9 (3)[a/]	65.5 ± 1.7	65.2 ± 1.7	68.6 ± 2.9
MCHB, MICRO MICROGMS.	16.7 ± 1.2	20.7 ± 1.0 (3)	21.8 ± 1.5[a/]	19.3 ± .5	20.7 ± 1.0
MCHBC, GM %	29.4 ± .5	29.2 ± 1.0 (3)	33.4 ± 2.6	29.6 ± .2	30.1 ± .7
PLATELETS ($X10^5$ /MM^3)	3.6 ± 1.0	6.1 ± .9 (3)	4.7 ± 1.1	4.6 ± .9	5.4 ± .8
LEUKOCYTES ($X10^3$ /MM^3)	4.2 ± .5	5.2 ± .6 (3)	6.3 ± .8	6.4 ± 1.2	6.8 ± 1.1
NEUTROPHILS, %	18.0 ± 4.3	27.0 ± 4.8	15.8 ± 2.3	18.8 ± 4.5	9.5 ± 2.1
LYMPHOCYTES, %	80.0 ± 5.1	71.3 ± 4.2	83.3 ± 2.0	79.3 ± 4.8	89.8 ± 1.8
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	1.0 ± .6	1.3 ± .5	.3 ± .3	.8 ± .5	.5 ± .3
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	1.0 ± .6	.5 ± .5	.8 ± .5	1.0 ± 1.0	.3 ± .3
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	.3 ± .3	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
SGPT, IU/L	70 ± 5 (2)	170 ± 59 (2)	119 ± 5 (2)	95 ± 2 (2)	282 ± 19 (2)[a/]
BUN, MG %	21.5 ± 2 (2)	28.5 ± 9 (2)		17.5 ± 1 (2)	19.0 ± 3 (2)
MACROPHAGES (NO./MM^3)	20 ± 5 (2)			31 ± 8 (3)	72 ± 24

Entries are mean ± S.E. of 4 mice except as noted in parentheses.

a/ Significantly different from the Control Group, $p < 0.05$, Dunnett's multiple comparison procedure.

TABLE 42

LABORATORY DATA OF FEMALE MICE AFTER EXPOSURE TO VC OR VDC FOR 1 MONTH

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
ERYTHROCYTES ($X10^6$ /MM^3)	7.47 ± .14	6.98 ± .66	7.21 ± .29	7.16 ± .33 (3)	7.40 ± .56 (3)
RETICULOCYTES, %	.96 ± .10	1.19 ± .31	1.60 ± .34	1.06 ± .14 (3)	1.71 ± .58
HEMATOCRIT, VOL. %	49.0 ± .9	47.5 ± 2.7	48.3 ± 2.4	44.7 ± 2.2 (3)	41.8 ± 7.4
HEMOGLOBIN, GM. %	14.5 ± .4	14.6 ± .8	14.5 ± .7	12.9 ± .7 (3)	15.0 ± .6 (3)
MCV, CUBIC MICRONS	65.6 ± 1.0	68.9 ± 3.2	66.9 ± 1.0	62.4 ± 2.0 (3)	66.6 ± 2.3 (3)
MCHH, MICRO MICROGMS.	19.5 ± .5	21.2 ± 1.0	20.2 ± .4	17.9 ± .2 (3)	20.4 ± .8 (3)
MCHHC, GM %	29.6 ± .6	30.8 ± .2	30.1 ± .3	28.8 ± .9 (3)	30.7 ± .1 (3)
PLATELETS ($X10^5$ /MM^3)	5.5 ± .8	6.3 ± .7	5.0 ± 1.3 (3)	4.1 ± .9 (3)	3.7 ± .4 (2)
LEUKOCYTES ($X10^3$ /MM^3)	9.0 ± 2.1	9.1 ± 2.0	8.9 ± 2.3	3.6 ± .3 (3)	5.3 ± 1.4 (3)
NEUTROPHILS, %	12.3 ± 2.0	15.3 ± 2.3	13.8 ± 3.1	24.7 ± 5.5 (3)	15.3 ± 4.8
LYMPHOCYTES, %	84.8 ± 2.8	81.3 ± 3.4	84.0 ± 4.0	73.0 ± 5.0 (3)	83.3 ± 5.5
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0 (3)	0.0 ± 0.0
EOSINOPHILS, %	1.5 ± .6	3.3 ± 1.4	2.0 ± .8	1.3 ± .0 (3)	1.0 ± .6
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0 (3)	0.0 ± 0.0
MONOCYTES, %	1.5 ± .6	.3 ± .3	.5 ± .3	.5 ± .5 (3)	.5 ± .3
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0 (3)	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0 (3)	0.0 ± 0.0
SGPT, IU/L	171 ± 47 (2)	197 ± 8 (2)	143 ± 84 (2)	201 (1)	311 ± 48 (2)
BUN, MG %	22.0 ± 1 (2)	21.5 ± 0.5 (2)		19.0 (1)	24.0 ± 0.0 (2)
MACROPHAGES (NO./MM^3)	71 ± 27 (3)			20 ± 5 (2)	20 ± 5 (2)

Entries are mean ± S.E. of 4 mice except as noted in parentheses.

TABLE 43

LABORATORY DATA OF MALE MICE AFTER EXPOSURE TO VC OR VDC FOR 2 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
ERYTHROCYTES ($\times 10^6$ /MM^3)	6.40 ± .17	6.00 ± .22	6.78 ± .26 (3)	6.59 ± .19	6.37 ± .19
RETICULOCYTES, %	1.18 ± .14	1.70 ± .07	.88 ± .13 (3)	1.10 ± .30	1.31 ± .11
HEMATOCRIT, VOL. %	48.0 ± 1.3	45.8 ± 1.3	50.0 ± 1.0 (3)	48.8 ± .6	45.3 ± .5
HEMOGLOBIN, GM. %	14.2 ± .5	13.6 ± .3	14.8 ± .5 (3)	14.3 ± .2	13.5 ± .1
MCV, CUBIC MICRONS	75.0 ± 1.2	76.3 ± .7	73.9 ± 2.0 (3)	74.0 ± 1.3	71.2 ± 1.8
MCHL, MICRO MICROGMS.	22.1 ± .4	22.7 ± .4	21.8 ± .1 (3)	21.7 ± .3	21.3 ± .6
MCHBC, GM %	29.5 ± .2	29.8 ± .3	29.5 ± .7 (3)	29.3 ± .1	29.9 ± .2
PLATELETS ($\times 10^5$ /MM^3)	5.8 ± .6	6.3 ± .7	5.9 ± .7	6.0 ± 1.0	4.8 ± .4
LEUKOCYTES ($\times 10^3$ /MM^3)	5.9 ± .8	4.4 ± .5	6.8 ± .7 (3)	6.1 ± .9	4.4 ± 1.4
NEUTROPHILS, %	40.8 ± 11.8	43.8 ± 7.9	38.1 ± 13.6	39.0 ± 11.1	31.0 ± 4.4
LYMPHOCYTES, %	57.5 ± 11.9	54.3 ± 7.3	60.5 ± 14.2	59.5 ± 10.7	68.5 ± 4.3
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	.3 ± .3	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	.3 ± .3	1.0 ± .6[a/]	.5 ± .3	1.0 ± .4	0.0 ± 0.0
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	1.5 ± 1.0	.3 ± .3	.5 ± .3	.5 ± .5	.5 ± .5
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	.3 ± .3	0.0 ± 0.0	0.0 ± 0.0
SGPT, IU/L	129 ± 40	87 ± 12	184 ± 14	163 ± 35	236 ± 24
BUN, MG %	35.5 ± 2.6	24.0 ± 3.4[a/]	23.0 ± 1.7[a/]	22.5 ± 1.2[a/]	15.8 ± 1.9
MACROPHAGES (NO./MM^3)	23 ± 13			162 ± 82 (3)	87 ± 50 (3)

Entries are mean ± S.E. of 4 mice except as noted in parentheses.

a/ Significantly different from the Control group, $P < 0.05$, Dunnett's multiple comparison procedure.

TABLE 44

LABORATORY DATA OF FEMALE MICE AFTER EXPOSURE TO VC OR VDC FOR 2 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
ERYTHROCYTES ($\times 10^6$ /MM^3)	5.94 ± .38	7.09 ± .24	6.52 ± .38	6.66 ± .30	6.90 ± .41
RETICULOCYTES, %	.78 ± .07	1.13 ± .17	1.04 ± .23	1.26 ± .24	1.58 ± .07[a/]
HEMATOCRIT, VOL. %	46.8 ± 3.3	54.0 ± 1.7	50.5 ± 1.2	49.5 ± 1.7	50.8 ± 1.9
HEMOGLOBIN, GM. %	13.8 ± 1.0	15.9 ± .5	15.1 ± .3	14.6 ± .5	15.2 ± .5
MCV, CUBIC MICRONS	78.7 ± 1.8	76.2 ± .5	78.0 ± 2.8	74.5 ± 2.1	73.8 ± 1.7
MCHB, MICRO MICROGMS.	23.2 ± .5	22.5 ± .1	23.4 ± 1.0	21.9 ± .7	22.1 ± .6
MCHBC, GM %	29.5 ± .2	29.5 ± .1	30.0 ± .6	29.5 ± .7	29.9 ± .2
PLATELETS ($\times 10^5$ /MM^3)	5.1 ± .6	4.1 ± .6	4.5 ± .3	5.7 ± .3	4.9 ± .5
LEUKOCYTES ($\times 10^3$ /MM^3)	5.0 ± .3	5.3 ± .3	5.8 ± .5	5.1 ± .5	4.8 ± .2
NEUTROPHILS, %	29.3 ± 6.8	26.8 ± 7.3	22.5 ± 8.6	29.0 ± 12.0	22.8 ± 6.2
LYMPHOCYTES, %	67.5 ± 5.9	71.0 ± 7.3	76.5 ± 8.6	68.8 ± 11.3	75.8 ± 5.6
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	2.5 ± .9	1.0 ± .6	.8 ± .5	1.8 ± 1.1	.5 ± .5
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	.8 ± .5	1.3 ± .9	.3 ± .3	.5 ± .3	1.0 ± .6
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	.3 ± .3
SGPT, IU/L	119 ± 18	200 ± 25	296 ± 72	222 ± 40	217 ± 50
BUN, MG %	23.3 ± .9	24.3 ± 1.3	27.5 ± 2.3	24.8 ± 1.0	33.3 ± 1.1[a/]
MACROPHAGES (NO./MM^3)	213 ± 123 (3)			18 ± 6	218 ± 148 (2)

Entries are mean ± S.E. of 4 mice except as noted in parentheses.

a/ Significantly different from the Control group, $p < 0.05$, Dunnett's multiple comparison procedure.

TABLE 45

LABORATORY DATA OF MALE MICE AFTER EXPOSURE TO VC OR VDC FOR 3 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
ERYTHROCYTES ($X10^6$ /MM^3)	7.52 ± .46 (3)	8.15 ± .2 (2)	8.01 ± .5 (2)	6.13 ± .68	7.14 ± .22
RETICULOCYTES, %	1.11 ± .33 (3)	1.25 ± .2 (2)	1.63 ± .4 (2)	1.53 ± .25	1.24 ± .20
HEMATOCRIT, VOL. %	48.3 ± .9 (3)	49.0 (1)	46.0 ±2.0 (2)	46.3 ± 1.2 (3)	44.0 ± .9
HEMOGLOBIN, GM. %	15.5 ± .4 (3)	16.3 ± .4 (2)	15.1 ± .7 (2)	13.3 ± 1.3	14.5 ± .4
MCV, CUBIC MICRONS	64.6 ± 3.4 (3)	58.8 (1)	57.5 ±1 (2)	68.1 ± .9 (3)	61.7 ± 1.2
MCH, MICRO MICROGMS.	20.7 ± .8 (3)	19.9 ± .1 (2)	19.1 ± .3 (2)	21.9 ± .7	20.3 ± .1
MCHC, GM %	32.1 ± .7 (3)	34.1 (1)	33.3 ± .1 (2)	31.3 ± .5 (3)	33.0 ± .5
PLATELETS ($X10^5$ /MM^3)	7.0 ± 1.2 (3)	6.2 (1)		6.8 ± .9 (3)	7.1 ± .7 (2)
LEUKOCYTES ($X10^3$ /MM^3)	6.2 ± 1.0 (3)	7.1 ± .8 (2)	3.9 ±1.0 (2)	3.8 ± .7	6.1 ± 1.2
NEUTROPHILS, %	22.3 ± 3.3	25.8 ± 12.6	30.5 ± 8.5	15.3 ± 2.1	19.0 ± 8.6
LYMPHOCYTES, %	77.0 ± 2.9	73.8 ± 12.7	67.8 ± 8.9	84.3 ± 2.1	80.8 ± 8.5
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	1.0 ± 1.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	.5 ± .3	.3 ± .3	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	.3 ± .3	.5 ± .3	.8 ± .8	.5 ± .5	.3 ± .3
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	2.0 ± 2.0	0.0 ± 0.0	0.0 ± 0.0
SGPT, IU/L	55.0 ± 9.1	96.7 ± 21.5 (3)	72.0 ± 6.9	86.0 ± 9.2 (3)	82.5 ± 5.9
BUN, MG %	20.0 ± 1.1	19.0 ± 1.2 (3)	24.8 ± 1.7	21.0 ± 2.1 (3)	27.0 ± 2.4
MACROPHAGES (NO./MM^3)	186 ± 124			53 ± 16	135 ± 99

Entries are mean ± S.E. of 4 mice except as noted in parentheses.

TABLE 46

LABORATORY DATA OF FEMALE MICE AFTER EXPOSURE TO VC OR VDC FOR 3 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
ERYTHROCYTES ($\times 10^6$ /MM^3)	6.73 ± .17 (3)	7.72 ± .47	7.12 ± .94 (3)	6.24 ± .77 (3)	5.83 ± .54 (3)
RETICULOCYTES, %	1.04 ± .07 (3)	1.22 ± .23	1.15 ± .21 (3)	1.54 ± .18 (3)	1.48 ± .25 (3)
HEMATOCRIT, VOL. %	44.3 ± 1.2 (3)	48.0 ± 1.2	44.7 ± 3.0 (3)	42.7 ± 3.5 (3)	39.3 ± 3.7 (3)
HEMOGLOBIN, GM. %	14.1 ± .5 (3)	15.9 ± .8	14.9 ± .8 (3)	14.0 ± 1.1 (3)	12.4 ± 1.0 (3)
MCV, CUBIC MICRONS	65.9 ± .3 (3)	62.6 ± 2.2	64.0 ± 4.8 (3)	69.2 ± 3.5 (3)	67.7 ± 1.6 (3)
MCHM, MICRO MICROGMS.	20.9 ± .2 (3)	20.7 ± .3	21.5 ± 2.1 (3)	22.7 ± 1.4 (3)	21.3 ± .3 (3)
MCHMC, GM %	31.6 ± .2 (3)	33.1 ± .8	33.4 ± .8 (3)	32.8 ± .5 (3)	31.5 ± .6 (3)
PLATELETS ($\times 10^5$ /MM^3)	5.9 ± .5 (2)	6.4 (1)	4.3 ± .5 (2)	6.0 ± .5 (2)	
LEUKOCYTES ($\times 10^3$ /MM^3)	3.2 ± .5 (3)	5.2 ± .4	6.1 ± 1.5 (3)	4.2 ± .7 (3)	3.1 ± .3 (3)
NEUTROPHILS, %	12.0 ± 3.2	8.5 ± 2.1	10.3 ± 1.7	8.8 ± 3.3	12.3 ± 5.1
LYMPHOCYTES, %	87.3 ± 3.6	90.3 ± 2.6	88.8 ± 2.0	91.0 ± 3.5	86.3 ± 4.9
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	.8 ± .5	.8 ± .5	.5 ± .5	0.0 ± 0.0	.5 ± .5
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	0.0 ± 0.0	.5 ± .	.5 ± .5	.3 ± .3	1.0 ± .4
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	.3 ± .3	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
SGPT, IU/L	116 ± 30	64 ± 8	127 ± 33	66 ± 6	105 ± 16
BUN, MG %	19.8 ± 1.4	22.8 ± 3.1	26.0 ± 3.8	20.8 ± 1.0	29.8 ± 2.4
MACROPHAGES (NO./MM^3)	24 ± 8			165 ± 89	86 ± 68

Entries are mean ± S.E. of 4 mice except as noted in parentheses.

TABLE 47

LABORATORY DATA OF MALE MICE EXPOSED TO VC OR VDC FOR 6 MONTHS

DOSE: PPM	CONTROL	50 PPM VC	250 PPM VC	1,000 PPM VC	55 PPM VDC
ERYTHROCYTES ($\times 10^6$ /MM^3)	7.21 ± .31	7.26 ± .22	7.39 ± .12	6.25 ± .26	6.76 ± .35
RETICULOCYTES, %	.97 ± .24	.79 ± .17	1.18 ± .18	1.38 ± .13	1.69 ± .35
HEMATOCRIT, VOL. %	45.5 ± 1.4	44.5 ± 1.2	47.3 ± .9	39.3 ± 2.3 a/	42.5 ± 1.3
HEMOGLOBIN, GM. %	14.2 ± .5	13.6 ± .6	14.4 ± .3	11.7 ± .6 a/	13.1 ± .5
MCV, CUBIC MICRONS	63.2 ± 1.2	61.3 ± .3	64.0 ± .1	62.7 ± 1.3	63.1 ± 2.1
MCHB, MICRO MICROGMS.	19.8 ± .4	18.8 ± .2	19.5 ± .4	18.8 ± .4	19.5 ± .5
MCHBC, GM %	31.3 ± .7	30.6 ± .5	30.5 ± .7	30.0 ± .6	30.9 ± .5
PLATELETS ($\times 10^5$ /MM^3)	3.7 ± .7	6.8 ± .9 a/	6.2 ± .4	5.1 ± .7	4.5 ± .6
LEUKOCYTES ($\times 10^3$ /MM^3)	8.4 ± 3.9	5.2 ± 1.1	6.0 ± 1.8	4.1 ± .7	3.4 ± .7
NEUTROPHILS, %	20.8 ± 4.6	26.5 ± 4.0	37.0 ± 10.1	51.5 ± 5.8 a/	35.5 ± 8.8
LYMPHOCYTES, %	79.0 ± 4.7	73.5 ± 4.0	62.8 ± 10.5	47.8 ± 5.9 a/	64.5 ± 8.8
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	1.0 ± .4	0.0 ± 0.0	.3 ± .3	.8 ± .5	0.0 ± 0.0
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
SGPT, IU/L	58.7 ± 11.1 (3)	49.3 ± 16.9 (3)	64.8 ± 10.5	83.5 ± 18.6	96.5 ± 17.8
BUN, MG %	28.3 ± 4.8	28.8 ± 7.8 (3)	17.8 ± 2.8	38.5 ± 17.6	40.8 ± 9.9
MACROPHAGES (NO./MM^3)	77 ± 39 (3)			629 ± 193	353 ± 173 (3)

ENTRIES ARE MEAN ± STANDARD ERROR OF 4 MICE EXCEPT AS NOTED IN PARENTHESES.

a/ Significantly different from Control group, $p < 0.05$, Dunnett's multiple comparison procedure.

TABLE 48

LABORATORY DATA OF FEMALE MICE EXPOSED TO VC OR VDC FOR 6 MONTHS

DOSE: PPM	CONTROL	50 PPM VC	250 PPM VC	1,000 PPM VC	55 PPM VDC
ERYTHROCYTES ($X10^6$ /MM^3)	6.83 ± .37 (2)	7.42 ± .68 (2)	7.35 ± .25	7.31 ± .15	6.26 ± 1.02
RETICULOCYTES, %	.85 ± .19 (3)	1.34 ± .18	.98 ± .19	1.41 ± .30	1.45 ± .49
HEMATOCRIT, VOL. %	44.5 ± 1.5 (2)	44.5 ± 4.5 (2)	48.0 ± 1.1	47.0 ± 1.9	39.3 ± 6.8
HEMOGLOBIN, GM. %	13.3 ± .5 (2)	14.3 ± 1.7 (2)	14.9 ± .8	14.6 ± .5	12.4 ± 2.0
MCV, CUBIC MICRONS	65.2 ± 1.3 (2)	59.9 ± .6 (2)	65.4 ± 1.0	64.5 ± 3.5	62.2 ± 1.9
MCHB, MICRO MICROGMS.	19.4 ± .2 (2)	19.3 ± .5 (2)	20.3 ± .5	20.1 ± 1.0	19.8 ± .3
MCHBC, GM %	29.8 ± .2 (2)	32.2 ± .5 (2)	31.0 ± 1.1	31.2 ± .6	31.8 ± .6
PLATELETS ($X10^5$ /MM^3)	4.1 ± 0.0 (2)	3.9 ± .9 (2)	4.6 ± .4	5.0 ± .8	4.6 ± .3
LEUKOCYTES ($X10^3$ /MM^3)	4.2 ± .3 (3)	3.9 ± 1.3 (2)	7.4 ± .7	6.4 ± 1.0	4.0 ± .7
NEUTROPHILS, %	18.7 ± 4.7 (3)	25.3 ± 8.4	20.0 ± 4.4	31.5 ± 7.1	23.8 ± 3.1
LYMPHOCYTES, %	79.3 ± 4.9 (3)	74.3 ± 8.1	79.0 ± 5.0	67.8 ± 6.8	76.0 ± 3.2
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	1.5 ± .9	.5 ± .5	1.0 ± .7	.8 ± .5	.3 ± .3
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
SGPT, IU/L	50 ± 6 (3)	51 ± 25 (2)	37 ± 6 (2)	51 ± 5	107 ± 29
BUN, MG %	23.0 ± 1.7 (3)	21.8 ± 2.1	14.0 ± 1.0 (2)	18.3 ± 1.3	33.3 ± 10.7
MACROPHAGES (NO./MM^3)	100 ± 40 (3)			400 ± 45 (3)[a/]	235 ± 83

ENTRIES ARE MEAN ± STANDARD ERROR OF 4 MICE EXCEPT AS NOTED IN PARENTHESES.

a/ Significantly different from Control group, $p < 0.05$, Dunnett's multiple comparison procedure.

TABLE 49

LABORATORY DATA OF MALE MICE EXPOSED TO VC OR VDC FOR 9 MONTHS

DOSE: PPM	Control	50 ppm VC	250 ppm VC	1000 ppm VC	55 ppm VDC
ERYTHROCYTES ($X10^6$ /MM^3)	6.13 ± .92	5.79 ± .21	6.56 ± .20	5.34 ± 1.08	6.56 ± .37
RETICULOCYTES, %	3.05 ± 1.43	1.80 ± .19	2.50 ± .46	5.52 ± 3.24	1.96 ± .08
HEMATOCRIT, VOL. %	39.5 ± 4.9	41.3 ± 1.8	43.3 ± 2.0	33.3 ± 4.8	42.5 ± .9
HEMOGLOBIN, GM. %	12.1 ± 1.7	13.9 ± .6	12.8 ± .6	10.8 ± 1.5	13.3 ± .4
MCV, CUBIC MICRONS	65.5 ± 2.9	71.3 ± 2.4	66.0 ± 3.2	65.5 ± 6.2	65.2 ± 2.7
MCHB, MICRO MICROGMS.	19.9 ± 1.2	24.0 ± .8	19.6 ± 1.3	21.5 ± 2.2	20.5 ± 1.3
MCHHC, GM %	30.4 ± 1.1	33.7 ± .2	29.8 ± 2.1	32.7 ± .6	31.4 ± .8
PLATELETS ($X10^5$ /MM^3)	4.7 ± .3	4.1 ± .9	4.7 ± .6	4.8 ± .7	5.5 ± .6
LEUKOCYTES ($X10^3$ /MM^3)	4.2 ± .8	5.0 ± .5	4.4 ± .9	3.3 ± 1.3	4.6 ± 1.5
NEUTROPHILS, %	48.5 ± 8.3	33.5 ± 3.6	23.8 ± 2.7	42.8 ± 6.7	39.0 ± 4.1
LYMPHOCYTES, %	59.0 ± 8.5	65.3 ± 4.7	76.8 ± 2.8	57.0 ± 6.5	60.5 ± 3.9
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	.3 ± .3
EOSINOPHILS, %	.5 ± .3	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	.3 ± .3
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	0.0 ± 0.0	0.0 ± 0.0	.3 ± .3	.3 ± .3	0.0 ± 0.0
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
SGPT, IU/L	38 ± 4	77 ± 45	60 ± 14	75 ± 23	154 ± 49
BUN, MG %	28.5 ± 5.2	19.0 ± 2.3	20.3 ± 1.7	60.3 ± 23.3	42.3 ± 3.9
MACROPHAGES (NO./MM^3)	88 ± 25	35 ± 4	44 ± 5	831 ± 162 a/	50 ± 8

ENTRIES ARE MEAN ± STANDARD ERROR OF FOUR MICE.

a/ Significantly different from the control group, $P < 0.05$, Dunnett's multiple comparison procedure.

TABLE 50

LABORATORY DATA OF FEMALE MICE EXPOSED TO VC OR VDC FOR 9 MONTHS

DOSE: PPM	Control	50 ppm VC	250 ppm VC	1000 ppm VC	55 ppm VDC
ERYTHROCYTES ($X10^6$ /MM ^{3})	6.84 ± .59	6.85 ± .53	4.38	5.44	7.88 ± .30
RETICULOCYTES, %	1.71 ± .35	1.42 ± .11	6.43	2.23	1.78 ± .10
HEMATOCRIT, VOL. %	44.3 ± 1.8	44.0 ± 1.3	30.0	39.0	46.5 ± .6
HEMOGLOBIN, GM. %	13.8 ± .5	13.5 ± .4	10.5	12.6	14.8 ± .8
MCV, CUBIC MICRONS	65.6 ± 1.8	65.1 ± 4.6	68.5	71.7	66.8 ± 3.6
MCHH, MICRO MICROGMS.	20.5 ± 1.4	20.1 ± 1.5	24.0	23.2	21.4 ± 2.0
MCHHC, GM %	31.2 ± .4	30.8 ± .2	35.0	32.3	31.8 ± 1.3
PLATELETS ($X10^5$ /MM ^{3})	4.2 ± 1.8	4.8 ± .2	2.5	2.3	4.9 ± .5
LEUKOCYTES ($X10^3$ /MM ^{3})	2.5 ± 1.1	2.6 ± .6	9.5	4.3	3.2 ± .7
NEUTROPHILS, %	42.8 ± 5.2	36.5 ± 7.8	29.0	66.0	33.3 ± 4.9
LYMPHOCYTES, %	58.0 ± 5.2	63.5 ± 7.8	70.8	34.0	66.8 ± 4.9
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0	0.0	0.0 ± 0.0
EOSINOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	1.0	0.0	0.0 ± 0.0
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0	0.0	0.0 ± 0.0
MONOCYTES, %	0.0 ± 0.0	0.0 ± 0.0	0.0	0.0	0.0 ± 0.0
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0	0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0	0.0	0.0 ± 0.0
SGPT, IU/L	93 ± 27	42 ± 5	55	46	141 ± 62
BUN, MG %	24.5 ± 2.6	23.5 ± 3.2	18.0	38.0	18.3 ± 4.4
MACROPHAGES (NO./MM ^{3})	83 ± 43	50 ± 16	295	225	16 ± 10

ENTRIES ARE MEAN ± STANDARD ERROR OF FOUR MICE EXCEPT FOR THE 250 ppm AND 1000 ppm VC GROUPS IN WHICH ONLY ONE MOUSE WAS TERMINATED IN EACH GROUP.

TABLE 51

LABORATORY DATA OF MALE MICE EXPOSED TO VC OR VDC FOR 12 MONTHS

DOSE: PPM	CONTROL	50 (PPM VC)	55 (PPM VDC)
ERYTHROCYTES ($X10^6$ /MM^3)	7.39 ± .09	7.88 ± .19	7.40 ± .26
RETICULOCYTES, %	3.04 ± 1.43	2.56 ± .34	2.56 ± .30 (7)
HEMATOCRIT, VOL. %	43.0 ± .4	44.0 ± 1.2	40.6 ± 3.7 (7)
HEMOGLOBIN, GM. %	13.2 ± .1	13.9 ± .5	12.8 ± 1.1
MCV, CUBIC MICRONS	58.2 ± .6	55.9 ± 1.0	54.3 ± 4.7 (7)
MCHB, MICRO MICROGMS.	17.9 ± .2	17.7 ± .3	17.3 ± 1.5
MCHBC, GM %	30.8 ± .2	31.7 ± .9	30.8 ± .6 (7)
PLATELETS ($X10^5$ /MM^3)	7.9 ± .7	6.1 ± .3	7.5 ± .7 (7)
LEUKOCYTES ($X10^3$ /MM^3)	5.8 ± 1.8	8.9 ± 1.7	4.3 ± .8
NEUTROPHILS, %	27.8 ± 4.6	36.0 ± 7.6	28.8 ± 5.0
LYMPHOCYTES, %	72.3 ± 4.6	63.7 ± 7.4	71.3 ± 5.0
BANDS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	0.0 ± 0.0	.3 ± .3	0.0 ± 0.0
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
SGPT, IU/L	41.8 ± 6.9	52.3 ± 4.9	99.0 ± 16.2 (7) a/
BUN, MG %	24.8 ± 3.9	30.8 ± 2.6	51.4 ± 5.6 (7) a/
MACHOPHAGES (NO./MM^3)	25 ± 6	395 ± 325 (2)	134 ± 53

Entries are mean ± standard error of 4(Control), 3(50 ppm VC) or 8(55 ppm VDC) mice unless otherwise indicated in parentheses.

a/ Significantly different from the control group, $P < 0.05$, Dunnett's multiple comparison procedure.

TABLE 52

LABORATORY DATA OF FEMALE MICE EXPOSED TO VDC FOR 12 MONTHS

DOSE: PPM	CONTROL	55 (PPM VDC)
ERYTHROCYTES ($X10^6$ /MM^3)	7.72 ± .15	7.39 ± .30
RETICULOCYTES, %	1.50 ± .20	2.20 ± .25 a/
HEMATOCRIT, VOL. %	43.9 ± .7	43.1 ± 1.6
HEMOGLOBIN, GM. %	13.9 ± .3	13.6 ± .6
MCV, CUBIC MICRONS	56.9 ± .9	58.4 ± .4
MCHG, MICRO MICROGMS.	18.0 ± .2	18.4 ± .2
MCHBC, GM %	31.6 ± .4	31.5 ± .4
PLATELETS ($X10^5$ /MM^3)	6.2 ± .6	7.1 ± 1.4 (6)
LEUKOCYTES ($X10^3$ /MM^3)	4.9 ± .8	3.6 ± .8
NEUTROPHILS, %	20.7 ± 4.2	32.5 ± 4.0
LYMPHOCYTES, %	78.6 ± 4.1	67.3 ± 4.1
BANDS, %	0.0 ± 0.0	0.0 ± 0.0
EOSINOPHILS, %	.3 ± .2	.3 ± .2
BASOPHILS, %	0.0 ± 0.0	0.0 ± 0.0
MONOCYTES, %	.4 ± .2	0.0 ± 0.0 a/
ATYPICAL, %	0.0 ± 0.0	0.0 ± 0.0
NUCLEATED RBC, %	0.0 ± 0.0	0.0 ± 0.0
SGPT, IU/L	103 ± 16	78 ± 5
BUN, MG %	23.1 ± 1.5	36.7 ± 4.6 (7) a/
MACROPHAGES (NO./MM^3)	58 ± 16	22 ± 5

Entries are mean ± standard error of 10 mice(Control) or 8 mice(55 ppm VDC) unless otherwise indicated in parentheses.

a/ Significantly different from the control group, $P < 0.05$, Dunnett's multiple comparison procedure.

TABLE 53

NUMBERICAL DISTRIBUTION OF CHROMOSOMES IN BONE MARROW OF MICE EXPOSED TO VC OR VDC

Treatment	No. of Mice	Chromosome Frequency ≤ 38	39	40	41	≥ 42	Tetraploids (4N) per 100 cells
After One Month							
Control	6	5[a/]	5	36	3	1	0.42 ± 0.20[b/]
VC (1,000 ppm)	6	6	4	39	1	0	0.25 ± 0.17
VDC (55 ppm)	6	2	5	40	2	1	0.25 ± 0.17
After Three Months							
Control	4	5	7	37	1	0	0.0 ± 0.0
VC (1,000 ppm)	4	6	6	37	1	0	0.0 ± 0.0
VDC (55 00m)	4	6	6	35	3	0	0.15 ± 0.15
After Six Months							
Control	6	7	4	37	1	1	0.50 ± 0.22
VC (1,000 ppm)	6	4	4	34	6	2	0.33 ± 0.21
VDC (55 ppm)	5	5	7	36	2	0	0.36 ± 0.22
After Nine Months							
VC (1,000 ppm)	5	2	3	42	2	1	0.0 ± 0.0
After Twelve Months							
VDC (55 ppm)	6	2	5	41	1	1	0.17 ± 0.17

a/ Mean
b/ Mean ± S.E.

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TABLE 54

MORPHOLOGICAL ABERRATIONS OF CHROMOSOMES IN BONE MARROW OF MICE EXPOSED TO VC OR VDC

Treatment	No. of Mice	Chromatid Gaps per 50 Cells	Chromatid Breaks per 50 Cells	Translocations per 50 Cells	Total Aberrations per 50 Cells
			After One Month		
Control	6	0.67 ± 0.33[a/]	0.0 ± 0.0	0.20 ± 0.20	0.86 ± 0.31
VC (1,000 ppm)	6	0.52 ± 0.23	0.17 ± 0.17	0.17 ± 0.17	0.86 ± 0.13
VDC (55 ppm)	6	0.97 ± 0.26	0.33 ± 0.21	0.17 ± 0.17	0.47 ± 0.43
			After Three Months		
Control	4	0.25 ± 0.25	0.0 ± 0.0	0.0 ± 0.0	0.25 ± 0.25
VC (1,000 ppm)	4	0.0 ± 0.0	0.25 ± 0.25	0.0 ± 0.0	0.25 ± 0.25
VDC (55 ppm)	4	0.50 ± 0.50	0.25 ± 0.25	0.0 ± 0.0	0.75 ± 0.48
			After Six Months		
Control	6	0.0 ± 0.0	0.0 ± 0.0	0.17 ± 0.17	0.17 ± 0.17
VC (1,000 ppm)	6	0.0 ± 0.0	0.0 ± 0.0	0.17 ± 0.17	0.17 ± 0.17
VDC (55 ppm)	5	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0

(continued to next page)

TABLE 54 (Concluded)

Treatment	No. of Mice	Chromatid Gaps per 50 Cells	Chromatid Breaks per 50 Cells	Translocations per 50 Cells	Total Aberrations per 50 Cells
			After Nine Months		
VC (1,000 ppm)	5	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
			After Twelve Months		
VDC (55 ppm)	6	0.33 ± 0.21	0.0 ± 0.0	0.0 ± 0.0	0.33 ± 0.21

a/ Mean ± S.E.

TABLE 55

ORGAN WEIGHTS OF MALE MICE AFTER EXPOSURE TO VC OR VDC FOR 1 MONTH

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
			Absolute Weight (gm)		
Terminal Body Weight	33.0 ± 1.0[a/]	31.0 ± 1.2	32.0 ± 0.7	32.5 ± 0.6	29.8 ± 0.8
Brain	0.51 ± 0.02	0.47 ± 0.01[b/]	0.47 ± 0.01[b/]	0.46 ± 0.01[b/]	0.46 ± 0.00[b/]
Liver	1.77 ± 0.24	1.34 ± 0.13	1.35 ± 0.12	1.31 ± 0.02	1.35 ± 0.03
Kidney	0.54 ± 0.03	0.51 ± 0.04	0.51 ± 0.02	0.54 ± 0.01	0.46 ± 0.02
Spleen	0.17 ± 0.02	0.13 ± 0.02	0.14 ± 0.01	0.13 ± 0.01	0.11 ± 0.01[b/]
Testes	0.26 ± 0.04	0.23 ± 0.01	0.24 ± 0.01	0.22 ± 0.02	0.24 ± 0.01
			Relative to Brain Weight (gm/gm)		
Liver	3.5 ± 0.5	2.9 ± 0.3	2.9 ± 0.3	2.8 ± 0.0	2.9 ± 0.1
Kidney	1.06 ± 0.08	1.09 ± 0.08	1.11 ± 0.06	1.17 ± 0.04	1.01 ± 0.05
Spleen	0.34 ± 0.05	0.27 ± 0.04	0.30 ± 0.02	0.27 ± 0.02	0.24 ± 0.02
Testes	0.52 ± 0.08	0.49 ± 0.03	0.52 ± 0.02	0.49 ± 0.04	0.52 ± 0.03

a/ Mean ± S.E. of four mice.

b/ Significantly different from control, $p < 0.05$, Dunnett's Multiple Comparison procedure.

TABLE 56

ORGAN WEIGHTS OF FEMALE MICE AFTER EXPOSURE TO VC OR VDC FOR 1 MONTH

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
			Absolute Weight (gm)		
Terminal Body Weight	23.3 ± 1.1[a/]	27.8 ± 1.4[b/]	26.5 ± 1.5	24.8 ± 0.9	26.5 ± 0.9
Brain	0.48 ± 0.01	0.47 ± 0.01	0.47 ± 0.01	0.49 ± 0.01	0.49 ± 0.01
Liver	1.13 ± 0.08	1.15 ± 0.07	1.12 ± 0.02	1.03 ± 0.06	1.31 ± 0.06
Kidney	0.33 ± 0.03	0.38 ± 0.02	0.37 ± 0.02	0.36 ± 0.01	0.39 ± 0.01
Spleen	0.10 ± 0.01	0.15 ± 0.02	0.13 ± 0.02	0.14 ± 0.03	0.13 ± 0.01
Ovaries	0.02 ± 0.01	0.01 ± 0.00	0.02 ± 0.00	0.02 ± 0.00	0.02 ± 0.00
			Relative to Brain Weight (gm/gm)		
Liver	2.36 ± 0.18	2.43 ± 0.12	2.40 ± 0.06	2.13 ± 0.07	2.69 ± 0.08
Kidney	0.69 ± 0.05	0.81 ± 0.03	0.79 ± 0.04	0.74 ± 0.01	0.80 ± 0.00
Spleen	0.21 ± 0.02	0.31 ± 0.04	0.27 ± 0.03	0.30 ± 0.08	0.27 ± 0.02
Ovaries	0.05 ± 0.16	0.03 ± 0.01	0.03 ± 0.01	0.05 ± 0.01	0.03 ± 0.01

a/ Mean ± S.E. of four mice.

b/ Significantly different from control, $p < 0.05$, Dunnett's Multiple Comparison procedure.

TABLE 57

ORGAN WEIGHTS OF MALE MICE AFTER EXPOSURE TO VC OR VDC FOR 2 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
			Absolute Weight (gm)		
Terminal Body Weight	33.5 ± 0.5[a/]	33.8 ± 1.9	34.3 ± 1.7	36.8 ± 1.4	32.0 ± 0.6
Brain	0.50 ± 0.01	0.47 ± 0.04	0.51 ± 0.01	0.48 ± 0.03	0.49 ± 0.02
Liver	1.72 ± 0.13	1.50 ± 0.08	1.50 ± 0.07	1.57 ± 0.09	1.60 ± 0.04
Kidney	0.69 ± 0.04	0.70 ± 0.08	0.66 ± 0.03	0.69 ± 0.02	0.52 ± 0.04
Spleen	0.11 ± 0.04	0,15 ± 0.03	0.15 ± 0.01	0.16 ± 0.00	0.11 ± 0.02
Testes	0.27 ± 0.02	0.26 ± 0.01	0.28 ± 0.02	0.26 ± 0.02	0.26 ± 0.02
			Relative to Brain Weight (gm/gm)		
Liver	3.4 ± 0.3	3.3 ± 0.4	2.9 ± 0.1	3.3 ± 0.2	3.3 ± 0.1
Kidney	1.37 ± 0.08	1.56 ± 0.29	1.29 ± 0.05	1.44 ± 0.10	1.06 ± 0.04
Spleen	0.23 ± 0.08	0.33 ± 0.05	0.30 ± 0.02	0.34 ± 0.03	0.22 ± 0.03
Testes	0.54 ± 0.03	0.58 ± 0.06	0.55 ± 0.05	0.55 ± 0.07	0.53 ± 0.02

a/ Mean ± S.E. of four mice.

TABLE 58

ORGAN WEIGHTS OF FEMALE MICE AFTER EXPOSURE TO VC OR VDC FOR 2 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
			Absolute Weight (gm)		
Terminal Body Weight	28.8 ± 0.6[a]	29.0 ± 1.9	29.3 ± 0.6	29.5 ± 1.2	28.0 ± 0.4
Brain	0.53 ± 0.02	0.53 ± 0.02	0.47 ± 0.01	0.54 ± 0.02	0.51 ± 0.01
Liver	1.28 ± 0.10	1.29 ± 0.07	1.25 ± 0.04	1.28 ± 0.07	1.32 ± 0.08
Kidney	0.43 ± 0.02	0.42 ± 0.01	0.39 ± 0.01	0.44 ± 0.02	0.42 ± 0.01
Spleen	0.14 ± 0.01	0.13 ± 0.01	0.17 ± 0.01	0.14 ± 0.01	0.12 ± 0.01
Ovaries	0.03 ± 0.00	0.04 ± 0.01	0.03 ± 0.00	0.03 ± 0.00	0.04 ± 0.01
			Relative to Brain Weight (gm/gm)		
Liver	2.44 ± 0.16	2.44 ± 0.09	2.66 ± 0.11	2.40 ± 0.12	2.60 ± 0.17
Kidney	0.81 ± 0.03	0.79 ± 0.03	0.84 ± 0.03	0.82 ± 0.05	0.82 ± 0.01
Spleen	0.26 ± 0.01	0.24 ± 0.02	0.36 ± 0.03[b]	0.26 ± 0.02	0.23 ± 0.02
Ovaries	0.06 ± 0.01	0.07 ± 0.01	0.07 ± 0.00	0.06 ± 0.00	0.07 ± 0.00

a/ Mean ± S.E. of four mice.

b/ Significantly different from Control, $p < 0.05$, Dunnett's Multiple Comparison procedure.

TABLE 59

ORGAN WEIGHTS OF MALE MICE AFTER EXPOSURE TO VC OR VDC FOR 3 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
			Absolute Weight (gm)		
Terminal Body Weight	34.9 ± 1.1[a/]	34.8 ± 1.1	32.8 ± 1.2	34.4 ± 1.2	28.3 ± 1.8[b/]
Brain	0.52 ± 0.02	0.49 ± 0.01	0.51 ± 0.02	0.52 ± 0.01	0.51 ± 0.01
Liver	1.64 ± 0.09	1.54 ± 0.08	1.46 ± 0.06	1.62 ± 0.08	1.50 ± 0.07
Kidney	0.63 ± 0.03	0.67 ± 0.06	0.64 ± 0.05	0.68 ± 0.03	0.50 ± 0.01
Spleen	0.12 ± 0.01	0.16 ± 0.02	0.14 ± 0.01	0.12 ± 0.01	0.12 ± 0.01
Testes	0.22 ± 0.02	0.30 ± 0.03	0.28 ± 0.01	0.27 ± 0.02	0.27 ± 0.02
			Relative To Brain Weight (gm/gm)		
Liver	3.19 ± 0.14	3.16 ± 0.13	2.88 ± 0.19	3.13 ± 0.16	2.97 ± 0.18
Kidney	1.23 ± 0.04	1.37 ± 0.10	1.25 ± 0.07	1.31 ± 0.07	0.99 ± 0.04
Spleen	0.23 ± 0.01	0.33 ± 0.04[b/]	0.27 ± 0.02	0.24 ± 0.01	0.23 ± 0.02
Testes	0.43 ± 0.03	0.62 ± 0.06[b/]	0.54 ± 0.02	0.52 ± 0.04	0.55 ± 0.05

a/ Mean ± S.E. of four mice.

b/ Significantly different from control, $p < 0.05$, Dunnett's Multiple Comparison procedure.

TABLE 60

ORGAN WEIGHTS OF FEMALE MICE AFTER EXPOSURE TO VC OR VDC FOR 3 MONTHS

	Control	VC 50 ppm	VC 250 ppm	VC 1,000 ppm	VDC 55 ppm
			Absolute Weight (gm)		
Terminal Body Weight	25.9 t 1.5[a/]	29.4 ± 1.2	26.0 ± 1.1	26.9 ± 0.7	25.9 ± 0.8
Brain	0.49 ± 0.01	0.51 ± 0.02	0.55 ± 0.01	0.51 ± 0.03	0.47 ± 0.03
Liver	1.18 ± 0.10	1.27 ± 0.06	1.12 ± 0.07	1.21 ± 0.07	1.32 ± 0.07
Kidney	0.50 ± 0.14	0.41 ± 0.02	0.38 ± 0.04	0.45 ± 0.07	0.41 ± 0.01
Spleen	0.12 ± 0.01	0.11 ± 0.01	0.14 ± 0.02	0.14 ± 0.01	0.13 ± 0.00
Ovaries	0.04 ± 0.01	0.04 ± 0.01	0.04 ± 0.01	0.04 ± 0.01	0.04 ± 0.01
			Relative to Brain Weight (gm/gm)		
Liver	2.38 ± 0.17	2.49 ± 0.04	2.03 ± 0.10	2.40 ± 0.21	2.81 ± 0.11
Kidney	1.01 ± 0.27	0.81 ± 0.03	0.70 ± 0.05	0.89 ± 0.11	0.87 ± 0.05
Spleen	0.24 ± 0.01	0.22 ± 0.01	0.24 ± 0.03	0.27 ± 0.02	0.28 ± 0.02
Ovaries	0.07 ± 0.01	0.09 ± 0.01	0.08 ± 0.01	0.08 ± 0.03	0.10 ± 0.02

a/ Mean ± S.E. of four mice.

TABLE 61

ORGAN WEIGHTS OF MALE MICE EXPOSED TO VC OR VDC FOR 6 MONTHS

	Control	50 ppm VC	250 ppm VC	1,000 ppm VC	55 ppm VDC
			Absolute Weight (gm)		
Terminal Body Weight	38.2 ± 1.5[a/]	36.1 ± 3.3	38.5 + 0.9	36.7 ± 0.5	36.5 ± 1.4
Brain	0.50 ± 0.01	0.52 ± 0.01	0.52 ± 0.04	0.55 ± 0.02	0.50 ± 0.01
Liver	1.89 ± 0.05	1.73 ± 0.17	1.81 ± 0.08	1.75 ± 0.14	1.94 ± 0.05
Kidney	0.63 ± 0.06	0.68 ± 0.03	0.74 ± 0.04	0.61 ± 0.04	0.57 ± 0.02
Spleen	0.14 ± 0.01	0.16 ± 0.04	0.15 ± 0.02	0.22 ± 0.04	0.16 ± 0.02
Testes	0.29 ± 0.01	0.28 ± 0.04	0.29 ± 0.02	0.33 ± 0.09	0.27 ± 0.00
			Relative to Brain Weight (gm/gm)		
Liver	3.8 ± 0.2	3.3 ± 0.4	3.5 ± 0.3	3.2 ± 0.2	3.9 ± 0.1
Kidney	1.27 ± 0.12	1.32 ± 0.07	1.45 ± 0.13	1.11 ± 0.09	1.15 ± 0.05
Spleen	0.29 ± 0.02	0.32 ± 0.08	0.31 ± 0.06	0.39 ± 0.06	0.32 ± 0.04
Testes	0.58 ± 0.03	0.54 ± 0.07	0.56 ± 0.03	0.61 ± 0.17	0.54 ± 0.02

a/ Mean ± S.E. of four mice.

TABLE 62

ORGAN WEIGHTS OF FEMALE MICE EXPOSED TO VC OR VDC FOR 6 MONTHS

Group	Control	50 ppm VC	250 ppm VC	1,000 ppm VC	55 ppm VDC
	Absolute Weight (gm)				
Terminal Body Weight	33.7 ± 1.9[a/]	31.0 ± 1.3	30.4 ± 1.8	31.9 ± 1.3	31.7 ± 1.4
Brain	0.51 ± 0.02	0.51 ± 0.03	0.52 ± 0.01	0.52 ± 0.02	0.53 ± 0.02
Liver	1.63 ± 0.10	1.43 ± 0.07	1.60 ± 0.10	1.53 ± 0.17	1.56 ± 0.14
Kidney	0.45 ± 0.04	0.42 ± 0.02	0.50 ± 0.01	0.46 ± 0.04	0.49 ± 0.02
Spleen	0.17 ± 0.02	0.19 ± 0.03	0.19 ± 0.02	0.18 ± 0.02	0.19 ± 0.01
Ovaries	0.05 ± 0.01	0.03 ± 0.00	0.06 ± 0.01	0.04 ± 0.01	0.04 ± 0.00
	Relative to Brain Weight (gm/gm)				
Liver	3.2 ± 0.3	2.8 ± 0.3	3.1 ± 0.2	2.9 ± 0.2	3.0 ± 0.3
Kidney	0.90 ± 0.08	0.84 ± 0.08	0.98 ± 0.04	0.88 ± 0.05	0.95 ± 0.06
Spleen	0.34 ± 0.04	0.37 ± 0.05	0.37 ± 0.03	0.35 ± 0.05	0.36 ± 0.03
Ovaries	0.09 ± 0.02	0.07 ± 0.01	0.11 ± 0.02	0.09 ± 0.01	0.08 ± 0.01

a/ Mean ± S.E. of four rats.

TABLE 63

ORGAN WEIGHTS OF MALE MICE EXPOSED TO VC OR VDC FOR 9 MONTHS

	Control	50 PPM VC	250 PPM VC	1,000 PPM VC	55 PPM VDC
Absolute Weight (gm)					
Terminal Body Weight	39 ± 3[a]	37 ± 2	38 ± 1	37 ± 3	38 ± 1
Brain	0.54 ± 0.02	0.48 ± 0.02[b]	0.50 ± 0.01	0.53 ± 0.01	0.47 ±
Liver	1.74 ± 0.12	1.49 ± 0.12	1.59 ± 0.09	1.71 ± 0.15	1.93 ±
Kidney	0.75 ± 0.17	0.70 ± 0.05	0.69 ± 0.03	0.66 ± 0.03	0.57 ± 0.04
Spleen	0.17 ± 0.04	0.16 ± 0.02	0.20 ± 0.02	0.31 ± 0.09	0.19 ± 0.03
Testes	0.36 ± 0.03	0.23 ± 0.01[b]	0.28 ± 0.02	0.27 ± 0.03[b]	0.30 ± 0.02
Relative to Brain Weight (gm/gm)					
Liver	3.2 ± 0.2	3.1 ± 0.3	3.2 ± 0.2	3.3 ± 0.3	4.1 ± 0.4
Kidney	1.38 ± 0.26	1.47 ± 0.11	1.39 ± 0.07	1.26 ± 0.06	1.20 ± 0.07
Spleen	0.31 ± 0.06	0.34 ± 0.02	0.39 ± 0.04	0.58 ± 0.17	0.40 ± 0.07
Testes	0.68 ± 0.08	0.49 ± 0.03	0.56 ± 0.03	0.51 ± 0.06	0.64 ± 0.05

a/ Mean ± S.E. of four mice.

b/ Significantly different from Control group, $p < 0.05$; Dunnett's multiple comparison procedure.

TABLE 64

ORGAN WEIGHTS OF FEMALE MICE EXPOSED TO VC OR VDC FOR 9 MONTHS

	Control	50 PPM VC	250 PPM VC	1,000 PPM VC	55 PPM VDC
			Absolute Weight (gm)		
Terminal Body Weight	34 ± 2[a/]	32 ± 3	35(1)	30(1)	30 ± 1
Brain	0.54 ± 0.01	0.54 ± 0.02	0.48(1)	0.51(1)	0.50 ± 0.03
Liver	1.36 ± 0.09	1.31 ± 0.13	1.93(1)	1.20(1)	1.34 ± 0.05
Kidney	0.47 ± 0.01	0.49 ± 0.04	0.45(1)	0.37(1)	0.46 ± 0.03
Spleen	0.14 ± 0.01	0.15 ± 0.02	0.55(1)	0.11(1)	0.16 ± 0.01
Ovaries	0.07 ± 0.01	0.05 ± 0.02	0.05(1)	0.02(1)	0.05 ± 0.01
			Relative to Brain Weight (gm/gm)		
Liver	2.54 ± 0.16	2.41 ± 0.15	4.04(1)	2.35(1)	2.68 ± 0.08
Kidney	0.88 ± 0.04	0.90 ± 0.05	0.93(1)	0.72(1)	0.92 ± 0.04
Spleen	0.25 ± 0.01	0.27 ± 0.04	1.14(1)	0.22(1)	0.33 ± 0.02
Ovaries	0.14 ± 0.02	0.10 ± 0.03	0.10(1)	0.05(1)	0.10 ± 0.01

a/ Mean ± S.E. of four mice except as noted in parentheses.

TABLE 65

ORGAN WEIGHTS OF MALE MICE EXPOSED TO VC OR VDC FOR 12 MONTHS

Group	Control	50 ppm VC	55 ppm VDC
	Absolute Weight (gm)		
Brain	0.490 ± 0.019[a/](4)	0.493 ± 0.020(3)	0.479 ± 0.010(8)
Liver	2.1 ± 0.0(4)	1.7 ± 0.0(3)	2.2 ± 0.2(8)
Kidney	0.78 ± 0.03(4)	0.73 ± 0.03(3)	0.57 ± 0.02[b/](8)
Spleen	0.17 ± 0.02(4)	0.12 ± 0.01(3)	0.26 ± 0.09(8)
Testes	0.302 ± 0.009(4)	0.283 ± 0.020(3)	0.269 ± 0.016(8)
	Relative to Brain Weight (gm/gm)		
Liver	4.3 ± 0.2(4)	3.6 ± 0.1(3)	4.6 ± 0.4(8)
Kidney	1.59 ± 0.02(4)	1.49 ± 0.07(3)	1.18 ± 0.04[b/](8)
Spleen	0.36 ± 0.04(4)	0.25 ± 0.02(3)	0.53 ± 0.18(8)
Testes	0.62 ± 0.05(4)	0.57 ± 0.03(3)	0.56 ± 0.02(8)

a/ Mean ± S.E. of number of rats indicated in parentheses.

b/ Significantly different from Control group, $p < 0.05$; Dunnett's multiple comparison procedure.

TABLE 66

ORGAN WEIGHTS OF FEMALE MICE EXPOSED TO VC OR VDC FOR 12 MONTHS

Group	Absolute Weight (gm) Control	55 ppm VDC
Brain	0.496 ± 0.008[a/]	0.466 ± 0.015
Liver	1.38 ± 0.06	1.63 ± 0.10[b/]
Kidney	0.44 ± 0.02	0.46 ± 0.02
Spleen	0.121 ± 0.007	0.150 ± 0.015
Ovary	0.04 ± 0.01	0.06 ± 0.02
	Relative to Brain Weight (gm/gm)	
Liver	2.8 ± 0.1	3.6 ± 0.3[b/]
Kidney	0.89 ± 0.04	0.98 ± 0.05
Spleen	0.24 ± 0.02	0.32 ± 0.03[b/]
Ovary	0.08 ± 0.01	0.14 ± 0.05

a/ Mean ± S.E. of ten rats (Control) or eight rats (55 ppm VDC).
b/ Significantly different from Control group, $p < 0.05$; Dunnett's multiple comparison procedure.

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TABLE 67

SUMMARY OF BRONCHIOLO ALVEOLAR ADENOMAS IN MICE AFTER EXPOSURE TO VC OR VDC

Exposure Time	Control ♂	Control ♀	50 ppm VC ♂	50 ppm VC ♀	250 ppm VC ♂	250 ppm VC ♀	1,000 ppm VC ♂	1,000 ppm VC ♀	55 ppm VDC ♂	55 ppm VDC ♀
1 month	0[a/]	0	0	0	0	0	0	0	0	0
2 months	0	0	0	0	1	0	1	2	0	0
3 months	0	0	1	0	1	0	2	1	0	0

a/ Number of adenomas in four mice of each sex.

TABLE 68

SUMMARY OF TUMORS THAT OCCURRED DURING 4 TO 6 MONTHS OF EXPOSURE TO VC OR VDC[a/]

Tumor[b/]	50 ppm VC					250 ppm VC									1,000 ppm VC										55 ppm VDC		
Sex	Male			Female		Male				Female						Male						Female						Male		
House No.	107[c/]	122	124	143[c/]	85	157	158	159	160	214[c/]	215[c/]	216[c/]	194	195	196	251[c/]	252[c/]	229	230	231	232	284[c/]	288[c/]	265	266	267	268	301	302	303
Week Terminated	22	26	26	26	26	26	26	26	26	24	24	24	26	26	26	21	26	26	26	26	26	22	25	26	26	26	26	26	26	26
Connective Tissue (adjacent to salivary gland)																														
Hemangioma																					1									
Lung																														
Bronchiolo-alveolar adenoma	1		1						2	1	2			2	1	2	3	3	1	3	3	2	2	3		2				1
Acinar proliferation		1			1	1	1	1					1												1		1	1		
Metastic squamous cell and/or anaplastic carcinoma												1										1	2			1				
Liver																														
Hemangiosarcoma													3		2					1	2	2		1		1				
Mammary Gland																														
Duct adenocarcinoma												2										2	2			1				
Squamous cell carcinoma												2											3			3				
Anaplastic carcinoma												2											3			2				
Hemangiosarcoma																						2				2				
Malignant Lymphoma				3												3														

a/ Includes only mice which were found to have tumors during 4 to 6 months of exposure to VC or VDC.
b/ Severity of lesion: 1 - mild; 2 - moderate; 3 - marked; 4 - severe; + - present; ± questionable.
c/ Died or unscheduled termination.

TABLE 69

SUMMARY OF TUMORS THAT OCCURRED IN MICE DURING 7 TO 9 MONTHS OF EXPOSURE TO 50 PPM VC[a]

Tumor[b]	Sex	Male			Female										
	Mouse No.	92	108[c]	105[c]	125	126	142[c]	141[c]	140[c]	139[c]	138[c]	137[c]	136[c]	135[c]	134[c]
	Week Terminated	39	27	39	39	39	28	28	33	33	33	34	35	36	36
Lung															
Bronchiolo alveolar adenoma		1		1	1	1					1				1
Metastatic squamous cell carcinoma							1			1					
Liver															
Hemangiosarcoma			±												
Mammary Gland															
Duct adenocarcinoma							1	1	1					2	3
Squamous cell carcinoma								1	1	1		1		2	3
Anaplastic carcinoma									1	3		1		2	3
Hemangiosarcoma							1								
Epididymus and Testes															
Hemangiosarcoma				1											
Mediastinum															
Hemangioma													2		

a/ Includes only mice which were found to have tumors during 7 to 9 months exposure to 50 ppm VC.
Five scheduled mice and two unscheduled mice were not found to have tumors.

b/ Severity of lesion: 1 - mile; 2 - moderate; 3 - marked; 4 - severe; ± - questionable.

c/ Died or unscheduled termination.

TABLE 70

SUMMARY OF TUMORS THAT OCCURRED IN MICE DURING 7 TO 9 MONTHS OF EXPOSURE TO 250 PPM VC[a]

Tumor[b]	Sex	Male								Female													
	Mouse No.	162	163	164	180[c]	179[c]	178[c]	177[c]	176[c]	197[d]	213[c]	212[c]	211[c]	210[c]	209[c]	208[c]	207[c]	206[c]	205[c]	204[c]	203[c]	202[c]	201[c]	200
	Week Terminated	39	39	39	27	32	32	33	34	39	27	27	30	30	31	32	32	32	32	33	33	34	34	34
Lung																								
Bronchiolo-alveolar adenoma		3	2	2			1	2		1		3	3		3	2				1	2			2
Metastatic squamous cell carcinoma													2											
Liver																								
Hemangiosarcoma		1			1	1		1	1	1	1		4	1	4	1	2	2	3	1	1	2	1	1
Mammary Gland																								
Duct adenocarcinoma																		1	1					
Squamous cell carcinoma																		1	1					
Anaplastic carcinoma																		2	1					
Malignant Lymphoma															1	1								
Heart																								
Hemangiosarcoma						±																		
Pancreas																								
Hemangiosarcoma																						1		
Skeletal Muscle																								
Hemangiosarcoma																							1	
Gastrointestinal Tract																								
Hemangiosarcoma																								1

a/ Includes only mice which were found to have tumors during 7 to 9 months exposure to 250 ppm VC. One scheduled and two unscheduled mice were not found to have tumors.

b/ Severity of lesion: 1 - mild; 2 - moderate; 3 - marked; 4 - severe; ± - questionable.

c/ Died or unscheduled termination.

d/ Only female that survived 39 weeks exposure to 250 ppm VC.

TABLE 71

SUMMARY OF TUMORS THAT OCCURRED IN MICE DURING 7 TO 9 MONTHS OF EXPOSURE TO 1,000 PPM VC[a]

Tumor[b]	Sex	Male													
	Mouse No.	233	234	235	236	250[c]	249[c]	247[c]	246[c]	245[c]	244[c]	243[c]	242[c]	241[c]	240[c]
	Week Terminated	39	39	39	39	28	29	31	34	34	34	34	35	36	38
Lung															
Bronchiolo-alveolar adenoma		3	3	3	3	3	3	3	2	2	3		3	1	3
Liver															
Hemangiosarcoma		4	1	2			3	1	3	3	2		3	3	3
Malignant Lymphoma												3			

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TABLE 71 (Concluded)

SUMMARY OF TUMORS THAT OCCURRED IN MICE DURING 7 TO 9 MONTHS OF EXPOSURE TO 1,000 PPM VC[a]

Tumor[b]	Sex / House No. / Week Terminated	Female 269B[d] 39	287♀[c] 27	286♀[c] 27	285♀[c] 27	283♀[c] 28	282♀[c] 28	281♀[c] 29	280♀[c] 30	279♀[c] 30	278♀[c] 30	277♀[c] 31	276♀[c] 31	275♀[c] 34	274♀[c] 34	273♀[c] 34	272♀[c] 34	271♀[c] 35	270♀[c] 36	269♀[c] 36	269A♀[c] 37
Lung																					
Bronchiolo-alveolar adenoma		1	3	2	3	3	3	1	3		2	3	3	1	3	3	1	1	3	3	1
Metastatic squamous cell carcinoma			2	2	2						1				3						
Metastatic anaplastic carcinoma															1						
Liver																					
Hemangiosarcoma		1	1	1	1			1	1	1	2		3	3	3				3	2	3
Mammary Gland																					
Duct adenocarcinoma			1	1	3			3													
Squamous cell carcinoma				1	1						3		3	3	3	2	2				
Anaplastic carcinoma														3	3	2	2				
Hemangiosarcoma								3						3	3	2	2				
Malignant Lymphoma										3		3			3						
Kidney																					
Hemangiosarcoma												1									
Mesenteric Lymph Nodes																					
Hemangiosarcoma													1								

a/ Includes only mice which were found to have tumors during 7 to 9 months exposure to 1,000 ppm VC. One unscheduled termination was not found to have any tumors.

b/ Severity of lesion: 1 - mild; 2 - moderate; 3 - marked; 4 - severe; ± - questionable.

c/ Died or unscheduled termination.

d/ Only female surviving 39 weeks exposure to 1,000 ppm VC.

TABLE 72

SUMMARY OF TUMORS THAT OCCURRED IN MICE DURING 10 TO 12 MONTHS EXPOSURE TO VC OR VDC[a/]

	50 ppm VC					250 ppm VC			55 ppm VDC									
Sex	Male					Female			Male								Female	
Mouse No.	95	94	93	104[c/]	103[c/]	132[c/]	131[c/]	129[c/]	177[c/]	171[c/]	321	320	316	315	314	312	311	310	350	360[c/]
Tumor[b/] Week Terminated	52	52	52	42	51	46	47	52	40	48	52	52	52	52	52	52	52	52	52	43
Lung																				
Bronchiolo-alveolar adenoma	1	1		1					3	1	1	1			1					
Liver																				
Hemangiosarcoma			3	3					4	2						2				1
Hepatoma																			3	
Hepatic cell carcinoma														2						
Mammary gland																				
Duct adenocarcinoma						3	2													
Squamous cell carcinoma						3	2													
Anaplastic carcinoma						3	2													
Hemangiosarcoma							2													
Mesentery																				
Hemangiosarcoma		1	3	1	3			1	2								2	2		
Kidney																				
Adenoma	1												1							
Skin																				
Keratoacanthoma				3																

a/ Includes only mice that were found to have tumors during 10 to 12 months exposure to VC or VDC

b/ Severity of lesions: 1 - mild; 2 - moderate; 3 - marked; 4 - severe; 1 - questionable.

c/ Death or unscheduled termination. No tumors were found in control mice during this period.

TABLE 73

CUMULATIVE TUMOR INCIDENCE IN MICE DURING 12 MONTHS EXPOSURE TO VC OR VDC

	Control		50 ppm VC		250 ppm VC		1,000 ppm VC		55 ppm VDC	
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Tumor										
Lung										
Bronchiolo alveolar adenoma	1/26[a/]	0/36	8/29	4/34	10/29	12/34	22/33	26/37	6/35	0/35
Acinar proliferation	0/26	0/36	1/29	1/34	3/29	1/34	0/33	2/87	2/35	0/35
Metastatic squamous cell carcinoma	0/26	0/36	0/29	2/34	0/29	2/34	0/33	8/37	0/35	0/35
Liver										
Hemangiosarcoma	0/26	0/36	3/29	0/34	7/29	16/34	13/33	18/37	2/35	1/35
Hepatoma	0/26	0/36	0/29	0/34	0/29	0/34	0/33	0/37	1/35	1/35
Hepatic cell carcinoma	0/26	0/36	0/29	0/34	0/29	0/34	0/33	0/37	1/35	0/35
Mammary gland										
Duct adenocarcinoma	0/26	0/36	0/29	8/34	0/29	3/34	0/33	7/37	0/35	0/35
Squamous cell carcinoma	0/26	0/36	0/29	9/34	0/29	3/34	0/33	10/37	0/35	0/35
Anaplastic carcinoma	0/26	0/36	0/29	8/34	0/29	3/34	0/33	6/37	0/35	0/35
Hemangiosarcoma	0/26	0/36	0/29	1/34	0/29	0/34	0/33	7/37	0/35	0/35
Malignant lymphoma	0/26	0/36	0/29	1/34	0/29	2/34	2/33	3/37	0/35	0/35
Hemangiosarcoma										
Heart	0/26	0/36	0/29	0/34	1/29	0/34	0/33	0/37	0/35	0/35
Skeletal muscle	0/26	0/36	0/29	0/34	0/29	1/34	0/33	0/37	0/35	0/35
Gastrointestinal tract	0/26	0/36	0/29	0/34	0/29	1/34	0/33	0/37	0/35	0/35
Kidney	0/26	0/36	0/29	0/34	0/29	0/34	0/33	1/37	0/35	0/35
Pancreas	0/26	0/36	0/29	0/34	0/29	1/34	0/33	0/37	0/35	0/35
Mesenteric lymph nodes	0/26	0/36	0/29	0/34	0/29	0/34	0/33	1/37	0/35	0/35
Epididymus and testes	0/26	0/36	1/29	0/34	0/29	0/34	0/33	0/37	0/35	0/35
Mesentery	0/26	0/36	4/29	1/34	1/29	0/34	0/33	0/37	2/35	0/35

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TABLE 73 (Continued)

CUMULATIVE TUMOR INCIDENCE IN MICE DURING 12 MONTHS EXPOSURE TO VC OR VDC

	Control		50 ppm VC		250 ppm VC		1,000 ppm VC		55 ppm VDC	
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Hemangioma										
Mediastinum	0/26	0/36	0/29	1/34	0/29	0/34	0/33	0/37	0/35	0/35
Connective tissue (adjacent to salivary gland)	0/26	0/36	0/29	0/34	0/29	0/34	1/33	0/37	0/35	0/35
Kidney										
Adenoma	0/26	0/36	1/29	0/34	0/29	0/34	0/33	0/37	1/35	0/35
Skin										
Keratoacanthoma	0/26	0/36	1/29	0/34	0/29	0/34	0/33	0/37	0/35	0/35

a/ Number of mice with tumors/total number of mice that died or were terminated during 12 months exposure to VC or VDC.

TABLE 74

SUMMARY OF TISSUE LESIONS AND M/E RATIOS IN MICE AFTER EXPOSURE TO VC OR VDC FOR 1 MONTH

Lesion[a/]	Controls								VC (1,000 ppm)								VDC (55 ppm)							
Sex:	Males				Females				Males				Females				Males				Females			
Rat No:	1	2	3	4	37	38	39	40	217	218	219	220	253	254	255	256	289	290	291	292	325	326	327	3
Heart																								
Myocarditis																								1
Liver																								
Focal degeneration and inflammation																						1	1	
Bile duct hyperplasia and cholelethiosis																								
Salivary Gland																								
Microfoci of mononuclear cells																							1	
Kidney																								
Chronic interstitial nephritis	2	1	2	2								1					1	1	1	1				
Tubular casts	2		2	1								1						1						
Tubular basophilia		1		1								1								1				
Microcalculi			1														1		1					
Skeletal Muscle																								
Myositis																							1	
Bone Marrow																								
M/E ratio	1·2	1·3	1·3	1·2	1·3	1·4	1·2	1·2	1·1	1·3	1·3	1·2	1·3	1·5	1·3	1·4	1·6	1·5	1·3	1·4	1·5	1·2	1·2	1

a/ Severity of lesion: 1 - mild, 2 - moderate, 3 - marked, 4 - severe, ± - questionable.

TABLE 75

SUMMARY OF TISSUE LESIONS AND M/E RATIOS IN MICE
AFTER EXPOSURE TO VC OR VDC FOR 2 MONTHS

Lesion[a/]	Controls								VC (1,000 ppm)								VDC (55 ppm)							
Sex:	Males				Females				Males				Females				Males				Females			
Rat No:	5	6	7	8	41	42	43	44	221	222	223	224	257	258	259	260	293	294	295	296	329	330	331	332
Heart																								
Myocarditis													1											
Lung																								
Bronchiolo-alveolar adenoma											1			1	1									
Liver																								
Microfoci of inflammatory cells			1										1									1	1	1
Focal mineralization															1									
Pancreas																								
Pancreatitis and degeneration															2	2								
Perianal Gland																								
Suppurative inflammation			3																					
Hyperplasia			2																					
Kidney																								
Chronic interstitial nephritis		1	1					1	1								1		2					
Tubular casts	1		1	1															2					
Microcalculi																			1					
Tubular basophilia			1																					
Dilation of pelvis										1		1												
Uterus																								
Acute metritis					1	1	1									1								
Brain																								
Mild, focal fatty change																					1			
Skeletal Muscle																								
Myositis															1									
Bone Marrow																								
M/E ratio	1·3	1·3	1·4	1·3	1·2	1·3	1·4	1·5	1·4	1·3	1·4	1·2	1·4	1·5	1·5	1·4	1·3	1·3	1·4	1·5	1·5	1·2	1·4	1·3

a/ Severity of lesion: 1 - mild, 2 - moderate, 3 - marked, 4 - severe, ± - questionable, + - present.

TABLE 76

SUMMARY OF TISSUE LESIONS AND M/E RATIOS IN MICE
AFTER EXPOSURE TO VC OR VDC FOR 3 MONTHS

Lesion[a/]	Sex	Control								VC (1,000 ppm)								VDC (55 ppm)						
		Male				Female				Male				Female				Male				Female		
	Rat No.	9	10	11	12	45	46	47	48	225	226	227	228	261	262	263	264	297	298	299	300	333	334	335
Heart																								
Focal myocardial degeneration																				1	1	1		1
Lung																								
Bronchiolo-alveolar adenoma													1	1										
Focal acinar epithelial proliferation												1												
Liver																								
Microfoci of mononuclear cells					1	1										1			1		1			
Intranuclear inclusions	+	+	+							+	+	+	+			+	+	+	+	+	+	+		+
Focal necrosis																					1			
Salivary Gland																								
Focal chronic inflammation												1				1								
Kidney																								
Focal, chronic interstitial nephritis	1		1										1		1		1		1		1	1		
Tubular casts	1	1		1														1	1	1	1			
Microcalculi		1																	1					
Bone Marrow																								
M/E ratio	1.6	1.6	1.7	1.4	1.7	1.5	1.6	1.4	1.5	1.6	1.7	1.5	1.5	1.7	1.6	1.5	1.7	1.7	1.7	1.6	1.7	1.6	1.8	

a/ Severity of lesions: 1 - mild, 2 - moderate, 3 - marked, 4 - severe, ± - questionable, + - present.

TABLE 77

SUMMARY OF TISSUE LESIONS (OTHER THAN TUMORS) AND M/E RATIOS IN MICE EXPOSED TO VC OR VDC FOR 6 MONTHS[a/]

Lesion[b/]	CONTROLS								VC (1,000 ppm)								VDC (55 ppm)							
Sex	Males				Females				Males				Females				Males				Females			
House No.	13	14	15	16	49	50	51	52	229	230	231	232	265	266	267	268	301	302	303	304	337	338	339	340
Heart																								
Focal myocarditis				1																				
Lung																								
Focal suppurative bronchopneumonia		1									1				1									
Macrophage and lymphoid infiltration			1		1		1	1			1		2		2						1			
Salivary gland																								
Focal, chronic inflammation		1				1		1			1		1		1			1						
Liver																								
Microfoci of mononuclear cells							1	1		1	1			1	1							1		
Increase in intranuclear cells									1				1				1	1	1	1				
Infiltration of nucleated RBC's											1	2	1											
Focal degeneration or necrosis											1	2	1			1								
Infiltration of inflammatory cells											1	2	1			1								
Kidney																								
Focal, chronic interstitial nephritis	1	1	2		1	1	1	1	1	1	1	3	1		1	1	1	1	1	1	1	1		1
Proteinaceous casts	1		2						1	1	1	1						1		1				
Focal tubular necrosis										1														
Brain																								
Focal inflammation										1														
Adrenal																								
Spindle cells infiltration			1	1		1	1	1		1	1		1		1	1	1		1	1			1	1
Focal vacuolation			1	1					1	2	1					1				1				
Bone marrow																								
M/E ratio	1·6	1·5	1·6	1·7	1·5	1·6	1·4	1·7	1·6	1·9	1·4	1·8	1·7	1·5	2·1	1·6	1·6	1·5	1·6	1·7	1·6	1·5	1·6	1·4

a/ Does not include deaths and unscheduled terminations that occurred during the 4 to 6 months.

b/ Severity of lesion: 1 - mild; 2 - moderate; 3 - marked; 4 - severe; ± - questionable.

TABLE 78

SUMMARY OF TISSUE LESIONS (OTHER THAN TUMORS) AND M/E RATIOS IN MICE EXPOSED TO VC OR VDC FOR 9 MONTHS[a/]

	Control								VC (1,000 ppm)					VDC (55 ppm)							
	Males				Females				Males				Females	Males				Females			
Lesion[b/]	17	18	19	20	53	54	55	56	233	234	235	236	2698	305	306	307	308	341	342	343	344
Heart																					
Hyocarditis					1	1	1					1	1	1	1	1	1		1	1	
Thickening of arterial wall and periarteritis														2							
Lung																					
Chronic murine pneumonia			1				1		1		1	2				1	1	1		1	
Mineralization												1									
Liver																					
Portal inflammation																	3				
Microfoci of mononuclear cells	1				1		1								1	2		2	2	2	2
Focal degeneration and necrosis	1											1		1	1	2	2	1	1	2	3
Intranuclear inclusions														2	2	3	2	3	2	2	
Large basophilic nuclei														2	3	3				2	
Salivary Gland																					
Chronic inflammation	1		1			1		1													
Cecum																					
Pinworms																1					
Kidney																					
Chronic interstitial nephritis	1	1	1	1	1	1	1	1		2	1	3		1	1	2	1		1		1
Tubular dilation and casts		1		1								2				1					
Glomerulonephritis (amyloidosis)																3					
Adrenal																					
Spindle cell infiltration					1			1								1	1		1		1
Large cells with yellowish vacuolated or foamy cytoplasm											1	2			2						1
Spleen																					
Lymphoid hyperplasia									2	1	1										
Vacuolization															2	2					
Extramedullary hematopoiesis																				1	
Mesenteric Lymph Node																					
Hemosiderosis												1									
Bone Marrow Smear																					
M/E ratio	1.7	1.5	1.7	1.5	1.5	1.5	1.6	1.7	1.9	1.7	1.7	1.5	--	1.7	1.4	1.5	1.6	1.7	1.5	1.9	1.8

a/ Does not include deaths or unscheduled terminations that occurred during 7 to 9 months.

b/ Severity of lesion: 1 - mild; 2 - moderate; 3 - marked; 4 - severe; ± - questionable.

TABLE 79

SUMMARY OF TISSUE LESIONS (OTHER THAN TUMORS) AND M/E RATIOS IN MICE EXPOSED TO VC OR VDC FOR 12 MONTHS[a/]

	Controls														VC (50 ppm)			VDC (55 ppm)											
	Males				Females										Males			Males							Females					
Lesion[b/]	21	22	23	24	57	58	59	60	61	62	63	64	65	66	93	94	95	309	310	311	312	313	314	315	316	345	346	347	348	349	350	351	352
Heart																																	
Myocarditis																			1	2	2	1		2	1							1	1
Lung																																	
Chronic murine pneumonia				2	2	2					1		1	1					1	1					1			1		1	1		1
Liver																																	
Distended sinusoids																					3	1											
Focal necrosis	2							2	2		2													3									
Microfoci of mononuclear cells							1	2	2			1						2	2			2	2			1	2		1	1	2	1	1
Degeneration		1	1					2	2									2	2	2		2	2	3	2	1	1	1	3	1	2	2	1
Intranuclear inclusions		1	1															3	2	3	2	3	3	2	2	2	2	1		2		3	2
Cyst and subacute inflammation											2																						
Bile duct hyperplasia											1																						
Small Intestine																																	
Amyloidosis	2	3	3		1	1		2					1	3	3	3	2	3	1	3	3	3	2	3	1	3	3	2	3	2		2	4
Cecum																																	
Pinworms in lumen						1								1						1									1				
Salivary Gland																																	
Microfoci of mononuclear cells			1	1				1	1	1																	1					1	
Kidney																																	
Chronic interstitial nephritis	1		1	1		1			1	1	1	1		1	1	1	1	1	1		2	1	1	1	1		1	1	1			1	
Amyloidosis		2														2		3	1	4	2	1		2	3	3							3
Tubular dilation and casts				1																2		1	1	1									
Ovary																										1							
Cyst																										3		3					4
Amyloidosis														2																			
Uterus																																	
Distended endometrial glands																										2		3	2				
Testis																																	
Tubular necrosis and mineralization																			1	1													
Amyloidosis																						2											
Adrenal																																	
Spindle cell infiltration		3	1	1		2					1					1							1						1	1		2	1
Mononuclear infiltration						1																											
Amyloidosis																		3	2	2				3	2	2							2
Spleen																																	
Amyloidosis		2																4															
Lymphoid hyperplasia																									2								
Extramedullary hematopoiesis																									1								
M/E Ratio	1.7	1.8	1.5	1.7	1.6	1.6	1.9	1.8	2.2	--	--	--	1.7	1.8	1.8	1.6	1.7	--	--	1.8	1.8	1.6	1.9	1.8	2.1	--	--	1.9	1.9	1.7	2.0	1.7	1.9

a/ Does not include deaths or unscheduled terminations that occurred during 7 to 9 months.

b/ Severity of lesions 1 - mild; 2 - moderate; 3 - marked; 4 - severe; ± questionable.

TABLE 80

DNA SYNTHESIS AND DNA CONCENTRATION OF LIVERS FROM MALE MICE EXPOSED TO 50 PPM VC FOR 11 MONTHS

VC (ppm)	DPM / mg DNA	mg DNA / g Liver
0	2886 ± 240(8)[a/]	2.3 ± 0.1
50	4232 ± 463(7)[b/]	2.5 ± 0.1

a/ Mean ± S.E. (Number of observations).
b/ Significantly different from control (two sample rank test[30/]).

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TABLE 81

HEPATIC ALA SYNTHETASE ACTIVITY IN
RATS EXPOSED TO VC FOR 12 MONTHS

VC Concentration	n Moles/mg Protein/hr	
	Male	Female
0 ppm	0.25 ± 0.03[a/]	0.22 ± 0.02
50 ppm	0.20 ± 0.01	0.24 ± 0.03
250 ppm	0.26 ± 0.04	--

a/ Mean ± S.E. for three determinations.

TABLE 82

URINARY ALA CONCENTRATION IN RATS EXPOSED TO VC FOR 12 MONTHS

VC (ppm)	Sex	Urine Volume(ml)[a/]	Urinary ALA Concentration[b/]
0	Male	3	1
	Male	6	1
	Female	3	1
	Female	27	1
50	Male	6	1
	Male	27	1
	Female	21	1
	Female	25	1
250	Male	13	1
	Male	7	1
	Female	31	1
	Female	7	1
1,000	Male	7	1
	Male	10	1
	Female	2	2

a/ Urine collected overnight

b/ Determined on a 0.5 ml sample of urine and expressed on a scale of 1 (0to 1 mg% ALA) to 6 (6 to 10 mg% ALA) with 2 equal to 1.0 to 1.5 mg% ALA.

TABLE 83

Number of Rats in Dominant Lethal Study
with Vinyl Chloride (VC) and Vinylidene Chloride (VDC)

	Chamber Concentration (ppm)				
	VC				VDC
	0	50	250	1000	55
No. of Male Rats					
Tested	12	12	12	12	12
Mated with 2 females	12	10	11	8[b/]	9
Mated with 1 female	0	2	1	2	2
Mated with 0 females	0	0	0	2	1
Fertile[a/]	12	11	10	10	10
No. of Female Rats					
Mated	24	22	23	18	20
Pregnant	24	20	16[b/]	14[b/]	13[b/]
with 1 dead implant	7	5	7	5	3
with 2 dead implants	3	2	0	1	1
with ≤ 3 dead implants	2	2	1	0	2

a/ Fathered at least one litter with one or more viable implants.

b/ Significantly different from control (Fisher's exact probability test,[31/] $p<0.05$).

TABLE 84

Mating Results in Dominant Lethal Study
with Vinyl Chloride (VC) and Vinylidene Chloride (VDC)

	Chamber Concentration (ppm)				
	VC				VDC
	0	50	250	1000	55
Corpora lutea/dam	15.8±0.6[a/]	14.3±0.8	15.2±0.3	15.1±0.6	15.1±0.5
Implants/dam	13.7±0.8	12.0±0.9	13.4±0.5	11.9±0.9	14.2±0.5
Implants/corpora lutea x 100	86±3	83±5	88±4	81±6	94±2
Viable/total implants x 100	92±2	92±3	93±3	95±2	93±3

a/ Mean ± S.E. for the values calculated on a dam basis for the number of pregnant rats indicated in Table 83.

TABLE 85

LEVELS OF ALPHA-FETOPROTEIN (AFP) IN RATS EXPOSED TO VC FOR 9 MONTHS

Rat No.	Sex	Exposure Group	µg AFP/mℓ of Serum
17	M	Control	<0.022
18	M	Control	<0.022
19	M	Control	<0.022
20	M	Control	<0.022
53	F	Control	<0.022
54	F	Control	<0.022
55	F	Control	<0.022
56	F	Control	<0.022
89	M	50 ppm VC	<0.022
90	M	50 ppm VC	<0.022
91	M	50 ppm VC	<0.022
92	M	50 ppm VC	<0.022
125	F	50 ppm VC	<0.022
126	F	50 ppm VC	<0.022
127	F	50 ppm VC	<0.022
128	F	50 ppm VC	<0.022
161	M	250 ppm VC	<0.022
162	M	250 ppm VC	<0.022
163	M	250 ppm VC	<0.022
164	M	250 ppm VC	<0.022
197	F	250 ppm VC	<0.022[a/]
198	F	250 ppm VC	<0.022
199	F	250 ppm VC	0.034
233	M	1,000 ppm VC	<0.022
234	M	1,000 ppm VC	<0.022
235	M	1,000 ppm VC	<0.022
236	M	1,000 ppm VC	<0.022
269	F	1,000 ppm VC	<0.022
270	F	1,000 ppm VC	<0.022[a/]
272	F	1,000 ppm VC	<0.022

a/ Rat found to have hepatic hemangiosarcoma.

TABLE 86

LEVELS OF ALPHA-FETOPROTEIN (AFP) IN MICE EXPOSED TO VC OR VDC

Mouse No.	Sex	Exposure Group	Length of Exposure(weeks)	µg AFP/mℓ of Plasma
35	M	Control	36	<0.04
133	F	50 ppm VC	36	<0.04
134	F	50 ppm VC	36	<0.04
135	F	50 ppm VC	36	<0.04
137	F	50 ppm VC	34	<0.04
177	M	250 ppm VC	33	0.29[a/]
201	F	250 ppm VC	34	<0.04[a/]
240	M	1,000 ppm VC	38	3.96[a/]
241	M	1,000 ppm VC	36	<0.04[a/]
244	M	1,000 ppm VC	34	<0.04[a/]
245	M	1,000 ppm VC	34	<0.04[a/]
248	M	1,000 ppm VC	30	<0.04
269	F	1,000 ppm VC	36	<0.04[a/]
269A	F	1,000 ppm VC	36	<0.04[a/]
270	F	1,000 ppm VC	36	<0.04[a/]
272	F	1,000 ppm VC	34	<0.04
273	F	1,000 ppm VC	34	<0.04
274	F	1,000 ppm VC	34	<0.04[a/]
275	F	1,000 ppm VC	34	<0.04[a/]
277	F	1,000 ppm VC	31	<0.04
278	F	1,000 ppm VC	30	<0.04[a/]
324	M	55 ppm VDC	36	1.92[b/]

a/ Mouse found to have hepatic hemangiosarcoma.
b/ Mouse found to have a hepatoma.

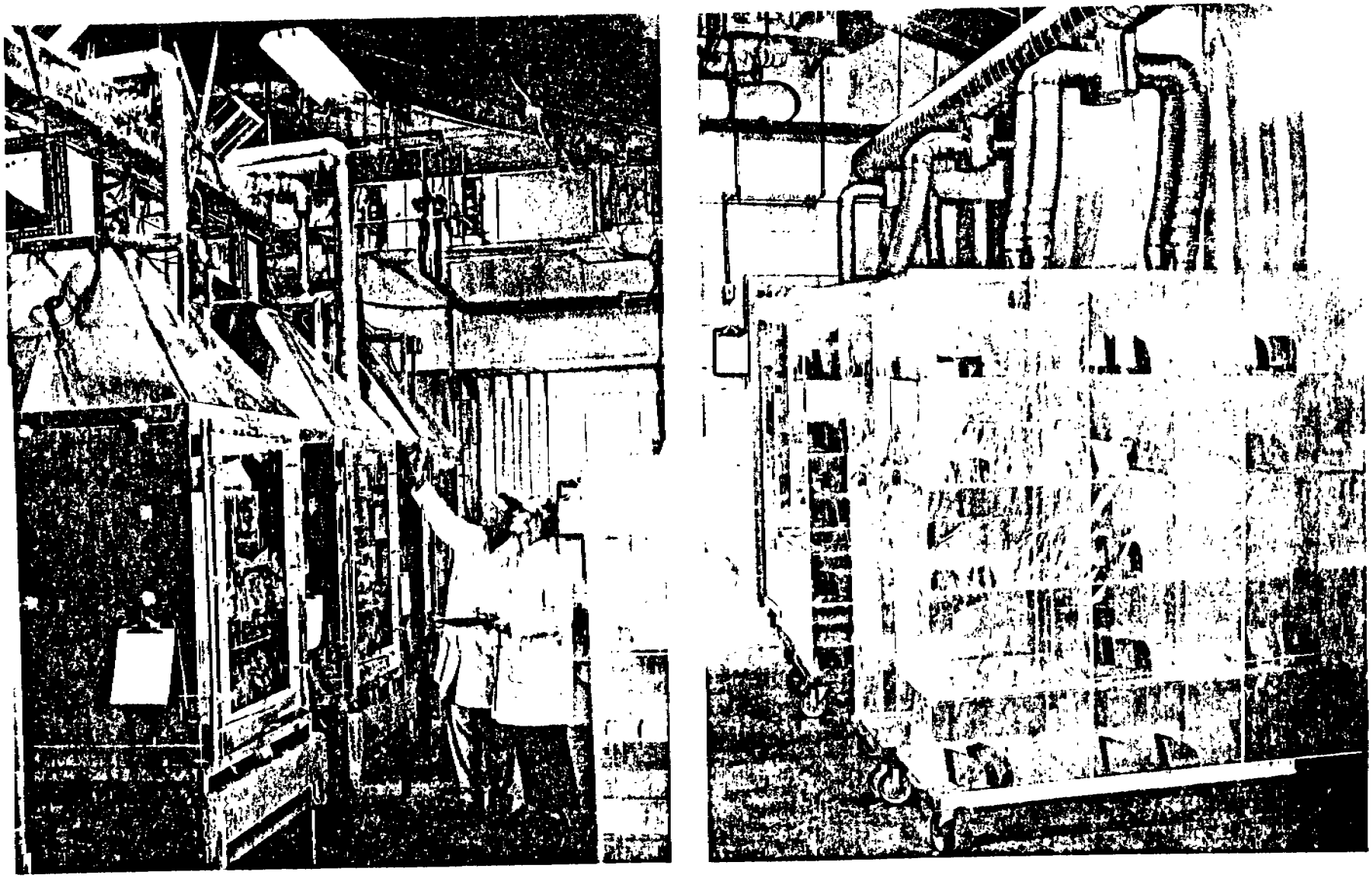

Figure [illegible]halation Chambers and Holding Racks.

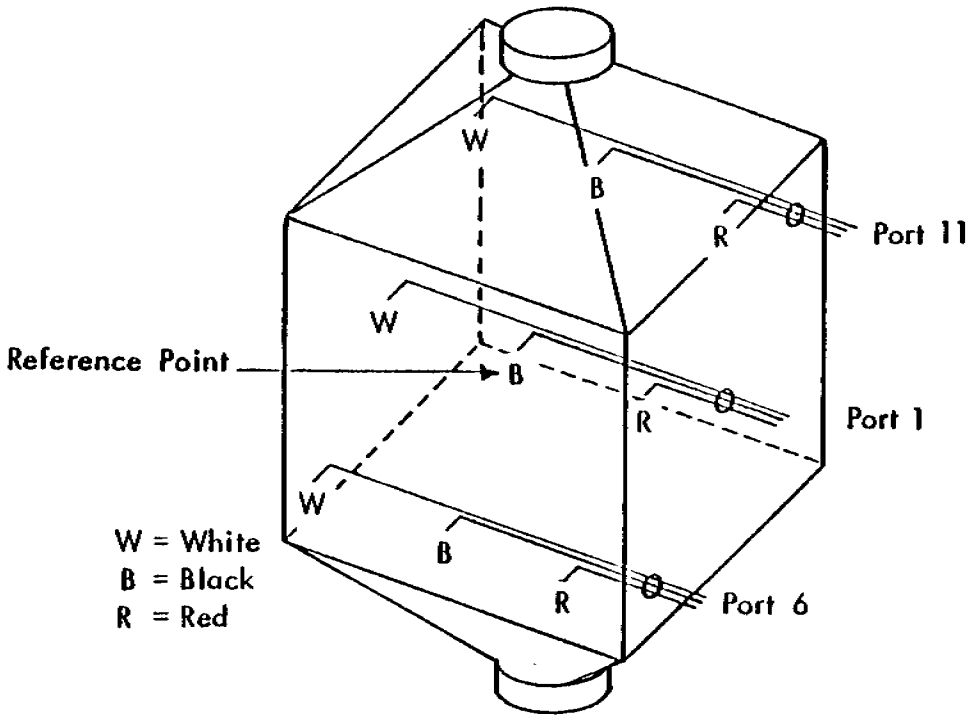

Figure 2 - Diagram of a Chamber Showing the Positions of Sampling Lines.

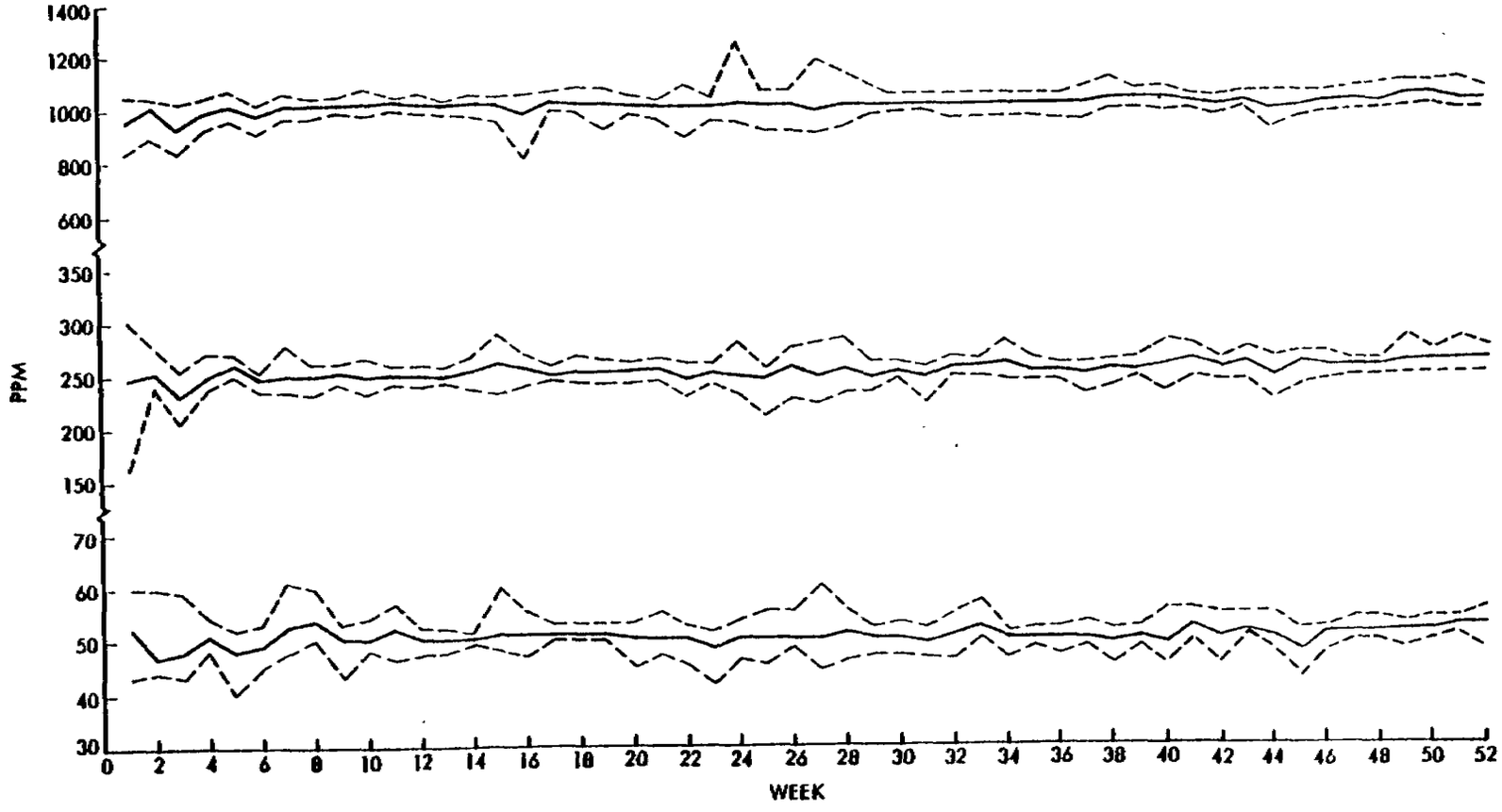

Figure 3 - Average Weekly Analytical Concentrations and the Range of all Samples for VC.

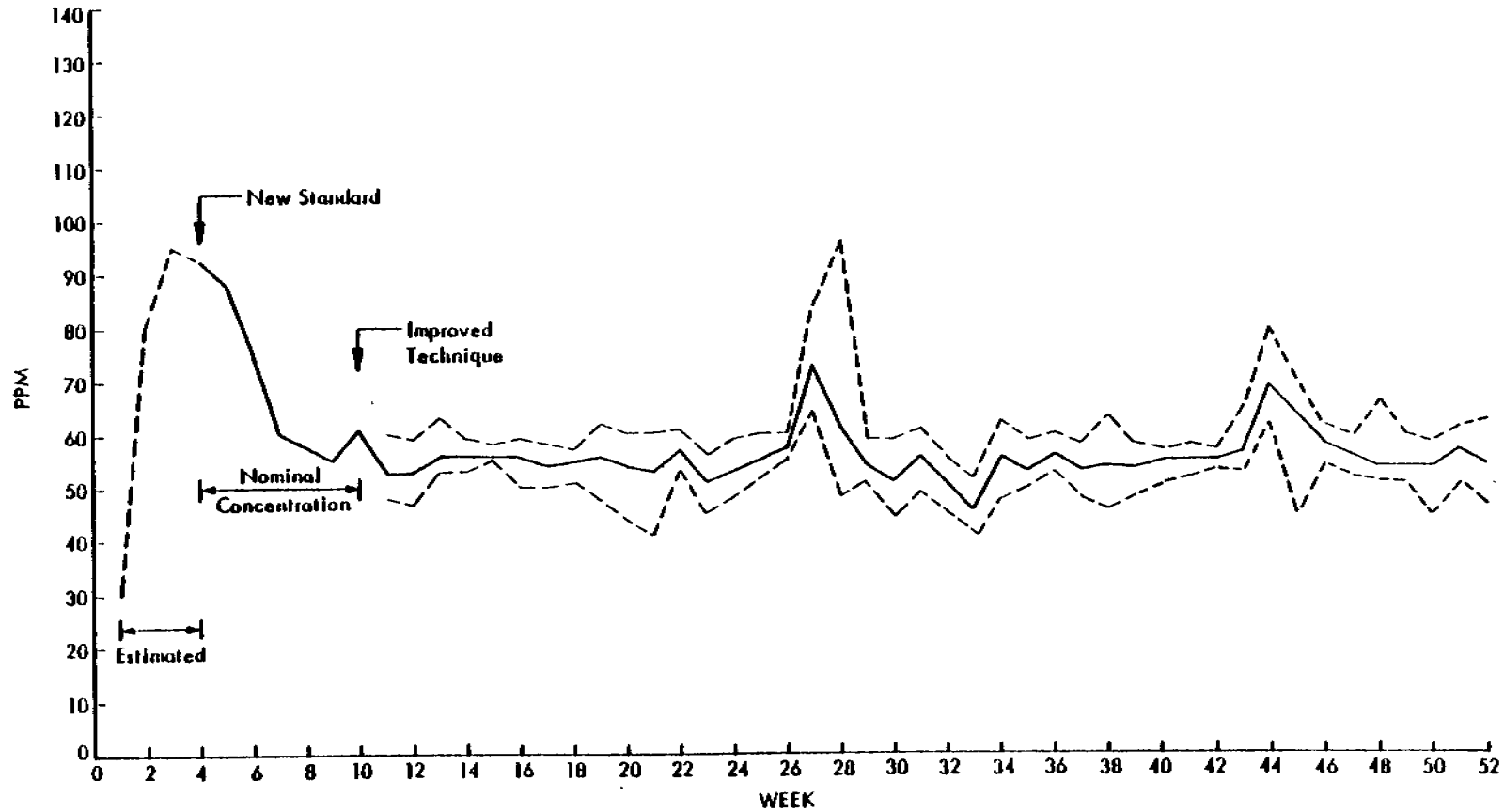

Figure 4 - Average Weekly Analytical Concentrations and the Range of all Samples for VDC.

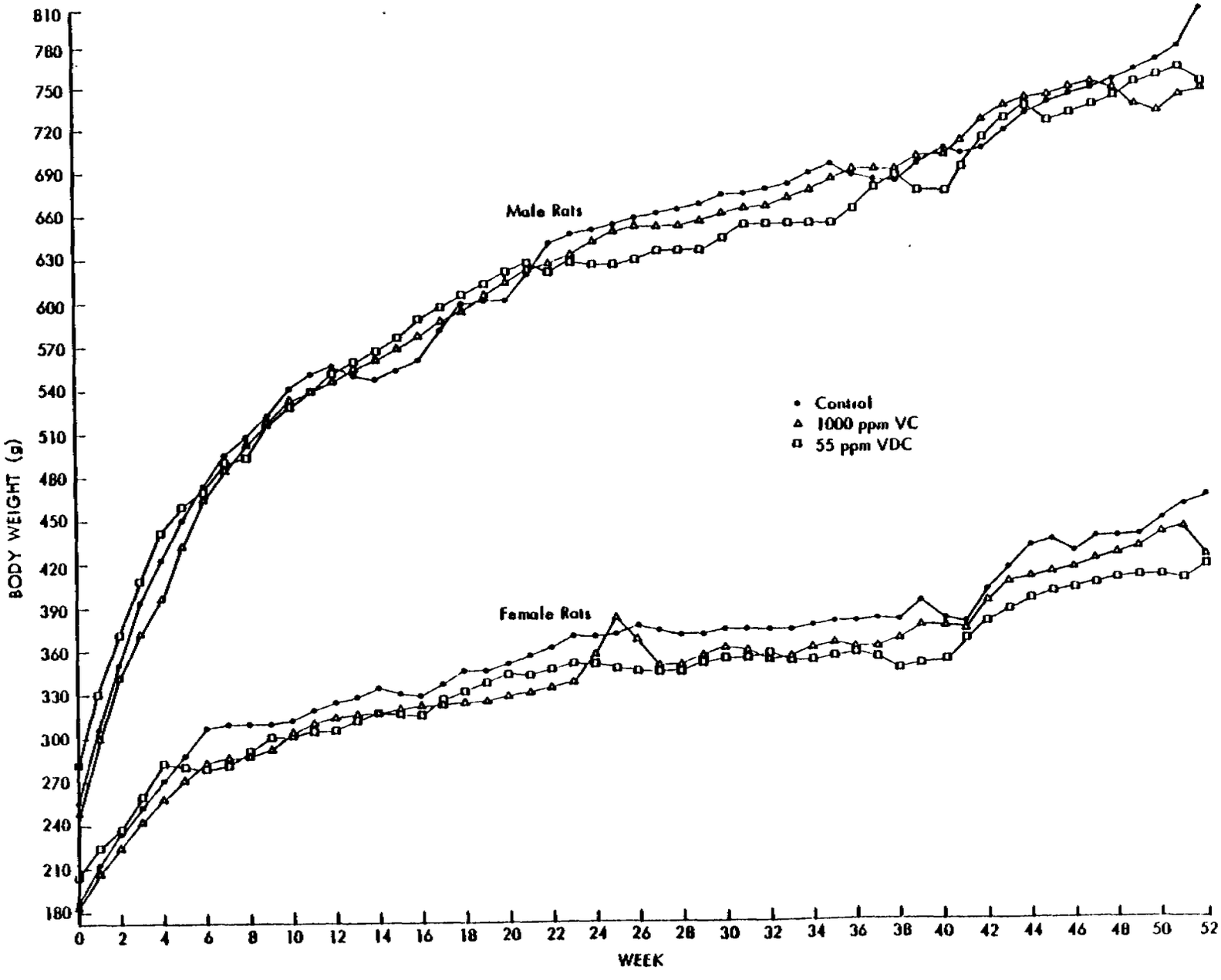

Figure 5 - Body Weights of Rats Exposed to VC or VDC.

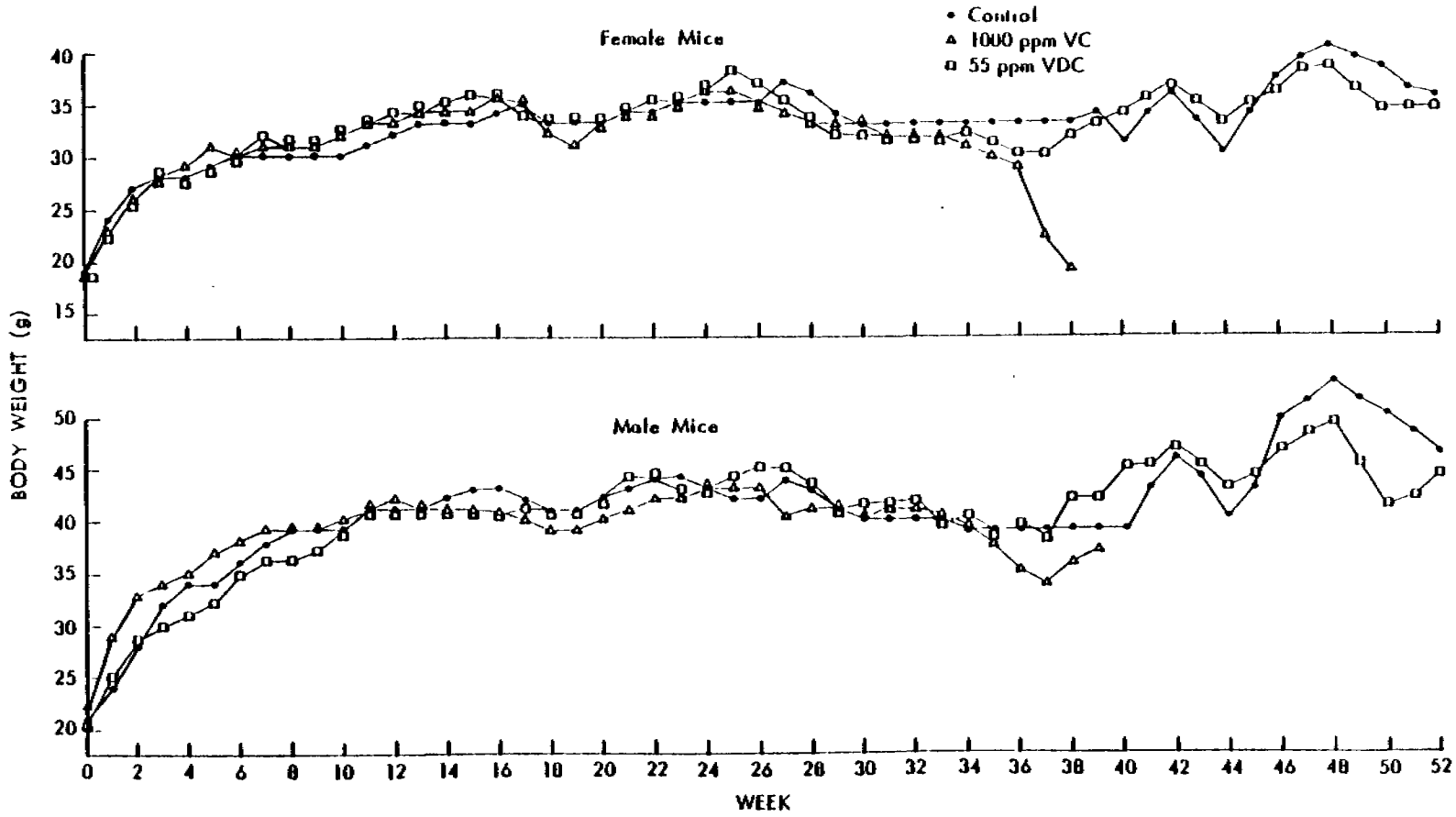

Figure 6 - Weight Gram of Mice Exposed to VC or VDC.

APPENDIX I

MANUAL FOR

HEMATOLOGY, CLINICAL LABORATORY TESTS, HISTOPATHOLOGY, STATISTICAL ANALYSIS, AND NORMAL VALUES

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HEMATOLOGY, CLINICAL LABORATORY TESTS, HISTOPATHOLOGY, STATISTICAL ANALYSIS, AND NORMAL VALUES

I. HEMATOLOGY AND CLINICAL LABORATORY TESTS

The usual blood sample from dogs is 8 ml, from monkeys 4 ml, and from rats 0.3 ml for hematology and about 8 ml for full analysis at termination.

A. Hematology

The following hematological analyses are performed on all blood samples from rats, dogs and monkeys.

1. Erythrocyte and leukocyte counts: A Coulter Electronic Particle Counter with 100 μ aperture is used.[1] Particle-free diluents (Isoton for RBC, Zap-Oglobin in Isoton for WBC, Coulter Electronics, Inc.) are counted to establish the background. Each blood sample is counted in duplicate. For each test day, two control blood samples (Diagnostic Technology, Inc.) are counted separately in duplicate.

2. Hematocrit: Hematocrit is determined in capillary tubes using a microcapillary centrifuge (International Equipment Company, Model MB). Two control blood samples (Diagnostic Technology, Inc.) are measured separately in duplicate.

3. Hemoglobin: Hemoglobin is measured as cyanomethemoglobin.[2] Each blood sample is measured in duplicate. Cyanomethemoglobin (Coulter Electronics, Inc.) is used as the standard. For each assay, two levels of the standard are used and two control blood samples (Diagnostic Technology, Inc.) are measured in duplicate.

4. Methemoglobin (Met-Hb): Met-Hb is measured by the method of Dubowski.[3] A positive control is made by adding potassium ferricyanide to control blood.

5. Heinz bodies: Heinz bodies are stained with methyl violet and the percent of Heinz bodies is calculated.

6. Mean corpuscular volume (MCV): MCV is calculated as follows:

$$\text{MCV } (\mu^3) = \frac{\text{Hematocrit x 10}}{\text{Erythrocytes in millions/mm}^3}$$

7. Mean corpuscular hemoglobin (MCHb): MCHb is calculated as follows:

$$\text{MCHb } (\mu\mu g) = \frac{\text{Hemoglobin (gm \%) x 10}}{\text{Erythrocytes in millions/mm}^3}$$

8. Mean corpuscular hemoglobin concentration (MCHbC): MCHbC is calculated as follows:

$$\text{MCHbC (gm \%)} = \frac{\text{Hemoglobin (gm \%) x 100}}{\text{Hematocrit}}$$

9. Differential leukocyte counts: Wright's stain is used to stain the leukocytes for examination.

10. Reticulocyte count: Reticulocytes are counted by the methylene blue method using the Miller disc.[4]

11. Platelet count: A Coulter Electronic Particle Counter with 70 μ aperture is used.[5] Particle-free Isoton is used as diluent and counted to establish the background. At weekly intervals, platelets are also visually counted in a hemocytometer with a phase microscope for comparison.[6]

12. Clotting time (dog and monkey): Clotting time is determined by the capillary tube procedure using two capillary tubes.[7] The time elapsed from the appearance of the blood from the animal and coagulation in either tube is measured.

B. Clinical Blood Tests

The following clinical blood chemistry tests [illegible]erformed on all blood samples from dogs and monkeys and on blood samp[illegible] from rats at termination.

1. Blood glucose: Fasting blood glucose is determined by Stein's hexokinase method.[8] Standard glucose solution (Dade) is used to establish a standard curve. For each assay, one level of the standard and two controls (Reference Serum, Worthington; and Validate, General Diagnostics) are measured.

2. Serum glutamic-oxaloacetic transaminase (SGOT): SGOT is measured by the method of Amador and Wacker.[9] Validate and Reference Serum are used as the enzyme reference for each assay.

3. Serum glutamic-pyruvic transaminase (SGPT): SGPT is measured by the method of Henry et al.[10] Validate and Reference Serum are used as the enzyme reference for each assay.

4. Alkaline phosphatase: Alkaline phosphatase is measured by the method of Bowers and McComb.[11] Validate and Reference Serum are used as the enzyme reference for each assay.

5. BUN: BUN is measured using the BUN Strate Kit (General Diagnostic) which is based on the urease method.[12] Three levels of Calibrate (General Diagnostics) are used to establish a standard curve. For each assay, two controls (Calibrate I and Validate) are used as the reference.

6. Creatinine: Creatinine is measured by a modified kinetic alkaline picrate procedure.[13] Creatinine Standard Solutions (Sigma Chemical Company) are used to establish a standard curve. For each assay, two levels of the standard and two controls (Calibrate I and Validate) are used as reference.

7. Lactate dehydrogenase (LDH): LDH is measured by the method of Wacker et al.[14] Precinorm E and Precipath E (Boehringer, Mannheim Corporation) are used as the enzyme controls for each assay.

8. α-Hydroxybutyrate dehydrogenase (α-HBDH): α HBDH is measured by the method of Rosalki and Wilkinson.[15] Precinorm E and Precipath E are used as the enzyme controls for each assay.

9. Creatine phosphokinase (CPK): CPK is measured by the improved procedure of Rosalki[16] based on the methods of Oliver.[17] Precinorm E and Precipath E are used as the enzyme controls for each assay.

C. Urinalysis

Urine samples are collected from animals before and during treatment as are the blood samples. The urine from rats is collected by slight manipulation of their body, and samples within each group are pooled. The monkeys and dogs are placed individually in metabolism cages, and urine is collected in the stainless steel pan. The urine from each dog and the pooled urine from rats are tested and examined for the following:

1. Protein: Urinary protein is determined with Labstix (Ames Company, Elkhart, Indiana).

2. Sugar: Urinary glucose and reducing substance are determined with Labstix (Ames Company).

3. Microscopic examination: Urine samples are centrifuged and the supernatant discarded. The residue is resuspended and examined microscopically for the presence of erythrocytes, leukocytes, epithelial cells, and crystals under high power field and for casts under low power field.

A positive urine control prepared with known amounts of protein and glucose in saline adjusted to pH 6.0 is run with each assay to check the reliability of the Labstix.

D. Occult Blood in Feces

Fecal samples are collected from animals before and during treatment as are the blood and urine samples. Occult blood in the feces is determined with Hematest Reagent Tablets (Ames Company, Elkhart, Indiana). A positive control (whole blood) and a negative control (distilled water) are included with each assay to check the reliability of the Hematest tablets.

E. Precision of Hematology and Clinical Blood Chemistry Tests

1. Reproducibility

For erythrocyte and leukocyte counts, hematocrit, hemoglobin, and the various clinical blood chemistry tests, the same control blood samples or control standards are used for day-to-day assays. The replication of results are excellent and are summarized in Table A.

The determination of differential leukocyte counts and reticulocyte counts are performed by experienced personnel. At weekly intervals, a blood sample is counted by two or more personnel to confirm the accuracy of the counting. Also at weekly intervals, the platelet counts obtained from a Coulter Electronic Particle Counter are compared with the direct visual counts in a hemocytometer using a phase microscope.

2. Reproducibility Within a Test Day

At monthly intervals, a blood sample is taken from a control dog and six or more determinations for erythrocyte, leukocyte, reticulocyte, and platelet counts, hemoglobin, and various clinical blood chemistry tests are performed to establish the reproducibility within an assay. The results are summarized in Table B.

3. Proficiency Test Service

We subscribe to the Proficiency Test Service of the Institute for Clinical Science, Hahnemann Medical College, Philadelphia, Pennsylvania (F. Wm. Sunderman, M.D., Director). On the first day of each month, this service sends two samples containing two different sera or solutions to all subscribers for measurements of one or more of the parameters usually analyzed in clinical laboratories. Participants report their results on a form furnished by the service. On the 15th day of the month, each participant receives a report from the service which includes: the results of a statistical analysis of the values reported by all the participating laboratories; a current review of pertinent methodology; a comprehensive bibliography; and validation of the results which the participating laboratory reported. This service enables each participating laboratory to obtain an unbiased and critical assessment of its proficiency in relation to that of 1,000 or so other clinical laboratories throughout the country. The service has been in continuous operation since 1949 and was given endorsement by the American Society of Clinical Pathologists in 1952 and by the Association of Clinical Scientists in 1957 and 1968. Our results have been found to be satisfactory and are summarized in Table C.

II. HISTOPATHOLOGY

A. Necropsy and Gross Examination

At termination or prior to imminent death, rats are killed with ether, and dogs and monkeys with an overdose of sodium pentobarbital. Animals that die on tests are kept refrigerated but not frozen until necropsy. The general physical condition and nutritional status of each animal at the time of death or termination are observed and recorded. Necropsy is performed as soon as possible after death. Gross changes of all tissues are carefully examined and recorded.

B. Organ Weights

The brain, liver, spleen, kidneys, adrenals, thyroids and gonads are trimmed free from surrounding tissues and weighed. The organ weight to body weight and/or brain weight ratios are then calculated.

C. Tissues for Microscopic Examination

Tissues to be examined include the eye, skin (breast), trachea, lung, tongue (except rat), salivary gland, liver, gallbladder (except rats), pancreas, esophagus, fundic and pyloric stomach, duodenum, jejunum, ileum, cecum, colon, kidneys, urinary bladder, gonads, and accessory organs, diaphragm and gracilis muscle, anterior pituitary, thyroids/parathyroids, adrenals, tonsil (except rat), thymus, spleen, prescapular (except rats) and mesenteric lymph nodes, rib bone with bone marrow, brain (sagittal section for rats; coronal sections of cerebral cortex, cerebellum, and brain stem for dog and monkey), spinal cord (lumbosacral plexus, dog and monkey), sciatic nerve and any other structures not mentioned which show abnormal gross changes.

D. Fixation and Staining of Tissues

All tissues are cut not to exceed 1 cm in thickness for fixation. For most tissues, neutral buffered 10% formalin is used. Sufficient volume of fixing solution is used and the tissues are changed to a fresh solution after 24 hours. The fixed tissues are processed in an Autotechnicon for dehydration, clearing, and infiltration and then embedded in paraffin. Routine H & E staining is used to stain the sectioned tissues for microscopic examination.

Supplementary tissue fixatives and staining techniques may be employed for more positive identification of special lesions such as calcification, pigments, fat deposition and other abnormal changes.

III. STATISTICAL ANALYSIS

Data are analyzed statistically using the Dunnett's multiple comparison procedure following an analysis of variance,[18] or our modification of this procedure for uneven numbers among groups. The chosen criterion significance is $p < 0.05$. The means of each group at various intervals during treatment are compared with pretreatment levels. For most experiments in beagles, three baseline (pretreatment) levels are obtained. The baseline levels for each animal are averaged and the mean is used in the analysis. In addition, the means of the various treated groups are compared with that of the control group at the respective time intervals.

IV. NORMAL VALUES

A. Hematology, Clinical Laboratory Tests and Bone Marrow

Since June 1971, we have used about 180 rhesus monkeys (Woodard Research Corporation, Herndon, Virginia, Primate Imports, Port Washington, New York, and PrimeLabs, Inc., Farmingdale, New Jersey) for various studies. The peripheral blood elements and clinical blood chemistry values of these monkeys before treatment and the myeloid/erythroid (M/E) ratio of the bone marrow of the monkeys used as normal controls varied among individual animals. The mean ± S.D. and the range of the various parameters for the males and females are summarized in Tables D and E, respectively.

Since September 1971, we have used about 525, 5 to 9 months old, beagles dogs (AKC registered, Hazelton Research Animals, Inc.). The peripheral blood elements, clinical blood chemistry values and the M/E ratio of the bone marrow varied considerably among individual dogs. The mean ± S.D. and the ranges of the various parameters for the males and females are summarized in Tables H and I, respectively.

During the same period, we have used about 500, 7 to 10 weeks old, male albino rats (CD® Strain, Charles River Breeding Laboratories). As for the dogs, the individual variations of the peripheral blood elements, clinical blood chemistry values and the M/E ratio of the bone marrow were large. The mean ± S.D. and the ranges of the various parameters for these male rats are summarized in Table L.

B. Absolute and Relative Organ Weights

Organ weights, both absolute and relative to body weight, of rhesus monkeys, beagle dogs, and albino rats are summarized in Tables F and G, J and K, and M, respectively. These were control animals used between June 1971 and December 1976.

C. Presence of Various Substances in the Urine

Various substances occasionally occurred in the urine of monkeys, dogs and rats. The results are summarized in Table N. Large percentage of urine samples from monkeys contained epithelial cells, i.e., 34.7% to 52.0%. Other substances occurred in 8.1% or less of the urine samples.

In dogs, protein, erythrocytes, leukocytes and epithelial cells were present in 19.1 to 21.6%, 16.5 to 19.8%, 22.6 to 24.6% or 24.7 to 25.7%, respectively, of the samples from dogs collected for analysis. Glucose,

crystals, and casts occurred in less than 2% of these samples. Some dogs had been bled and returned to the metabolism cages before the urine was removed for analysis. The high incidence of some of these substances in the urine of these dogs might be due to contamination with the fecal material and traces of blood dropped in the cage. Special care to avoid contamination has been undertaken.

In rats, large percentage of urine samples contained protein, i.e., 29.8 to 36.0%. A few samples contained erythrocytes, leukocytes, epithelial cells and crystals.

D. Occult Blood in the Feces

Less than 10% of the feces samples from monkeys or dogs was positive with the Hematest for occult blood. The results are summarized in Table 0.

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TABLE A

REPRODUCIBILITY AMONG TEST DAYS ON THE SAME CONTROL SAMPLES OR STANDARDS[a/]

	No. of Determinations	Mean ± S.D.	Range
Erythrocytes (x $10^6/mm^3$)			
Normal level	20	4.51 ± 0.07	4.36 - 4.67
Abnormal level	20	2.32 ± 0.04	2.25 - 2.40
Hematocrit (vol %)			
Normal level	20	44.3 ± 0.40	44 - 45
Abnormal level	20	22.8 ± 0.60	22 - 24
Hemoglobin (gm %)			
Normal level	20	14.2 ± 0.20	13.6 - 14.5
Abnormal level	20	7.4 ± 0.20	6.9 - 7.8
Leukocyte Counts (x $10^3/mm^3$)			
Normal level	20	7.3 ± 0.50	6.8 - 8.7
Abnormal level	20	17.6 ± 0.80	16.3 - 18.7
Fasting Blood Glucose (mg %)	20	163.0 ± 7.5	151 - 178
SGOT (IU/ℓ)	23	61.7 ± 3.9	55 - 68
SGPT (IU/ℓ)	23	51.3 ± 2.6	46 - 55
Creatinine (mg %)	18	2.2 ± 0.3	1.6 - 2.6
BUN (mg %)	19	9.8 ± 0.2	9.5 - 10.2
Bilirubin (mg %)	11	0.8 ± 0.1	0.8 - 1.0
Alkaline Phosphatase (IU/ℓ)	22	71.6 ± 5.4	62 - 80
CPK	11	153.0 ± 7.7	139 - 161
LDH	8	98.0 ± 2.4	95 - 101
HBDH	8	226.0 ± 7.2	214 - 238

a/ Performed in December 1976.

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TABLE B

REPRODUCIBILITY WITHIN A TEST DAY
ON THE SAME SPECIMEN[a/]

	Mean ± S.D.[b/]	Range
Erythrocytes (x 10^6/mm^3)	5.90 ± 0.14	5.73 - 6.08
Reticulocytes (%)	0.63 ± 0.12	0.44 - 0.79
Hematocrit (vol %)	46.8 ± 0.6	46.0 - 47.5
Hemoglobin (gm %)	16.1 ± 0.2	15.8 - 16.1
Platelets (x 10^5/mm^3)	1.56 ± 0.07	1.49 - 1.66
Leukocytes (x 10^3/mm^3)	10.8 ± 0.4	10.2 - 11.3
Bands (%)	0 ± 0	0 - 0
Neutrophils (%)	64.3 ± 3.1	61 - 69
Lymphocytes (%)	29.0 ± 4.9	23 - 35
Eosinophils (%)	3.2 ± 0.8	2 - 4
Basophils (%)	0 ± 0	0 - 0
Monocytes (%)	3.4 ± 0.9	3 - 5
Atypical (%)	0 ± 0	0 - 0
Nucleated RBC (%)	0 ± 0	0 - 0
Methemoglobin (gm %)	0 ± 0	0 - 0
Fasting Glucose (mg %)	96.7 ± 3.0	32 - 101
SGOT (IU/ℓ)	23.2 ± 2.8	21 - 28
SGPT (IU/ℓ)	25.3 ± 2.1	24 - 28
Creatinine (mg %)	0.6 ± 0.1	0.5 - 0.6
BUN (mg %)	9.0 ± 0.0	9 - 9
Alkaline Phosphatase (IU/ℓ)	63.5 ± 1.1	62 - 65
CPK	44.0 ± 1.6	43 - 46
LDH	38.5 ± 1.6	37 - 40
HBDH	42.0 ± 1.6	40 - 43

a/ Performed in October 1976.
b/ Six determinations from an adult beagle blood sample.

TABLE C

PROFICIENCY TEST SERVICE (PTS) REPORTS (1975-1976)[a/]

Unknowns	MRI Results	PTS Results	Participating Laboratories (10-90 Percentiles) Median	Mean	Acceptable Performance[b/]
Hemoglobin	13.8 gm %	13.8	13.8	13.8	13.6 - 14.0
	18.1 gm %	17.9	17.9	17.8	17.6 - 18.2
Serum Protein	6.6 mg %	7.1	7.0	7.0	6.7 - 7.3
Fasting Glucose	272.0 mg %	264.5	266.0	263.0	240 - 290
	229.0 mg %	221.4	220.5	222.5	200 - 240
BUN	12.1 mg %	12.0	12.0	12.2	11.0 - 13.0
	38.4 mg %	40.1	40.3	39.2	36.0 - 44.0
Creatinine	1.0 mg %	1.0	1.0	1.0	0.8 - 1.3
	4.3 mg %	4.4	4.5	4.4	3.9 - 4.9
Bilirubin	3.9 mg %	4.16	4.15	4.14	3.5 - 4.6
	1.3 mg %	1.78	1.80	1.77	1.5 - 2.1
Cholesterol	175.0 mg %	161.4	161.0	162.0	145 - 175
	100.0 mg %	109.8	109.4	111.0	98 - 120
Ca	15.7 meq/ℓ	15.4	15.4	15.3	14.1 - 16.4
	9.5 meq/ℓ	9.8	9.8	9.8	9.2 - 10.3
Na	156.0 meq/ℓ	155.8	156.0	155.5	153 - 158
K	7.3 meq/ℓ	7.5	7.5	7.5	7.3 - 7.7
Cl	96.0 meq/ℓ	97.8	98.0	97.5	96 - 101
	78.0 meq/ℓ	79.4	79.0	80.0	77 - 83
Mg	1.0 meq/ℓ	1.1	1.1	1.2	0.9 - 1.4
	1.9 meq/ℓ	2.0	2.0	2.1	1.8 - 2.3

a/ To date, we have received unknowns for phosphorus, uric acid, and serum iron. We do not routinely perform these determinations.

b/ Based on values submitted by participants by 10th of month.

TABLE 9

HEMATOLOGY, CLINICAL BLOOD CHEMISTRY VALUES, AND BONE MARROW (MYELOID/ERYTHROID) RATIOS OF MALE RHESUS MONKEYS[a/]

	Male Rhesus Monkeys			
	Number Studied	Body Weight (kg) Mean ± S.D.	Observed Results Mean ± S.D.	Range
Erythrocytes (x 10^6/mm^3)	108	3.74 ± 0.50	5.51 ± 0.45	3.75 - 6.61
Reticulocytes (%)	108	3.74 ± 0.50	0.97 ± 0.82	0.07 - 2.41
Hematocrit (vol %)	108	3.74 ± 0.50	43.0 ± 2.6	37.0 - 50.0
Hemoglobin (gm %)	108	3.74 ± 0.50	13.4 ± 0.8	10.8 - 15.4
MCV (μ^3)	108	3.74 ± 0.50	77.8 ± 7.0	69.6 - 117.3
MCHb ($\mu\mu$g)	108	3.74 ± 0.50	24.4 ± 1.8	21.0 - 31.6
MCHbC (mg %)	108	3.74 ± 0.50	31.4 ± 1.3	27.2 - 34.1
Platelets (x 10^5/mm^3)	99	3.74 ± 0.50	3.08 ± 0.45	0.80 - 7.10
Leukocytes (x 10^3/mm^3)	108	3.74 ± 0.50	10.4 ± 4.9	3.8 - 30.1
Neutrophils I (%)	108	3.74 ± 0.50	0.18 ± 0.45	0 - 2
Neutrophils M (%)	108	3.74 ± 0.50	39.30 ± 17.72	10 - 83
Lymphocytes (%)	108	3.74 ± 0.50	56.83 ± 17.74	13 - 84
Eosinophils (%)	108	3.74 ± 0.50	1.91 ± 2.42	0 - 11
Monophils (%)	108	3.74 ± 0.50	1.37 ± 1.58	0 - 7
Basophils (%)	108	3.74 ± 0.50	0.04 ± 0.20	0 - 2
Atypical cells (%)	108	3.74 ± 0.50	0.00 ± 0.00	0 - 0
Nucleated RBC (%)		3.74 ± 0.50	0.00 ± 0.00	0 - 0
Fasting Glucose (mg %)	100	3.76 ± 0.51	96.9 ± 15.2	59 - 127
SGOT (IU/ℓ)	100	3.76 ± 0.51	31.7 ± 9.2	20 - 60
SGPT (IU/ℓ)	100	3.76 ± 0.51	31.3 ± 7.8	15 - 46
Alkaline Phosphatase (IU/ℓ)	100	3.76 ± 0.51	360.0 ± 116.0	143 - 501
BUN (mg %)	100	3.76 ± 0.51	19.5 ± 7.5	12 - 65
Proth. Time (sec)	62	3.91 ± 0.44	10.2 ± 0.7	9.3 - 11.9
Serum Creat. (mg %)	100	3.76 ± 0.51	1.1 ± 0.3	0.6 - 1.8
Bilirubin				
Total (mg %)	62	3.91 ± 0.44	0.1 ± 0.2	0.0 - 0.8
Direct (mg %)	62	3.91 ± 0.44	0.0 ± 0.0	0.0 - 0.0
BSP 15 min (% ret.)	62	3.91 ± 0.44	18.0 ± 7.4	2 - 34
Na (mEq/ℓ)	62	3.91 ± 0.44	154.0 ± 19.1	144 - 179
K (mEq/ℓ)	62	3.91 ± 0.44	4.8 ± 0.6	3.9 - 5.7
Cl (mEq/ℓ)	62	3.91 ± 0.44	109.0 ± 6.4	93 - 118
Ca (mEq/ℓ)	62	3.91 ± 0.44	5.2 ± 0.4	4.2 - 6.3
Mg (mEq/ℓ)	62	3.91 ± 0.44	1.6 ± 0.1	1.2 - 1.8
Bone Marrow				
Myeloid/erythroid ratio	15	3.65 ± 0.41	1.5 ± 0.3	1.5 - 2.1

a/ Data collected between June 1971 and December 1976.

TABLE E

HEMATOLOGY, CLINICAL BLOOD CHEMISTRY VALUES, AND BONE MARROW (MYELOID/ERYTHROID) RATIOS OF FEMALE RHESUS MONKEYS[a/]

	Female Rhesus Monkeys			
	Number Studied	Body Weight (kg) Mean ± S.D.	Observed Results Mean ± S.D.	Range
Erythrocytes (x 10^6/mm^3)	81	3.51 ± 0.48	5.33 ± 0.40	4.25 - 6.03
Reticulocytes (%)	81	3.51 ± 0.48	1.07 ± 0.54	0.35 - 3.31
Hematocrit (vol %)	81	3.51 ± 0.48	41.5 ± 2.8	30.0 - 46.0
Hemoglobin (gm %)	81	3.51 ± 0.48	13.1 ± 1.0	7.9 - 14.1
MCV (μ^3)	81	3.51 ± 0.48	77.7 ± 5.3	66.5 - 95.2
MCHb ($\mu\mu$g)	81	3.51 ± 0.48	24.6 ± 1.7	17.6 - 29.7
MCHbC (mg %)	81	3.51 ± 0.48	31.6 ± 1.4	26.6 - 34.2
Platelets (x 10^5/mm^3)	81	3.51 ± 0.48	3.11 ± 1.23	1.85 - 7.90
Leukocytes (x 10^3/mm^3)	81	3.51 ± 0.48	9.5 ± 1.9	3.2 - 24.8
Neutrophils I (%)	81	3.51 ± 0.48	0.10 ± 0.43	0 - 3
Neutrophils M (%)	81	3.51 ± 0.48	36.41 ± 13.32	13 - 56
Lymphocytes (%)	81	3.51 ± 0.48	60.38 ± 13.26	41 - 79
Eosinophils (%)	81	3.51 ± 0.48	2.28 ± 3.10	0 - 18
Monophils (%)	81	3.51 ± 0.48	0.75 ± 0.98	0 - 4
Basophils (%)	81	3.51 ± 0.48	0.05 ± 0.22	0 - 1
Atypical cells (%)	81	3.51 ± 0.48	0.00 ± 0.00	0 - 0
Nucleated RBC (%)	74	3.56 ± 0.50	0.00 ± 0.00	0 - 0
Fasting Glucose (mg %)	81	3.51 ± 0.48	92.1 ± 15.3	57 - 116
SGOT (IU/ℓ)	81	3.51 ± 0.48	32.1 ± 7.6	20 - 70
SGPT (IU/ℓ)	81	3.51 ± 0.48	30.1 ± 7.6	12 - 39
Alkaline Phosphatase (IU/ℓ)	81	3.51 ± 0.48	349.9 ± 112.3	148 - 572
BUN (mg %)	81	3.51 ± 0.48	17.3 ± 4.2	11 - 29
Proth. Time (sec)	59	3.56 ± 0.43	10.5 ± 0.9	9.7 - 12.3
Serum Creat. (mg %)	81	3.51 ± 0.48	1.1 ± 0.3	0.6 - 1.7
Bilirubin				
Total (mg %)	81	3.51 ± 0.48	0.1 ± 0.1	0.0 - 0.8
Direct (mg %)	81	3.51 ± 0.48	0.0 ± 0.0	0.0 - 0.0
BSP 15 min (% ret.)	59	3.56 ± 0.43	16.4 ± 8.3	5 - 34
Na (mEq/ℓ)	59	3.56 ± 0.43	158.2 ± 6.5	147 - 174
K (mEq/ℓ)	59	3.56 ± 0.43	4.8 ± 0.7	3.9 - 6.2
Cl (mEq/ℓ)	59	3.56 ± 0.43	109.0 ± 6.1	95 - 113
Ca (mEq/ℓ)	59	3.56 ± 0.43	5.3 ± 0.5	4.3 - 6.3
Mg (mEq/ℓ)	59	3.56 ± 0.43	1.6 ± 0.2	1.3 - 2.0
Bone Marrow				
Myeloid/erythroid ratio	11	3.49 ± 0.62	1.4 ± 0.3	1.0 - 1.8

a/ Data collected between June 1971 and December 1976.

TABLE F

ABSOLUTE AND RELATIVE ORGAN WEIGHTS OF MALE RHESUS MONKEYS[a/]

Organ Weight	Absolute Mean ± S.D.	Range
Liver (gm)	82 ± 17	64 - 122
Spleen (gm)	4.6 ± 1.8	2.0 - 9.3
Kidneys (gm)	15.1 ± 3.8	8.0 - 22.0
Adrenals (gm)	0.73 ± 0.15	0.45 - 0.86
Thyroids (gm)	0.57 ± 1.30	0.37 - 0.81
Testes (gm)	1.29 ± 0.67	0.53 - 3.30
	Relative (per kg body weight) Mean ± S.D.	Range
Liver (gm)	23.4 ± 2.5	18.8 - 30.4
Spleen (gm)	1.25 ± 0.47	0.57 - 2.38
Kidneys (gm)	4.13 ± 0.92	2.20 - 6.43
Adrenals (mg)	201 ± 44	129 - 254
Thyroids (mg)	154 ± 42	86 - 250
Testes (gm)	0.34 ± 0.11	0.18 - 0.53

a/ Data collected between September 1971 and December 1976 from 17 monkeys weighing 3.71 ± 0.48 kg, used as control animals.

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TABLE G

ABSOLUTE AND RELATIVE ORGAN WEIGHTS OF FEMALE RHESUS MONKEYS[a/]

Organ Weight	Absolute Mean ± S.D.	Absolute Range
Liver (gm)	83 ± 17	64 - 122
Spleen (gm)	3.8 ± 1.4	2.0 - 6.0
Kidneys (gm)	14.5 ± 2.8	11.0 - 20.0
Adrenals (gm)	0.68 ± 0.16	0.53 - 1.14
Thyroids (gm)	0.60 ± 0.20	0.37 - 1.11
Ovaries (gm)	0.28 ± 0.10	0.14 - 0.45
	Relative (per kg body weight)	
	Mean ± S.D.	Range
Liver (gm)	25.4 ± 5.8	19.2 - 37.4
Spleen (gm)	1.16 ± 0.49	0.60 - 1.89
Kidneys (gm)	4.40 ± 0.86	3.20 - 6.25
Adrenals (mg)	212 ± 80	138 - 438
Thyroids (mg)	173 ± 66	97 - 346
Ovaries (mg)	82 ± 28	43 - 140

a/ Data collected between September 1971 and December 1976 from 11 monkeys weighing 3.39 ± 0.58 kg, used as controls.

TABLE H

HEMATOLOGY, CLINICAL BLOOD CHEMISTRY VALUES, AND BONE MARROW (MYELOID/ERYTHROID) RATIOS OF MALE BEAGLE DOGS[a/]

	Male Beagle Dogs				
	Number Studied	Age (months)	Body Weight (kg) Mean ± S.D.	Observed Results Mean ± S.D.	Range
Erythrocytes (x 10^6/mm^3)	276	4 - 7	8.3 ± 1.7	5.55 ± 0.73	3.62 - 7.60
Reticulocytes (%)	284	4 - 7	8.3 ± 1.7	0.72 ± 0.46	0.04 - 4.35
Hematocrit (vol %)	276	4 - 7	8.3 ± 1.7	41.6 ± 3.5	31 - 50
Hemoglobin (gm %)	276	4 - 7	8.3 ± 1.7	13.5 ± 1.4	10.0 - 16.9
MCV (μ^3)	276	4 - 7	8.3 ± 1.7	75.6 ± 8.3	56.7 - 127.1
MCHb ($\mu\mu$g)	276	4 - 7	8.3 ± 1.7	24.6 ± 3.0	17.1 - 41.7
MCHbC (mg %)	276	4 - 7	8.3 ± 1.7	32.5 ± 1.5	28.1 - 40.3
Platelets (x 10^5/mm^3)	270	4 - 7	8.4 ± 1.7	2.91 ± 1.02	0.93 - 6.35
Leukocytes (x 10^3/mm^3)	284	4 - 7	8.3 ± 1.7	11.9 ± 3.5	4.6 - 24.6
Neutrophils I (%)	284	4 - 7	8.3 ± 1.7	0.55 ± 1.06	0 - 6
Neutrophils M (%)	284	4 - 7	8.3 ± 1.7	56.81 ± 9.47	22 - 80
Lymphocytes (%)	284	4 - 7	8.3 ± 1.7	37.94 ± 9.26	13 - 71
Eosinophils (%)	284	4 - 7	8.3 ± 1.7	2.76 ± 2.93	0 - 16
Monophils (%)	284	4 - 7	8.3 ± 1.7	1.78 ± 1.84	0 - 11
Basophils (%)	284	4 - 7	8.3 ± 1.7	0.01 ± 0.10	0 - 2
Atypical cells (%)	284	4 - 7	8.3 ± 1.7	0.11 ± 0.37	0 - 2
Nucleated RBC (%)	284	4 - 7	8.3 ± 1.7	0.02 ± 0.10	0 - 2
Fasting Glucose (mg %)	284	4 - 7	8.3 ± 1.7	100.9 ± 12.6	66 - 134
SGOT (IU/ℓ)	276	4 - 7	8.3 ± 1.7	23.2 ± 7.4	11 - 59
SGPT (IU/ℓ)	276	4 - 7	8.3 ± 1.7	25.7 ± 7.9	8 - 46
Alkaline Phosphatase (IU/ℓ)	276	4 - 7	8.3 ± 1.7	73.3 ± 18.5	21 - 133
BUN (mg %)	284	4 - 7	8.3 ± 1.7	12.1 ± 3.3	4 - 23
Bone Marrow					
Myeloid/erythroid ratio	34	5 - 9	9.4 ± 1.6	1.6 ± 0.4	1.1 - 3.0

a/ Data collected between September 1971 and December 1976.

TABLE I

HEMATOLOGY, CLINICAL BLOOD CHEMISTRY VALUES, AND BONE MARROW (MYELOID/ERYTHROID) RATIOS OF FEMALE BEAGLE DOGS[a/]

	Female Beagle Dogs			Observed Results	
	Number Studied	Age (months)	Body Weight (kg) Mean ± S.D.	Mean ± S.D.	Range
Erythrocytes (x 10^6/mm^3)	257	4 - 7	6.9 ± 1.3	5.59 ± 0.73	3.27 - 7.75
Reticulocytes (%)	265	4 - 7	6.9 ± 1.3	0.74 ± 0.52	0.04 - 5.05
Hematocrit (vol %)	257	4 - 7	6.9 ± 1.3	42.3 ± 3.5	32 - 51
Hemoglobin (gm %)	257	4 - 7	6.9 ± 1.3	13.7 ± 1.3	11.0 - 18.6
MCV (μ^3)	257	4 - 7	6.9 ± 1.3	76.7 ± 9.7	55.8 - 128.4
MCHb ($\mu\mu$g)	257	4 - 7	6.9 ± 1.3	24.8 ± 3.3	17.1 - 41.6
MCHbC (mg %)	257	4 - 7	6.9 ± 1.3	32.3 ± 1.6	28.7 - 40.4
Platelets (x 10^5/mm^3)	227	4 - 7	6.9 ± 1.3	3.08 ± 1.15	1.08 - 7.95
Leukocytes (x 10^3/mm^3)	265	4 - 7	6.9 ± 1.3	10.9 ± 3.4	3.8 - 26.9
Neutrophils I (%)	265	4 - 7	6.9 ± 1.3	0.54 ± 1.16	0 - 7
Neutrophils M (%)	265	4 - 7	6.9 ± 1.3	57.08 ± 10.10	31 - 85
Lymphocytes (%)	265	4 - 7	6.9 ± 1.3	37.15 ± 10.46	10 - 61
Eosinophils (%)	265	4 - 7	6.9 ± 1.3	2.37 ± 2.25	0 - 13
Monophils (%)	265	4 - 7	6.9 ± 1.3	1.94 ± 2.01	0 - 9
Basophils (%)	265	4 - 7	6.9 ± 1.3	0.01 ± 0.09	0 - 1
Atypical cells (%)	265	4 - 7	6.9 ± 1.3	0.11 ± 0.43	0 - 4
Nucleated RBC (%)	265	4 - 7	6.9 ± 1.3	0.03 ± 0.17	0 - 2
Fasting Glucose (mg %)	248	4 - 7	6.9 ± 1.3	99.6 ± 14.4	55 - 130
SGOT (IU/ℓ)	257	4 - 7	6.9 ± 1.3	23.5 ± 7.2	6 - 52
SGPT (IU/ℓ)	257	4 - 7	6.9 ± 1.3	25.3 ± 7.0	8 - 49
Alkaline Phosphatase (IU/ℓ)	257	4 - 7	6.9 ± 1.3	73.5 ± 19.2	30 - 146
BUN (mg %)	265	4 - 7	6.9 ± 1.3	12.4 ± 3.3	4 - 26
Bone Marrow					
Myeloid/erythroid ratio	34	5 - 9	7.8 ± 1.4	1.4 ± 0.3	1.1 - 2.4

a/ Data collected between September 1971 and December 1976.

TABLE J

ABSOLUTE AND RELATIVE ORGAN WEIGHTS OF MALE BEAGLE DOGS[a/]

Organ Weight	Absolute Mean ± S.D.	Absolute Range
Liver (gm)	264 ± 51	166 - 384
Spleen (gm)	58 ± 25	22 - 167
Kidneys (gm)	53 ± 10	32 - 71
Adrenals (gm)	1.12 ± 0.26	0.74 - 1.75
Thyroids (gm)	1.03 ± 0.32	0.55 - 2.50
Testes (gm)	6.60 ± 4.56	1.32 - 18.00
	Relative (per kg body weight)	
	Mean ± S.D.	Range
Liver (gm)	27.9 ± 4.2	19.6 - 42.3
Spleen (gm)	6.0 ± 2.0	2.8 - 12.5
Kidneys (gm)	5.6 ± 0.8	4.0 - 7.7
Adrenals (mg)	117 ± 25	70 - 165
Thyroids (mg)	108 ± 34	56 - 211
Testes (gm)	0.67 ± 0.39	0.13 - 1.67

a/ Data collected between September 1971 and December 1976 from 51 dogs, weighing 9.3 ± 1.8 kg, used as control animals.

TABLE L

HEMATOLOGY, CLINICAL BLOOD CHEMISTRY VALUES, AND BONE MARROW (MYELOID/ERYTHROID) RATIOS OF MALE ALBINO RATS[a/]

	Male Rats			Observed Results	
	Number Studied	Age (weeks)	Body Weight (gm) Mean ± S.D.	Mean ± S.D.	Range
Erythrocytes (x 10^6/mm^3)	527	5 - 7	168 ± 22	5.84 ± 0.54	3.24 - 7.60
Reticulocytes (%)	461	5 - 7		3.04 ± 1.80	0.30 - 6.83
Hematocrit (vol %)	525	5 - 7	168 ± 22	45.1 ± 3.2	40 - 58
Hemoglobin (gm %)	525	5 - 7	168 ± 22	13.7 ± 0.9	11.8 - 17.1
MCV (μ^3)	525	5 - 7	168 ± 22	78.1 ± 16.3	62.3 - 104.6
MCHb ($\mu\mu$g)	525	5 - 7	168 ± 22	23.7 ± 2.6	19.2 - 41.0
MCHbC (mg %)	525	5 - 7	168 ± 22	30.5 ± 1.8	21.1 - 36.9
Platelets (x 10^5/mm^3)	473	5 - 7	164 ± 24	4.93 ± 1.23	2.30 - 7.95
Leukocytes (x 10^3/mm^3)	448	5 - 7	164 ± 24	15.4 ± 4.0	6.3 - 20.8
Neutrophils I (%)	448	5 - 7	164 ± 24	0.07 ± 0.31	0 - 3
Neutrophils M (%)	448	5 - 7	164 ± 24	14.1 ± 6.2	4 - 29
Lymphocytes (%)	448	5 - 7	164 ± 24	83.63 ± 6.75	52 - 96
Eosinophils (%)	448	5 - 7	164 ± 24	0.64 ± 0.91	0 - 6
Monophils (%)	448	5 - 7	164 ± 24	1.23 ± 1.73	0 - 13
Basophils (%)	448	5 - 7	164 ± 24	0.01 ± 0.15	0 - 2
Atypical cells (%)	448	5 - 7	164 ± 24	0.01 ± 0.12	0 - 2
Nucleated RBC (%)	448	5 - 7	164 ± 24	0.10 ± 0.42	0 - 4
Fasting Glucose (mg %)	125	10 - 12	348 ± 72	130.9 ± 17.2	94 - 165
SGOT (IU/ℓ)	125	10 - 12	348 ± 72	108.2 ± 34.5	63 - 223
SGPT (IU/ℓ)	125	10 - 12	348 ± 72	34.2 ± 16.5	17 - 120
Alkaline Phosphatase (IU/ℓ)	125	10 - 12	348 ± 72	94.9 ± 30.0	32 - 153
BUN (mg %)	125	10 - 12	348 ± 72	16.4 ± 4.7	8 - 41
Bone Marrow					
Myeloid/erythroid ratio	109	10 - 12	349 ± 63	1.7 ± 0.5	1.0 - 2.6

a/ Data collected between September 1971 and December 1976.

TABLE M

ABSOLUTE AND RELATIVE ORGAN WEIGHTS OF MALE ALBINO RATS[a/]

Organ Weight	Absolute Mean ± S.D.	Absolute Range
Liver (gm)	10.89 ± 2.87	7.18 - 15.09
Spleen (gm)	0.65 ± 0.11	0.34 - 0.89
Kidneys (gm)	2.64 ± 0.37	1.84 - 3.58
Adrenals (mg)	63.6 ± 9.5	21.9 - 73.5
Thyroids (mg)	26.3 ± 5.8	14.3 - 37.7
Testes (gm)	2.98 ± 0.51	1.76 - 3.81
	Relative (per 100 gm body weight)	
	Mean ± S.D.	Range
Liver (gm)	2.96 ± 0.42	2.09 - 4.01
Spleen (gm)	0.19 ± 0.08	0.10 - 0.30
Kidneys (gm)	0.76 ± 0.10	0.22 - 0.88
Adrenals (mg)	18.6 ± 5.8	5.8 - 22.4
Thyroids (mg)	7.6 ± 2.7	4.2 - 12.7
Testes (gm)	0.87 ± 0.15	0.23 - 1.09

a/ Data collected between September 1971 and December 1976 from 139 rats, weighing 352 ± 59 gm, used as control animals.

TABLE N

PRESENCE OF VARIOUS SUBSTANCES IN THE URINE OF MALE AND FEMALE MONKEYS, DOGS AND MALE RATS

Species:		Monkeys		Dogs		Rats[a]	
No. of Animals:		141[b]	18	615[b]	112	84[b]	18
No. of Collections:		141	98[c]	615	565[c]	84	56[d]
Glucose:	< 250 mg %	0[e]	2.0 (2)	0.2 (1)	0.7 (4)	0	0
	> 250 mg %	0	0	0.5 (3)	0.2 (1)	0	0
Protein:	< 100 mg %	3.5 (5)	6.1 (6)	19.3 (119)	17.3 (98)	29.8 (25)	36.0 (18)
	> 100 mg %	0	2.0 (2)	2.3 (14)	1.8 (10)	0	0
RBC:[f]	Moderate	1.4 (2)	3.1 (3)	16.4 (101)	13.3 (75)	3.6 (3)	8.0 (4)
	Excessive	0	0	3.4 (21)	3.2 (18)	0	0
WBC:[f]	Moderate	1.4 (2)	2.0 (2)	18.7 (115)	20.9 (118)	0	4.0 (2)
	Excessive	0	0	3.9 (24)	3.7 (21)	0	0
Epithelium:[g]	Moderate	31.2 (44)	44.9 (44)	21.0 (129)	21.9 (124)	0	8.0 (4)
	Excessive	3.5 (5)	7.1 (7)	4.7 (29)	2.8 (16)	0	0
Crystal:[h]	Moderate	0.7 (1)	2.0 (2)	0.2 (1)	0.7 (4)	0	2.0 (1)
	Excessive	0	0	0.2 (1)	0.7 (4)	0	2.0 (1)
Casts:	Positive	0.7 (1)	5.1 (5)	0	0.9 (5)	0	0

a/ Pooled sample of 4-20 rats.
b/ Baseline data collected from all animals employed between September 1971 and December 1976.
c/ Data collected at weekly intervals for 4-7 collections from controls employed between September 1971 and December 1976.
d/ Data collected at 2-week intervals for 2-4 collections from control rats employed between September 1971 and December 1976.
e/ Percent of total (number of samples).
f/ Normal, 10 or less cells; moderate, 10-100 cells; excessive, > 100 cells/field (x 440).
g/ Normal, 5 or less cells; moderate, 5-25 cells; excessive, > 25 cells/field (x 100).
h/ Normal, none; moderate, 1-5 crystals; excessive, > 5 crystals/field (x 100).

TABLE O

PRESENCE OF OCCULT BLOOD IN THE FECES OF MALE AND FEMALE MONKEYS AND DOGS

Species:	Monkeys		Dogs	
No. of Animals:	44[a]	8	118[a]	30
No. of Collections:	44	48[b]	118	156[b]
Occult Blood: Negative	90.9 (40)[c]	95.8 (46)	94.1 (111)	91.7 (143)
Positive	9.1 (4)	4.2 (2)	5.9 (7)	8.3 (13)

a/ Baseline data collected from all animals employed between July 1974 and December 1976.

b/ Data collected at weekly intervals for 4-7 collections from controls employed between July 1974 and December 1976.

c/ Percent of total (number of samples).