FINAL REPORT

on

A CHRONIC INHALATION TOXICOLOGY STUDY IN MONKEYS AND RATS EXPOSED TO FIBROUS GLASS

(Project Number G-7188)

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to

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

October 25, 1982

Volume I

by

Ralph I. Mitchell, Robert B. Reif, Arnold T. Mosberg, Daryl C. Thake, Melanie M. Connell, David J. Donofrio, Hugh H. Harroff, and Albert J. Roese

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Columbus Laboratories
505 King Avenue
Columbus, Ohio 43201

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SUMMARY

The objective of this study was to determine the extent of potential toxicologic effects of fibrous glass particles during long-term inhalation exposure of Fisher 344 rats and Cynomolgus monkeys. The investigation, under a National Institute for Occupational Safety and Health (NIOSH) contract, was conducted at the Battelle Memorial Institute's Columbus Laboratories, Columbus, Ohio. This 18-month inhalation study was initiated on September 28, 1978, and exposures begun on March 12, 1979 with 100 rats (50 of each sex) and on June 19, 1979 with 12 male Cynomolgus monkeys for each of the 5 exposure levels.

glass as follows:

Test Group	Fiber	Concentration (mg/m^3)
1	4 to 6 μm diameter; > 20 μm length with red binder	15
2	0.5 to 3.5 μm diameter; > 10 μm length with yellow binder	15
3	< 3.5 μm diameter; > 10 μm length	5
4	< 3.5 μm diameter; < 10 μm length	5
5 (Control)	None	0

The test atmospheres were generated by dispersing pre-sized fibrous glass in conditioned clean air for 7 hours per day, 5 days per week (excluding holidays) for 18 months (monkeys) and 21 months (rats) respectively. Control groups of animals were subjected to the same procedures as the test groups except that exposure was to clean air. During nonexposure periods, the control and test animals were housed in separate rooms. The exposures were terminated during the interval of 12-24-80 to 1-17-81.

Body weights, clinical signs of toxic effects, and mortality were followed throughout the study. Blood samples were taken for hematologic and clinical chemistry analyses twice before treatment and at weeks 16, 32, 48, and 64 during exposure (monkeys) and just prior to necropsy for rats and monkeys. Respiratory function was evaluated before exposure, after 9 months of exposure, and at sacrifice following 18 months of exposure (monkeys). Rats were held an additional 3 months, after their last exposure (age of 27 months), before they were sacrificed. A complete gross pathologic examination was conducted after sacrifice and a predetermined selection of tissues were taken.

After the 18 months of exposure, the mean fibrous glass concentrations in the chambers during exposure periods were calculated and compared with

the targeted concentrations given below:

Rats (21 months of fibrous glass exposure)

Group	Target (mg/m^3)	Measured (mg/m^3)
FO 1	15	13.96 ± 4.16
FO 2	15	14.94 ± 4.55
FO 3	5	4.85 ± 1.66
FO 4	5	4.78 ± 1.52
FO 5 (Control)	0	0.00 ± 0.00

Monkeys (18 months of fibrous glass exposure)

Group	Target (mg/m^3)	Measured (mg/m^3)
FO 1	15	14.72 ± 3.78
FO 2	15	15.62 ± 4.06
FO 3	5	5.04 ± 1.58
FO 4	5	4.78 ± 1.44
FO 5 (Control)	0	0.00 ± 0.00

Mortality

During the exposure period, 187 rats died spontaneously or were terminated in moribund condition. Two monkeys did not survive through the test period. One died early with a syndrome analagous to diabetes mellitus and the other was sacrificed in moribund condition. Neither death is considered to be the result of exposure.

Ophthalmologic Examinations

There were no postexposure lesions attributed to fibrous glass exposure.

Clinical Observations

None of the clinical signs recorded for monkeys or rats is considered to be the result of exposure to the fibrous glass test material.

Body Weights

There were no significant effects upon body weight from exposure of the rats or monkeys to any of the levels of fiber during the course of the experiment.

Hematology and Clinical Chemistry

In monkeys, there were no changes in group mean values that were outside the expected range nor were there biologically significant variations from control values that were associated with fiberous glass exposure. Also, in rats, there were no exposure related changes in hematology or serum chemistry values.

Pulmonary Function Evaluations

Pulmonary physiology measurements were performed in all monkeys in this study at 0 months, 9 months, and 18 months postexposure. Only a limited number of parameters were observed to deviate from control values during the study. The 9 and 18 month evaluations produced different patterns of respiratory response. Neither the 9 month nor the 18 month pattern was representative of restrictive or obstructive lung impairment. At the level of statistical significance chosen ($P < 0.05$), the changes could not be interpreted as lung debilitation.

Histopathology

Based on the histopathological investigation the following observations and conclusions summarize the findings of this study.

- The only unequivocal responses induced by fibrous glass inhalation in monkeys were macrophage aggregates with phagocytized fibrous glass in the lungs and tracheobronchial lymph nodes.
- The pulmonary responses in the rat induced by fibrous glass inhalation were characterized by macrophage aggregates and granulomas which contained fibrous glass fibers. The grossly visible plague like foci resulted from accumulations of granulomatous foci in pleural and subpleural locations. These lesions were limited to granulomatous foci, there was no fibrosis and there were no growth alterations in adjacent tissues, therefore there is no evidence in these animals that any further sequelae would result beyond that observed.
- There was no evidence of a fibrous glass induced fibrogenic response in either monkeys or rats.
- The most severe lesions in rats were in the F04 group (< 10 micrometers x 1 micrometer, no binder) whereas the response in the F01 group (>20 micrometers x 4 to 5 micrometers, with binder) was minimal.
- The severity of response in monkeys was similar for all exposed groups except the F01 group (>20 micrometers x 4 to 6 micrometers, with binder) in which the response was minimal. Group F01 also had monkeys which had mildly increased numbers of lymphoid nodules or aggregates in peribronchiolar and perivascular areas. The significance of the increase in the lymphoid aggregates is unknown but the most probable explanation would be a mild stimulation from an antigen such as the binder.
- The fibrous glass induced lesions were similarly distributed among all lobes of the lung in monkeys; in rats, the lesions were most prominent in posterior lobes in all but the F04 group where there was more equal distribution throughout the lung.

- The relative influence of fiber diameter, fiber length, concentration, and binder could not be evaluated due to variation of more than one factor in each animal group.
- The only evidence of translocation of fibers occurred in macrophage transport to draining pulmonary lymph nodes in many animals (rats and monkeys) and to mesenteric lymph nodes in two rats.
- The mononuclear cell leukemia was statistically significant when each test group was individually compared to the control group. The possibility of an exposure related incidence of this neoplasm cannot be ruled out.
- This study showed no evidence of pulmonary or mesothelial carcinogenicity associated with inhaled fibrous glass.

Data and Tissue Storage

Raw data, protocol, and a copy of the Final Report will be stored in the BCL Biological Sciences Department Archive. Tissue specimens, paraffin blocks, and slides will be transmitted to the Sponsor upon completion of the contract.

INTRODUCTION

The fibrous glass industry is a little less than 50 years old and within one generation has become one of the most versatile manufactured products, with a myriad of uses. In 1982, the annual production is between 3.5 to 4 billion pounds per year, with a value of approximately 2 billion dollars; however, because of its use for insulation and its ability to replace asbestos, the production rate should increase significantly. NIOSH estimates that 200,000 persons in the U.S. may be exposed occupationally to fibrous glass.[1]

To date, the major biological effects in human exposure to fibrous glass have been irritations to the skin and mucous membranes, as well as a very slight indication of an excess mortality risk due to nonmalignant respiratory diseases.[2] Although there has been concern that long term inhalation of fibers would produce a variety of pulmonary diseases, there has been little verification from most of the epidemiologic studies conducted so far. Most of the epidemiologic studies have been poorly designed and have failed to include the health outcomes of many workers who have been occupationally exposed for long periods of time.

A possible explanation for the fact that few health effects in humans have been found after fibrous glass exposure is that the nose is essentially 100 percent efficient in removing particles with aerodynamic diameters larger than 10 μm in diameter (depending upon the respiration rate) and can be completely efficient for particles as small as 6 μm. Essentially all of the fibers which are produced are greater than 4 μm in diameter and most of the fibers have a nominal diameter of 6 μm and the aerodynamic diameter of a fiber can be shown to be approximately 3 to 4 times the fiber diameter regardless of its length.[3] Thus, there is a low probability that such fibers can reach the lung during nasal breathing. This is verified by information obtained by Gross et al.[4] who showed that most of the fibers contained in the lungs of fibrous glass workers ranged between 1.5 and 2.5 μm in diameter and less than 6 percent of the fibers were greater than 4 μm. Consequently there is little reason to believe that typical worker exposure to the bulk of fibrous glass manufacture should produce an adverse pulmonary response.

However, micro fibers with diameters in the 1 μm size range should be of concern. Although these fibers only represent 1 to 2 percent of the total fibrous glass production, they are respirable and potentially carcinogenic. Animals that have been exposed to fibrous glass by various routes have shown fibrosis after intratracheal,[5,6] intrapleural,[7,8] and intraperitoneal[9,10,11] administration. Neoplasms have been observed after intrapleural and intraperitoneal administrations. Many of these studies demonstrated a relationship between fiber diameter and length and a specific biologic response.[12-14]

Although there have been several animal inhalation studies, they have produced inconsistent results. Some of the defects of these studies have been related to characteristics of the fibers, questionable mode of administration, insufficient exposure durations, lack of controls, etc.

Therefore, the National Institute for Occupational Safety and Health (NIOSH) initiated an 18-month inhalation study at Battelle Columbus Laboratories on September 28, 1978. The objectives of the study were to assess the adequacy of the current OSHA standard and to determine the character of pulmonary physiological and pathological responses produced by fibrous glass particles.

The study, which is reported herein, was initiated with 50 rats of each sex for each exposure concentration on March 12, 1979, and with 12 male Cynomolgus monkeys for each exposure level on June 19, 1979. Exposures to fiber glass were terminated during the interval 12-24-80 to 1-17-81. The monkeys were sacrificed immediately following the last exposure and the rats were held without exposure until they reached 27 months of age. The study was conducted and scheduled in accordance with the protocol in Appendix A. Deviations from the protocol are noted in the text. Appendix A also includes the standard operating procedures.

QUALITY ASSURANCE STATEMENT

This study was inspected by the Quality Assurance Unit and reports were submitted to management and the Principal Investigator as follows:

Phase	Date
Chamber Sampling	2/6/80
Pulmonary Function	4/23/80; 1/15/81
Blood Collection/Analysis	6/25/80; 11/3/80
Animal Body Weights	11/14/80
Animal Observations	11/14/80
Chamber Flushing	11/14/80
Ophthalmic Examinations	12/31/80
Animal Necropsy	12/23/80; 1/15/81
Data Audits	12/1/79; 4/28/81; 5/18/81; 6/5/81; 6/11/81; 6/12/81; 6/15/81; 6/18/81; 6/19/81; 11/11/81; 11/16/81; 12/3/81; 12/19/81; 12/28/81; 12/29/81
Report Audits	1/21/82; 4/30/82; 9/24/82
Reports to Principal Investigator and Management	Same as Data/Report Audits Above

To the best of my knowledge the methods described were the methods followed and the data presented accurately represent data generated during the study.

MATERIALS AND METHODS

EXPERIMENTAL ANIMAL STUDY PROCEDURES

Experimental Animals

On October 24, 1978, Battelle received 64 male Cynomolgus monkeys, (all young adults) from Primate Imports, Long Island, N.Y. for use in this study. The monkeys were individually housed in stainless steel cages and were quarantined in rooms 7C-317 and 7C-318 of the Battelle Columbus Laboratories' animal facility. The monkeys were isolated in these rooms until three consecutive TB tests, three consecutive fecal flotations and three consecutive fecal cultures (for enteric pathogens) administered at 2 week intervals were all negative. Then they were released for study. During the week prior to the start of exposure, all monkeys' eyes were examined for possible lesions or abnormalities. Animals with eye defects would have been rejected before the randomization and group assignment procedure, but no lesions warranting such action were found.

On February 16, 1979, 275 male and 275 female Fischer 344 rats were received from Charles River Breeding Laboratories, Wilmington, Mass. to be used in the chronic fibrous glass study. The rats were 5 weeks of age when received. These animals were housed five per cage in conventional polycarbonate cages and quarantined in room 7C-316 of the Battelle Columbus Laboratories' animal facility. The rats were held in isolation in this room and were observed twice daily by a veterinary technician for 7 days after arrival and then released for study.

Group Assignments (Randomization)

The male and female rats were randomized separately by computer-generated group assignment. The monkeys were randomized in a similar fashion. The group composition was structured so that mean body weights were statistically similar across groups and so that there was no inter-group heterogeneity of variance.

The first step in the randomization process was to enter the individual body weight and identification number for each animal into the computer programmed to generate random numbers. The program presented a standard distribution of body weights for all animals in each category. In the case of rats, animals with weights at the extreme tails of the distribution (about 8 percent of the total) were eliminated before randomization. The animals were then assigned to groups so that congruent body weight distribution curves were assured. Rats were randomly assigned to individual cage compartments alternating female and male animals within each cage. Monkeys were kept in individual cages.

Housing

During the quarantine and set-up period before exposure, the rats were housed in polycarbonate cages containing bottle waterers. At the time of randomization, the rats were placed into stainless steel wire mesh cages for the duration of the study.

The cages, manufactured by Allentown Caging Company of Allentown, N.J., are 58 inches long, 12 inches wide, and 7 inches high. There are 12 compartments for animals and each compartment is 7 inches high, 5 inches wide, and 12 inches long. The cage and compartment dimensions are fully compatible with Institute of Laboratory Animal Resources/American Association for Accreditation of Laboratory Animal Care (ILAR/AAALAC) caging requirements. The two end compartments on either end are only 4 inches wide. Nine such cages were contained on one mobile stainless steel rack 60 inches long, 28 inches wide, and 70 inches high. Each rack was fitted with an automatic watering system manifold (manufactured by Hardco of Cincinnati, Ohio) located centrally on the rack. A quick-disconnect coupling was used to attach each rack watering system to the room supply. The stainless steel nipples protruded approximately 1 inch into each compartment when the cages were placed on their assigned rack. Beneath each pair of cages on a rack was a stainless steel pan to catch animal wastes. The racks were wheel mounted to facilitate transport of cages from holding rooms to the chamber room and back.

The monkeys were individually housed in stainless steel cages with automatic watering nipples that both fit into the exposure chambers and slid

During the study, animals in their respective cages and racks were housed in environmentally controlled animal holding rooms for approximately 18 hours per day. Of the 18 hours in the holding rooms, 12 hours were in darkness and 6 hours were in light. All test animals were housed separately from control animals. The rooms were identical in every respect. The animals were provided with a minimum of 15 fresh air changes per hour with conditioned air programmed for a temperature of 70° ± 2°F and a relative humidity of 45 ± 5 percent.

On an exposure day, racks were wheeled from holding rooms to the inhalation exposure room for loading into the exposure chambers according to a standard operating protocol. Exposure followed for a period of approximately 6 hours, including start up and shut down time. After exposure, the animal cages were loaded back onto transfer racks for the trip back to the animal holding rooms. During final loading, rat cages were relocated on the transfer racks daily according to a standard procedure in which a given cage was placed one position down on the rack. Thus, each cage systematically progressed through all possible positions within the exposure chambers.

Monkey cages were transported back and forth from the exposure chambers to the holding rooms via a wheeled cart. Monkey cages were returned to the same position in the holding room after each exposure but they were rotated within the chamber according to a similar plan.

All holding rooms and racks were washed down daily while the animals were in the exposure chambers and all cages and racks were changed and washed each weekend. Exposure chambers were washed daily after the exposure period ended and the animals removed.

Feed

The rats were fed Purina Rodent Chow 5001 (manufacturer's minimum content of 23 percent protein, 4.5 percent fat, and 6.0 maximum percent fiber). The feed blocks were placed in troughs fixed to the front of the compartments at the end of the daily exposure period. The feed troughs were left in place over the weekends.

The monkeys were fed Purina Monkey Chow 5038 (manufacturer's minimum content of 15 percent protein, 5 percent fat, and 5.0 maximum percent fiber). The biscuits were given to the monkeys in stainless steel cups at the end of the daily exposure period and in the morning and evening on weekends.

Monitoring Individual Animal Identification

During the pretest period, each rat was fitted with a numbered monel metal ear tag (manufactured by National Band and Tag Co., Newport, Kentucky). The tag number was the animal's individual identification for the duration of the study and duplicate sets of tags were purchased in case replacements were needed. At the time of randomization, master locator maps were constructed to record the placement of rats, one per compartment. Each animal was placed in a specific cage and compartment throughout the study. The monkeys were identified with an individual chest tatoo.

Clinical Observations

All animals (monkeys and rats) were observed twice daily throughout the pretest and study periods by experienced technicians.

During observation, each rat was designated as being normal (N) or abnormal (A) by a check mark in the appropriate box on the clinical observations form (see example in Appendix B). If the animal was designated as being abnormal, a free text description of the abnormality was recorded on the animal obervations form (see example in Appendix B).

For monkeys, the normal/abnormal designations for morning and evening observations and the free text descriptions of the abnormalities were all recorded on the Record of Daily Clinical Observations form (see example in Appendix B).

The observations were made between 6 and 9 AM before the animals were loaded into the chambers between 3 and 6 PM after the animals were removed from the chambers. On weekends, the observations were made before and after cage changing, feeding, weighing, and room cleaning.

Mortality was recorded on daily record sheets, in the Project Death Record Log, and in the computerized body weight data file.

Ophthalmoscopic Examinations

Pre-exposure and post-exposure eye examinations were performed on all monkeys in this study. Before examination, the pupils were dilated by instillation of a few drops of Mydriacyl (Alcon Laboratories, Fort Worth, Texas) into the eye of each animal (the monkeys were restrained for instillation and examination by trained animal handlers). Approximately 15 minutes later, the eyes were examined using a Welch-Allyn Direct Ophthalmoscope for fundoscopic examination and an American Optical Slit-Lamp Biomicroscope for examination of the iris, lens, cornea, and conjunctivae. A trained veterinarian, experienced in laboratory animal ophthalmology, conducted all ophthalmoscopic examinations.

Body Weight Determinations

The weights of all animals were recorded at the beginning of the study, weekly for the first month, and biweekly thereafter for the duration of the study. The rats were weighed individually using an automatic capture and recording system. The system consisted of Mettler PL 3000 digital balances, Hazeltine 1400 CRT terminals, Techtran cassette tape drives, paper printers, and programmable microprocessors. Data tapes containing the current animal census based on master locator maps generated by the master data base record were used to program the microprocessor.

Once the microprocessor was programmed, the technicians were given cage and compartment identification and the associated animal census. Weight data signals from the balance were collected on a cassette data tape (to be read later to the master data base) and were simultaneously printed on a paper copy. The paper copy was used to check the completed update of the data base.

Because weighing was done when the cages were changed on a week-end day, two teams of two technicians were required to weigh the animals, record their weights, and place all animals into clean cages. A strict standard operating procedure required the following:

(1) Positive cage identification by reading the metal plate in the first compartment for each cage.

(2) Positive animal identification on the rat in Compartment Number 1 (Cages 1 through 9).

(3) Recording the identification number of (2) above on the form.

(4) Weighing all animals (individual rats) in a systematic manner by weighing each compartment 1 through 12, left to right.

(5) Checking the animal census against the master locator maps.

Monkeys were individually weighed in their cages on a table balance. The cage weight was subtracted from the gross weight to give the

Hematology and Clinical Chemistry

Monkeys

Blood for hematologic and serum chemical analyses was collected twice before the initiation of exposures; at weeks 16, 32, 48, and 64 following exposure; and immediately prior to necropsy. The parameters that were evaluated at each interval included the following.

Hematology. Hematocrit, hamoglobin, RBC count, WBC count, reticulocyte count, platelet count, and differential count.

Serum Chemistry. BUN, glucose, creatinine, inorganic phosphorus, calcium, total bilirubin, cholesterol, LDH, SGOT, sodium, and potassium. Blood samples were obtained from the femoral vein following a fast of approximately 12 to 16 hours. Specific procedures used for the determination of each factor are described in Appendix C. Results are evaluated by qualitative examination of group means for baseline and terminal sampling periods.

Rats

Blood for hematology and serum chemistry analyses was collected just prior to termination. Blood was collected by cardiocentesis after anesthetization of the rats with pentobarbital sodium injected intraperitoneally. The parameters evaluated were the same as those described above for the monkeys. Ten rats per sex were selected randomly for these evaluations.

Results were evaluated by qualitative examination of group means and standard deviations of exposed rats as compared to the control group.

Pulmonary Function Evaluation

One aspect of determining the health effects of long term, low level inhalation exposure to fibrous glass is the assessment of the alteration of pulmonary performance in exposed individuals. The value of respiratory physiology measurements is that such evaluations, which are designed to assess the subtle impairment of respiratory function relative to occupational exposure and to monitor those changes with time, may be useful is predicting the disease course in man. Although some respiratory function debilitation may not be life threatening, it may be costly both in terms of human suffering and economic impact. It is, therefore, important to understand the nature and degree of functional alterations of the respiratory system. To that end, Battelle selected a battery of pulmonary function tests for this study.

The following pulmonary function tests were selected: dynamic lung resistance (R_L), dynamic lung compliance (C_L), inspiratory capacity (IC), functional residual capacity (FRC), expiratory reserve volume (ERV), carbon monoxide diffusing capacity (DLCO), closing volume (CV), anatomical dead space (VADS), phase III slope ($\%N_2$/100 ml), forced vital capacity (FVC), peak expiratory flow rate (PEFR), forced expiratory flow at 50%, 25%, and 10% of lung volume (FEF @n%), and forced expiratory volume at 0.5 (FEV5) and 1 second (FEV1). In addition, some parameters were normalized to lung volumes, when appropriate, to compensate for size differences and limiting effects of smaller volumes. Table 1 is a list of all of the pulmonary function parameters measured or calculated for this study.

Lung mechanics evaluations were determined using the techniques of Neergaard and Wirz[15] after direct recording of transpulmonary pressure, lung airflow rate, and respired gas volume onto an Electronics for Medicine VR-6 recorder. Dynamic lung volumes were obtained from recordings of lung volume plotted relative to airflow rate. Respiratory maneuvers necessary for these evaluations were induced by a positive-pressure plethysmograph by Charles Spanger and Associates. The design and operation of this device is described in detail by Moorman, Lewis, and Wagner.[16] A picture of this device is shown in Figure 1.

TABLE 1. PULMONARY ASSESSMENT PARAMETERS

R_L	Dynamic Airways Resistance	($CMH_2O/l/sec$)
C_L	Dynamic Lung Compliance	(ml/CMH_2O)
FVC	Forced Vital Capacity	(ml)
FEV.5/FVC	Forced Expiratory Volume in 0.5 seconds normalized to FVC	(%)
FEV1/FVC	Forced Expiratory Volume in 1 second normalized to FVC	(%)
PEFR	Peak Expiratory Flow Rate	(ml/sec)
FEF @n%	Forced Expiratory Flow at n% of lung volume	(ml/sec)
FEF @n%/FVC	Normalized FEF @n%	(FVC/sec)
IC	Inspiratory Capacity	(ml)
FRC	Functional Residual Capacity	(ml)
ERV	Expiratory Reserve Volume	(ml)
RV	Residual Volume	(ml)
TLC	Total Lung Capacity	(ml)
RV/TLC	Ratio of RV to TLC	(%)
DLCO	Diffusing Capacity of Carbon Monoxide	(ml STPD/min/mmHg)
CV	Closing Volume Ratio to Vital Capacity	(%)
CV+RV/TLC	Sum of CV and RV normalized to TLC	(%)
VADS	Anatomical Dead Space	(ml)
$\%N_2/100$ ml	Slope of Phase III N_2 Washout	(%)
Viso	Volume of Helium Isoflow	(ml)
Viso/FVC	Viso normalized to FVC	(%)

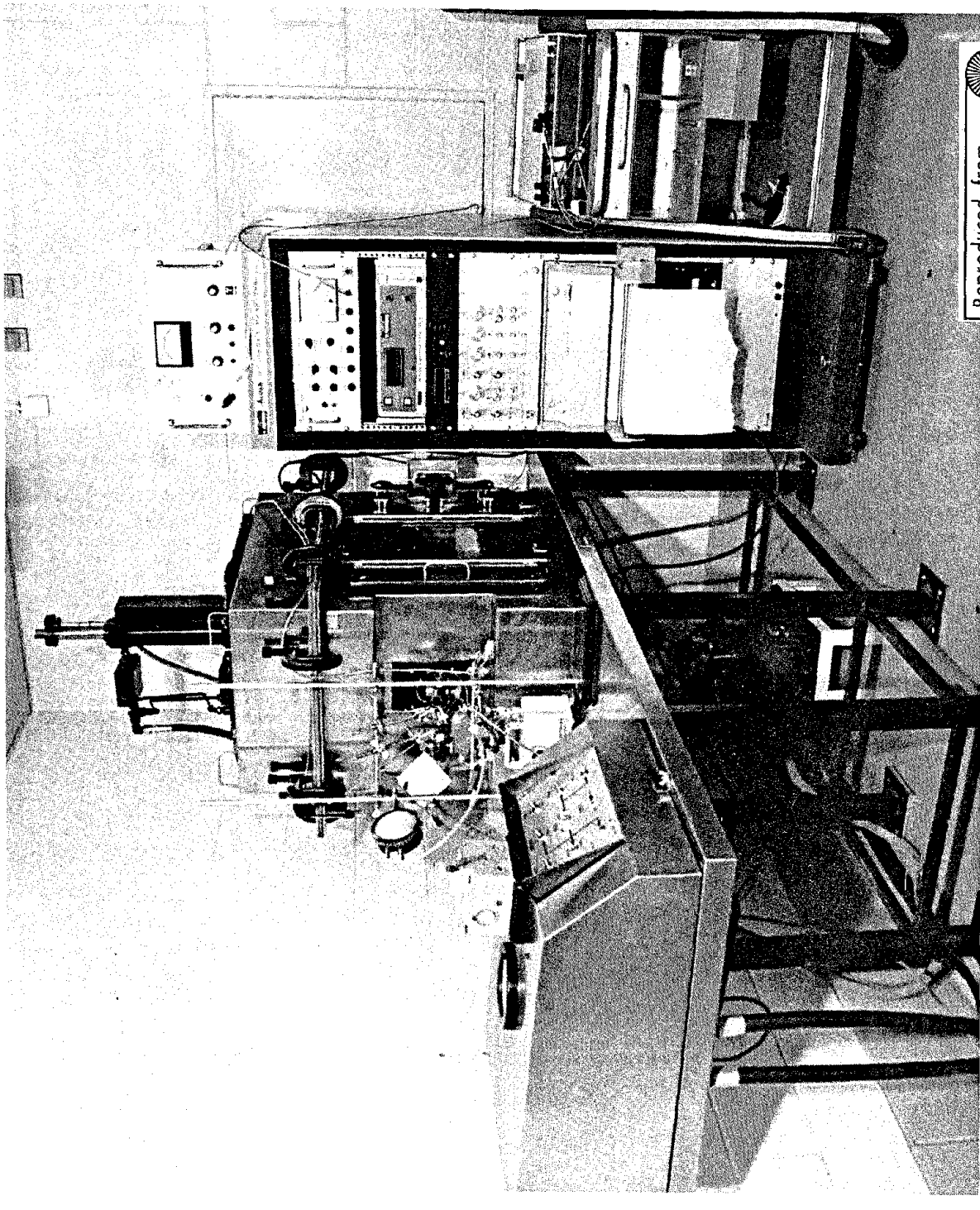

FIGURE 1. POSITIVE-PRESSURE PLETHYSMOGRAPH

The dynamic response characteristics of transducer systems used to evaluate pulmonary function information must exceed the frequency components inherent in the measured signals. Quiet breathing and forced expiratory maneuvers studied during this program do not typically exceed 4 Hz. No amplitude distortion or phase shift was observed in signals normalized to a simple harmonic motion device which provided reference flows up to 7 Hz. The plethysmograph compression time measured from -70 cm H_2O to +70 cm H_2O was determined to be 172 msecs $\pm$ 14 msecs with an n=10 trial. Transit time was measured by signals generated by electromechanical position switches used to control diaphragm excursion.

The volume of helium isoflow, the diffusing capacity of the lung for carbon monoxide, and the multiple breath N_2 washout test were executed as outlined by Hutcheon et al.[17], Ogilvie et al.[18], and Lewis et al.[19], respectively.

The 60 adult Cynomolgus monkeys were divided into 5 groups of 12 monkeys each for exposure and evaluation during this program. The generation and exposure conditions are discussed elsewhere in this report. Pulmonary function evaluations were performed at three time periods during the course of this study: once before the initiation of exposure, once after 9 months of exposure, and once after 18 months of exposure. Anesthesia was induced approximately 15 minutes before the beginning of the respiratory physiology measurements by the sequential introduction of ketamine (35 mg/kg) and Xylazine (5 mg/kg). Additional anesthetic was used, if necessary, to maintian adequate depth of anesthesia during the period of evaluation. The duration of evaluation was typically 30 minutes in length. The anesthesia regimen was selected because of its ease of introduction and its degree of safety.

Once the desired plane of anesthesia had been reached, the test subject was intubated with a shortened 20 FR Magill endotracheal tube and placed, sitting upright, in the plethysmograph. In addition, an esophageal balloon was placed in the lower third of the esophagus and the balloon was maneuvered to demonstrate maximum pressure fluctuations with minimal cardiac artifacts. The airflow through the endotracheal tube was monitored by a Hans Rudolph pneumotachograph and Validyne MP-45 pressure transducer. The esophageal pressures were also determined by a calibrated Validyne pressure transducer. The signals from these transducers, as well as the flow integrator and Med-Sciences

Nitrogen Analyzer, were recorded as necessary on an Electronics for Medicine VR-6 recorder. These recordings were subsequently evaluated to determine the respiratory performance of the test subject. After evaluations were completed, the subjects were returned to their cages to recover. Most monkeys appeared fully recovered after about 2 hours.

Gross and Microscopic Pathology

Monkeys

Detailed gross examinations were conducted on all monkeys and pertinent observations were recorded. Monkeys were terminated by anesthetization with pentobarbitol sodium, followed by exsanguination. The following tissues were removed and fixed in 10 percent neutral formalin.

Larynx	Urinary bladder
Trachea	Testes
Lung (section from each lobe)	Prostate gland
Heart	Ovaries
Liver	Uterus
Esophagus	Spleen
Stomach	Pancreas
Ileum	Kidneys
Colon	Adrenal glands
Pleural membrane	Pituitary gland
Nasal passages	Brain
Paranasal sinus	Thyroid gland
Tracheobronchial lymph node	Lesions or masses
Mesenteric lymph node	*Eyes

The tissues listed above were processed in the routine manner, embedded in paraffin, cut at 5 μm, stained with hematoxylin and eosin, and examined microscopically. Histochemical stains were utilized on specific tissues at the discretion of the pathologist to aid in interpretation of changes.

Rats

Detailed gross examinations were conducted on all rats and pertinent observations were recorded. Rats were terminated by intraperitoneal injections of pentobarbital sodium followed by exsanguination (if blood was collected for hematology and serum chemistry) or by CO_2 inhalation followed by exsanguination (if blood was not used for clinical laboratory procedures). Tissues removed for fixation and subsequent histologic examination were the same as those listed above for monkeys.

Statistical Analysis

Body Weights

The statistical analyses consist of body weight and weight gain analyses across dose groups at 0, 9, and 18 months for monkeys, and at 0, 9, and 21 months each for male and female rats. Percent weight changes over the entire measurement period, over the first 9 months, and over the remaining months were also analyzed across dose groups for monkeys and for each sex in rats. A survival analysis for rats only was performed, as only two deaths occurred among the sixty monkeys. These two early deaths were excluded from monkey body weight analyses as outliers because their weights were much lower than the other monkeys.

For each time period, the assumptions underlying a one-way analysis of variance were tested. Histograms and normal probability plots were used to determine the appropriate statistical test and to assess the normality within each dose group. Homogeneity of variance was tested by the method of Levene[20].

If the Levene statistic was not significant ($p > .05$), a one-way analysis of variance (ANOVA) was performed. If the ANOVA was significant ($p < .05$), a Dunnett's test[21] was used to compare each treatment with the control group. If the Levene statistic was significant ($p < .05$), a weighted ANOVA according to Welch[22] was performed. A t-test with Bonferroni's correction, assuming unequal variances was performed to compare treatment means with the control if the Welch test was significant. Because of outliers in the data for rats, a Kruskal-Wallis[23] nonparametric ANOVA followed by Dunn's[24] multiple comparisons was sometimes considered a more appropriate test. Such cases are noted and explained in the text.

Survival Analysis

Mortality data for rats was analyzed by the actuarial life table

method developed by Berkson and Gage[25]. For each group, survival information was printed and a nonparametric test devised by Desu[26] was used to compare groups.

All analyses were performed on Battelle's CDC 5600 and Cyber 74 computer systems using packaged programs[27-29]. For all analyses, the level of significance was $\alpha = .05$.

Chamber Concentrations

For each day and chamber, concentration levels were measured at various times throughout the day. Based on the measured reading obtained each time, the concentration level in the chamber was then manually adjusted toward a target level for the chamber. The data collected for each day and chamber included the measured concentration levels and the time period covered by each reading.

Statistical measures were computed to globally describe the concentration levels present in the chamber for each day. These measures included a time-weighted average of the concentration levels, a weighted measure of the variability in concentration levels, and the minimum and maximum levels. The assumptions upon which these descriptive statistics were based on as follows:

(1) There were two sources of variation for the concentration levels throughout the day:

- Variation due to manual adjustments of the levels.
- Random variation over time between each manual adjustment.

(2) The random variation was small relative to the variation due to manual adjustments. That is, a steady state condition existed between adjustments.

The formula used to compute the time-weighted average of the concentration levels is given by

$$\bar{X} = 1/T \sum_{i=1}^{N} T_i C_i \quad , \tag{1}$$

where T_i is the length of time covered by the i^{th} measured concentration level, C_i, $T = \sum_{i=1}^{N} T_i$ is the total length of time the animals were subjected to fiber glass during the day, and N is the number of readings taken in the chamber on the given day.

The variability of the concentration levels throughout the day was estimated by

$$S^2 = 1/T \sum_{i=1}^{N} T_i (C_i - \bar{X})^2 \quad , \tag{2}$$

where $\bar{X}$ and T are given in (1). Note that the formula given by (2) slightly underestimated the total variability in concentration levels since it does not include a component for the random variation over time between each manual adjustments. However, from Assumption 2, this component would be relatively small. The results for each day and chamber are given in Appendix D.

Finally, an average concentration level for each chamber over each quarter was computed by averaging the values for each day in the quarter. In addition, the lengths of test time for all the days were summed to get a total value for each quarter. The results for each quarter are given in Table 23.

Pulmonary Function

The one way analysis of variance (ANOVA) and the Kruskal-Wallis one way rank analysis of variance were used to evaluate the group statistics for the pulmonary data. Bartlett's test was used to validate the ANOVA. Those parameters that demonstrated non-homogeneous variance (Bartlett's $P > 0.05$) were tested by the non-parametric Kruskal-Wallis evaluation. For all procedures, the 95% level of significance was used.

FIBER PREPARATION

Four glass fiber fractions were required for the animal exposure program with general specifications of (1) 4 to 6 micrometer diameter fiber > 20 micrometers long, (2) 0.5 to 3.5 micrometer diameter fiber > 10 micrometers long, (3) < 3.5 micrometer diameter fiber > 10 micrometers long, and (4) < 3.5 micrometer diameter fiber < 10 micrometers long. Appropriate commercial production glass fibers were selected; and techniques were developed for grinding and classifying the fibers into fractions to meet these specifications.

During the 18 month animal exposure program, the four fiber fractions were produced on a lot basis and delivered daily for use in the exposure chambers. Each lot was examined and characterized to confirm that the fibers met the specifications for the exposure program.

Material Selection

Commercial grade glass fibers used in filters and insulation products were selected for making the required fiber fractions. The initial selection criteria were quantity production and fiber diameter in the required size ranges. Binders (formaldehyde based resins) were required on fibers in two of the fractions.

Four commercial products were selected for evaluation as follows:

(1) FG Insulation Fiberglas*, 4 to 12 micrometer diameter fiber with 4.5 percent binder (red - urea and phenol formaldehyde)

(2) FM Series Air Filter Media*, 1 micrometer diameter fiber with 12.5 percent binder (yellow - phenol formaldehyde)

(3) FM Series Air Filter Media*, 1 micrometer diameter fiber without binder

(4) Tempstran Code 100/475**, 1 micrometer diameter fiber without binder.

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* Owens-Corning Fiberglas Corporation, Newark, Ohio 43657

** Manville Corporation, Denver, Colorado 80217

Based on grinding and classification tests, the red FG Insulation Fiberglas and yellow FM Series Air Filter Media were selected for making the two fiber fractions with binders, and the Tempstran Code 100/475 glass fiber was selected for the two fractions with < 3.5 micrometer fibers > 10 micrometers and < 10 micrometers long.

Size Reduction

To meet the length requirements of the four fiber fractions, various grinding methods were investigated to break up the commercial glass fibers without destroying fiber integrity. Appropriate methods were selected to produce the fibers in the relatively large quantities needed in the inhalation program.

Several grinding mills (see below) were evaluated for (1) fiber production rate, (2) retention of fiber integrity with minimum overgrind, and (3) minimum contamination.

Name of Mill	Type of Mill	Manufacturer
Mikro Atomizer	High Speed Mechanical Pulverizer	Pulverizing Machinery Co., Summit, N.J.
Ball Mill	Ball Cascade	---
Glen Creston Mill	Hammer Mill	Glen Creston Ltd., Middlesex, Eng.
Fitz Mill	Hammer Mill	The W.J. Fitpatrick Co., Chicago, Ill.
Waring Blendor (Century 8)	Sluar	Dynamic Corp. of America, New Hartford, Conn.
Gem-T Mill	Fluid Energy	Geo. W. Helme Co., Inc. Helmetta, N.J.
Rod Mill	Rod Cascade	Denver Equip. Co., Denver, Col.
Willy Bleuler Apparatebau	High Energy Ring Mill	Zollikon-Schweiz, Switzerland
Planetary Mill	High Energy Ball Mill	Steel and Cowlishaw Ltd., Hanley, Stoke-on-Trent, England

Test grinds from each of the grinders yielded different results. The Waring Blendor and Gem-T fluid energy mill separated the fiber bundles but did little grinding on the 4 to 12 micrometer diameter Insulation FG

Fiberglas. The hammer mills such as the Fitzmill, Glen Creston mill, and the high speed Mikro Atomizer generally produced fiber lengths of 100 to 400 micrometers in the large diameter fibers. However, the hammer mills and high speed mechanical pulverizer were not effective in grinding the 1 micrometer diameter fibers. The fibers apparently charged electrically and collected in the housing and on the hammers.

Ball milling and grinding with the Willy Bleuler Apparatebau grinder were the most effective techniques for producing short fibers from the commercial glass fibers.

Ball Mill

Ball milling in 1.5 ℓ ceramic jars reduced the length of the 1 micrometer fibers but overground the 4 to 12 micrometer fibers when the ball jars were loaded with 1.2 kg of 0.5 cm ceramic balls and 3 grams of fiber. The 4 to 12 micrometer diameter fibers were reduced in diameter as well as in length. The best results were achieved by dry grinding with a rotational speed of about 75 rpm. The 1 micrometer diameter fibers without binder generally ground to 95 percent < 5 micrometers in 4 to 6 hours. This material was satisfactory for making the < 10 micron fractions. A shorter grind of 30 to 45 minutes produced fibers that were predominately (90 percent) in the range of 10 to 30 micrometers, satisfactory for making the > 10 micrometer fractions.

Wet grinding with 300 ml of water per load reduced the grinding rate. Only about 75 percent of 1 micrometer fiber with binder was in the range of 1 to 10 micrometers long after 30 hours of grinding. By comparison, 24 hours of dry grinding of the same fiber yielded about 90 percent that were less than 10 microns.

Fiber fractions produced by dry grinding of the 1 micrometer Tempstran fiber for periods of 0.75, 2, and 4 hours are shown at 500X magnification in Figures 2, 3, and 4 respectively.

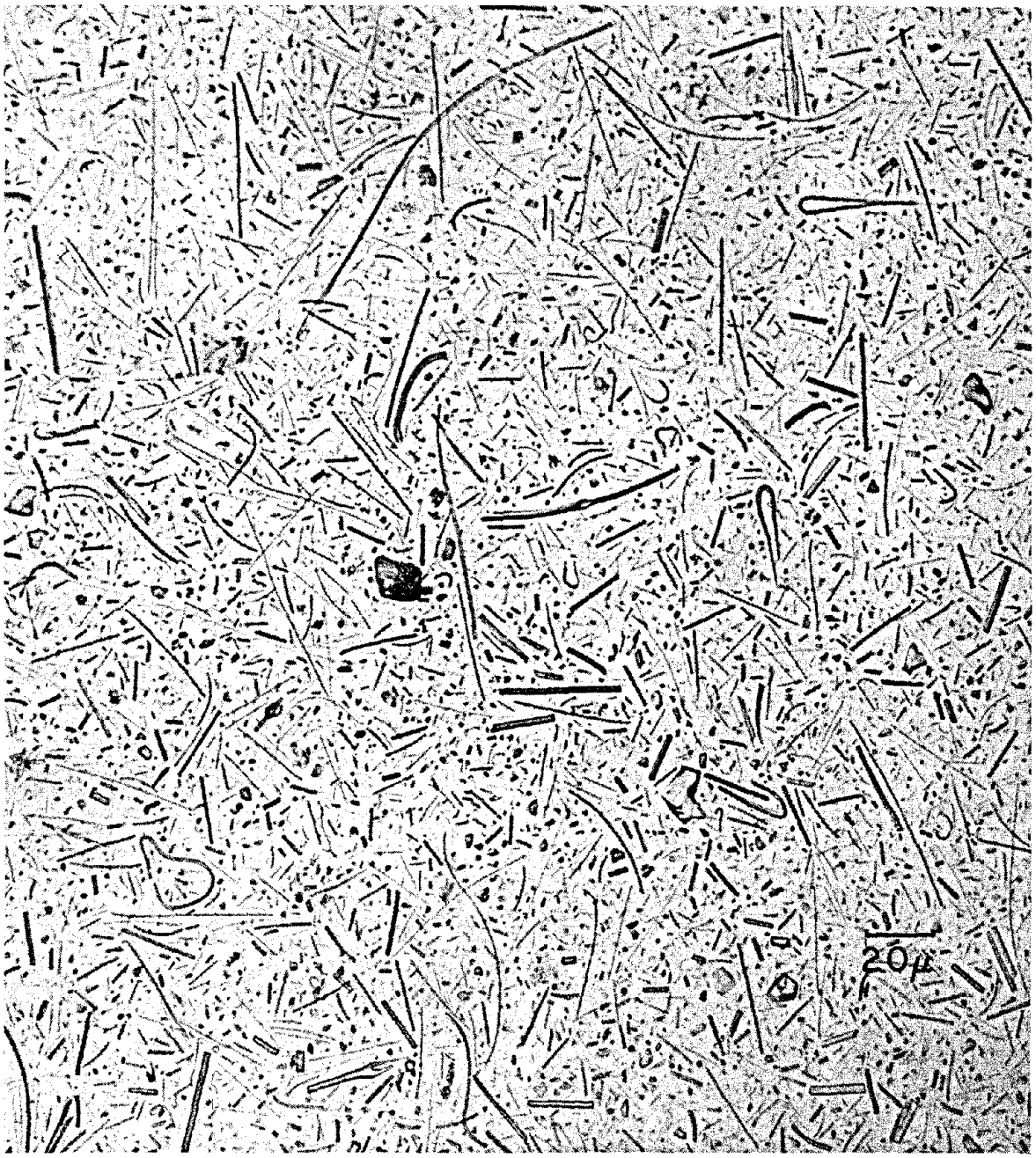

FIGURE 2. FIBER PRODUCED BY 3/4-HOUR BALL MILLING

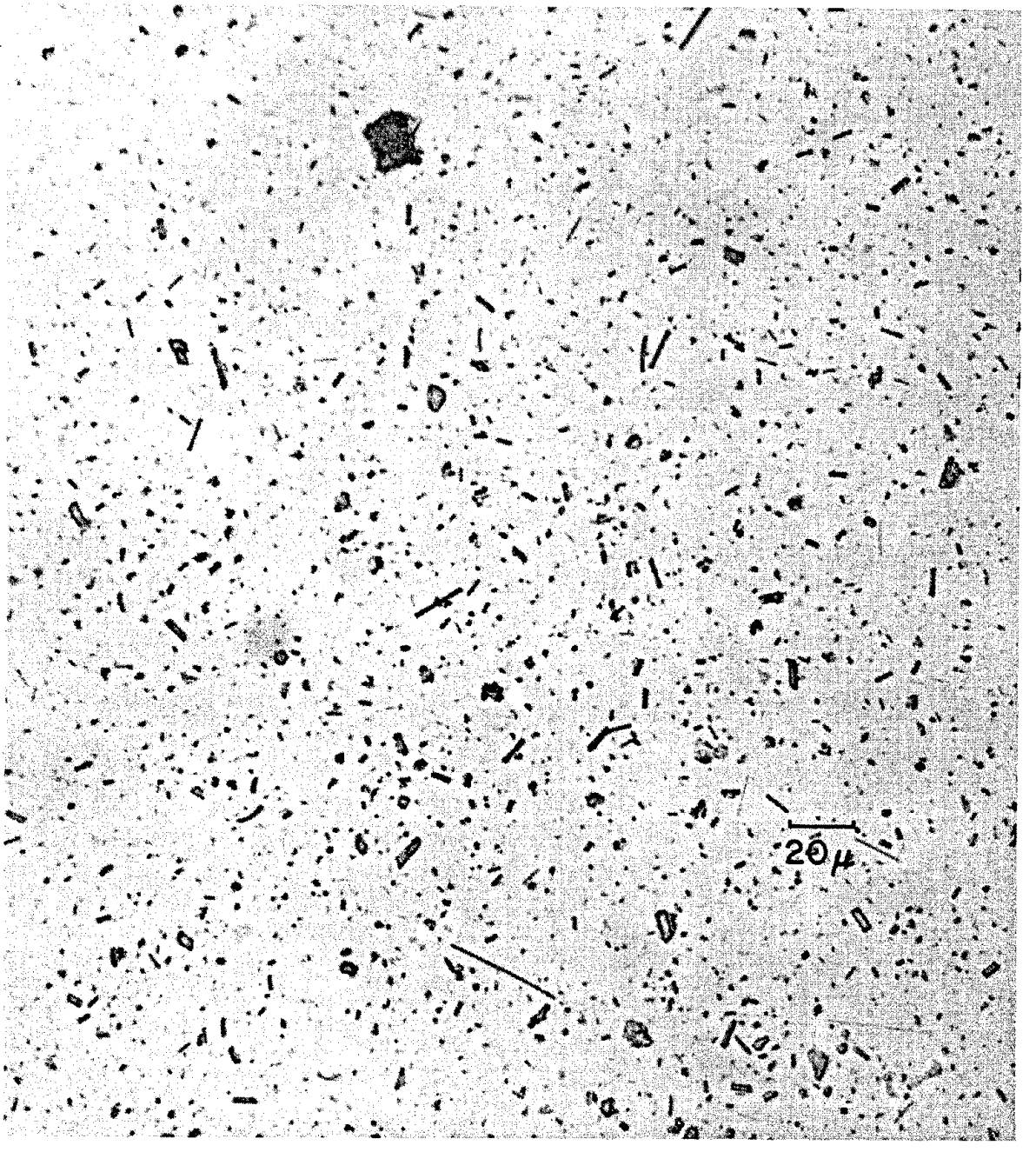

FIGURE 3. FIBER PRODUCED BY 2-HOUR BALL MILLING

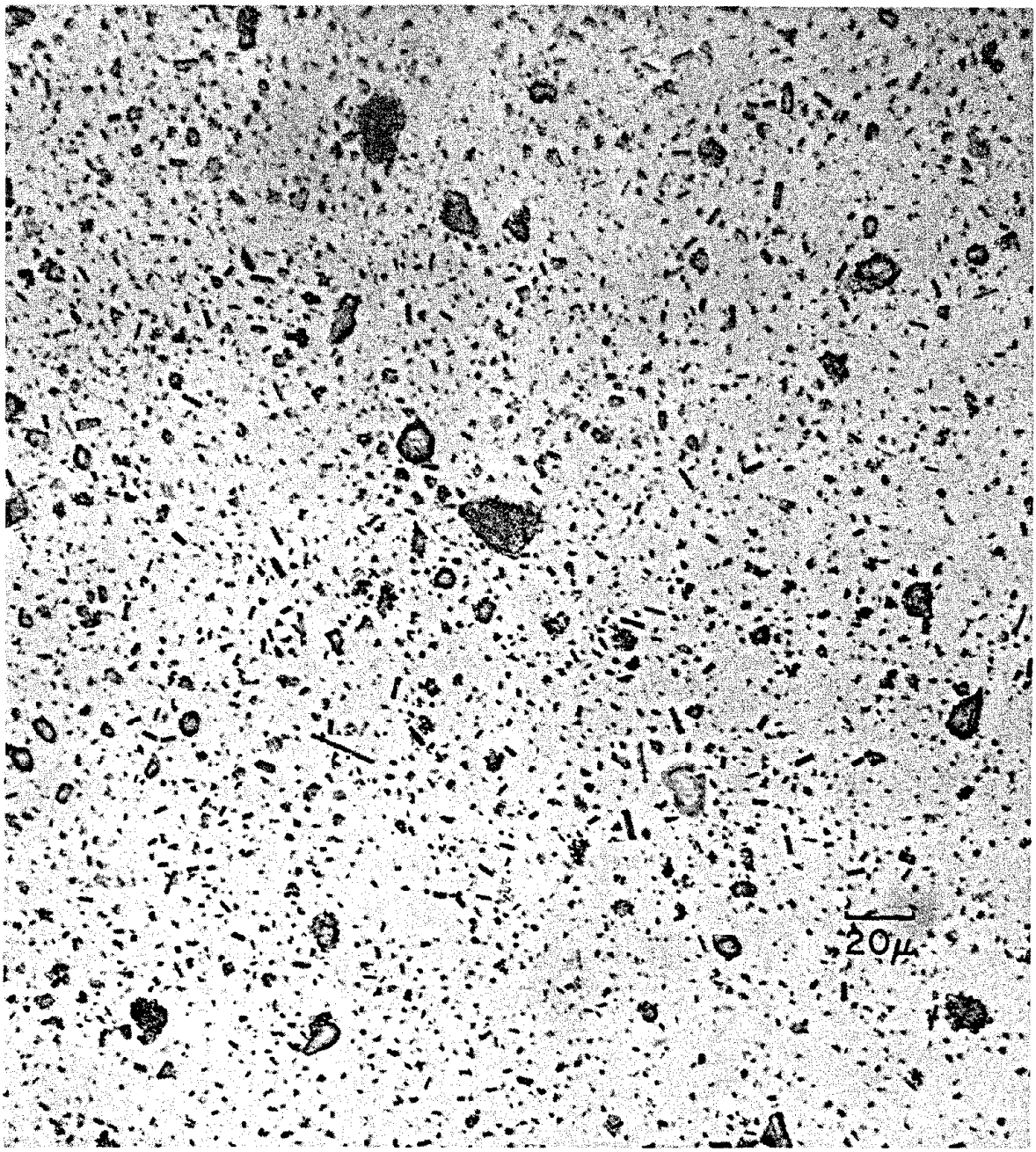

FIGURE 4. FIBER PRODUCED BY 4-HOUR BALL MILLING

High Speed Hammer Mill

The No. 5 Mikro Atomizer is a high-speed mechanical pulverizer that has a built-in air classifier. It generally produces particles in the range of 1 to 50 microns. The Mikro Atomizer might grind the 4 to 12 micrometer fibers if the fiber would clear the grinding chamber. However, cooling the fiber with dry ice failed to get the fibers to clear the grinding chamber and mixing the fiber with a hard resin to control the grinding failed. About 30 parts of fiber was hot blended with 70 parts of a hard resin, cooled, and ground. Low molecular weight Dow PS-SL-312 polystyrene* released the fiber too easily, and high molecular weight Dow 666-10 polystyrene was too tough to grind.

Ring Mill

The 4 to 12 micrometer FG Insulation Fiberglas with binder was ground successfully in a Willy Bleuler Apparatebau grinder. The Willy Bleuler has a set of three concentric solid and hollow cylinders that shake vigorously. The fiber length was reduced to approximately 20 microns in 30 seconds to 1 minute.

Figure 5 is a photograph of 200X magnification of 4 to 12 micrometer diameter fibers ground of 0.5 minute in the Willy Bleuler Apparatebau grinder. Longer grinding produced shorter fibers.

After the initial milling evaluations were completed, the Willy Bleuler Apparatebau grinder was selected for preparing all the fiber fractions required in the exposure program. A 30 second grind reduced the 4 to 12 micrometer diameter FG Insulation Fiberglas with binder to a mean length of about 20 micrometers. A 1 minute grind reduced the 1 micrometer diameter Tempstran Code 100/475 to a mean length longer than 10 micrometers, and a 3.5 minute grind reduced the 1 micrometer diameter Tempstran Code 100/475 fiber to a mean length of less than 10 micrometers. Grinding 1 micrometer diameter FM Series Air Filter Media with binder for 30 seconds produced fibers with lengths longer than 10 micrometers.

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*Dow Chemical Company, Midland, Michigan

FIGURE 5. FIBER PRODUCED BY 0.5-MINUTE GRIND IN WILLY BLEULER APPARATEBAU GRINDER

Classification

All of the grinding techniques which produced glass fibers in the desired size ranges also produced large numbers of particles and fibers with length to diameter ratios smaller than 3 to 1 as well as a few fibers that were up to several hundred micrometers long. Further processing was necessary to remove undersize and/or oversize particles and fibers to meet the required sizes. Consequently, various techniques, including centrifuging, wet filtration, and settling techniques, were developed to remove the oversize and undersize fibers and particles.

Initially, about 3 grams of ground material was dispersed ultrasonically in about 300 ml of water and filtered through a 325 mesh sieve. The dispersion was stirred rotationally and the sieve was vibrated to prevent plugging. The long fiber was retained on the sieve. Following sieving, the filtrate was allowed to settle for about 1 hour and the supernatant liquid, which contained extremely fine fragments, was poured off. The process was repeated several times. Reduction of the fines in the product was evident; however, some fine fragments still remained even after 5 such washings. The fines removed by this treatment ordinarily remain suspended for days producing a milky supernatant liquid; but after each rinsing treatment, the supernatant cleared more rapidly. Significant upgrading of the fiber fractions was achieved, confirming the results reported in two recent studies at Johns-Manville[30] and at the Institut fur Aerobiologie[31].

Long fiber fractions were prepared from the settled fraction while the short fiber fraction was recovered from the supernatant. Additional washings prepared the four required fiber fractions as follows:

Fiber Fraction	Fiber	Production Method
1) 4 to 6 micrometer diameter fiber greater than 20 micrometers long with binder	4 to 12 micrometer diameter FG Insulation Fiberglas with binder	Ground for 0.5 minute, wet sieved through a 325 mesh sieve, washed twice to remove fines, collected on filter, and sieved to break up cake.
2) 0.5 to 3.5 micrometer diameter fiber greater than 10 micrometers long with binder	1-micrometer FM Series Air Filter Media with binder	Ground for 0.5 minute, wet sieved through 325 mesh sieve, washed 4 times to removes fines, collected on filter, dried, and sieved to break up agglomerates.
3) less than 3.5 micrometer diameter fiber greater than 10 micrometers long	1 micrometer Tempstran Code 100/475	Ground for 1 minute, wet sieved through 325 mesh sieve, washed 4 times to remove fines, collected on filter, dried, and sieved to break up agglomerates.
4) less than 3.5 micrometer diameter fiber less than 10 micrometers long	1 micrometer Tempstran Code 100/475	Ground for 3.5 minutes, suspended material filtered, dried, and sieved to break up agglomerates.

Figures 6 to 9 are photographs of these fiber fractions at 800X. One centimeter on the photographs represents 12.5 micrometers at 800X. Although the fibers in Figures 8 and 9 were from the same parent material, nominally 1 micrometer diameter fiber, the diameters of the fibers in the settled fraction in Figure 8 were significantly larger than the diameters of the fibers in the supernatant fraction in Figure 9. The same effect can be seen in the fibers in Figure 7 from the settled fraction of fibers from parent fibers with nominal diameters of about 1 micrometer.

Since this technique required extensive time, liquid and air elutriation methods were evaluated. In elutriation, the opposite of sedimentation, the upward flow of the liquid or air interacts with the normal settling of the fibers. The large fibers settle whereas the small fibers move upward with the classification media. Some success was achieved with this technique, but the time required to size a fiber fraction was not acceptable.

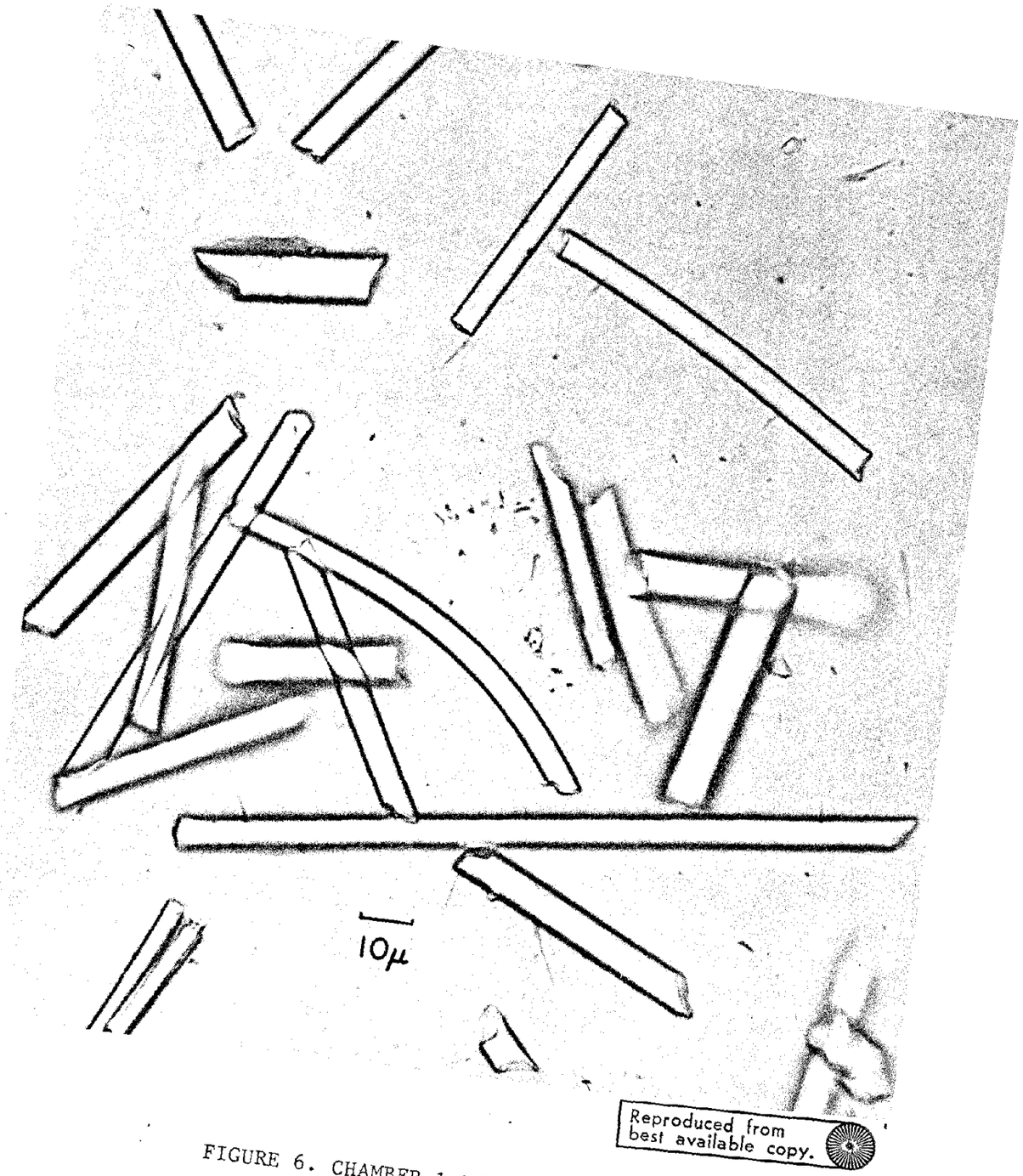

FIGURE 6. CHAMBER 1 FIBERS (800X)

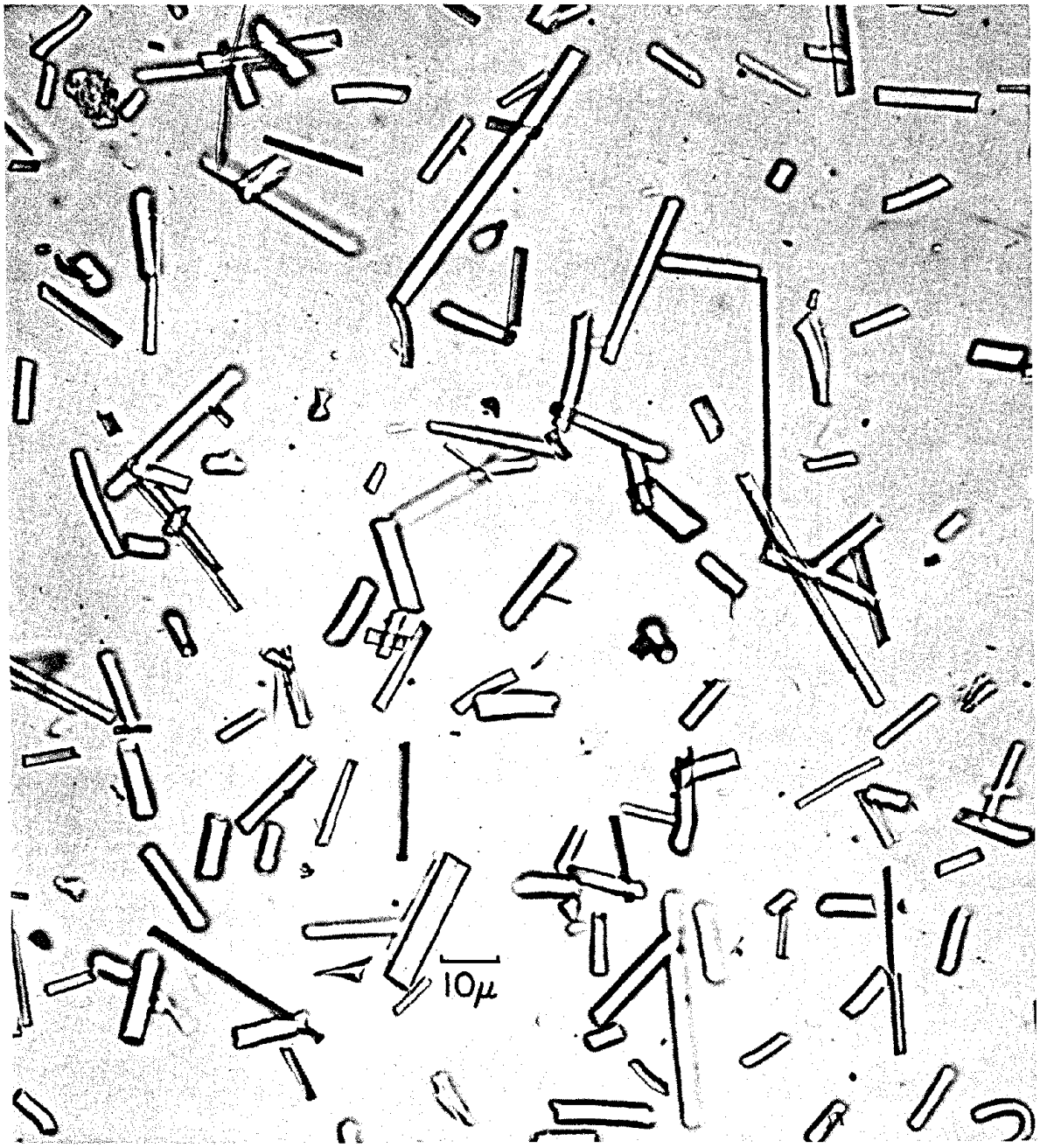

FIGURE 7. CHAMBER 2 FIBERS (800X)

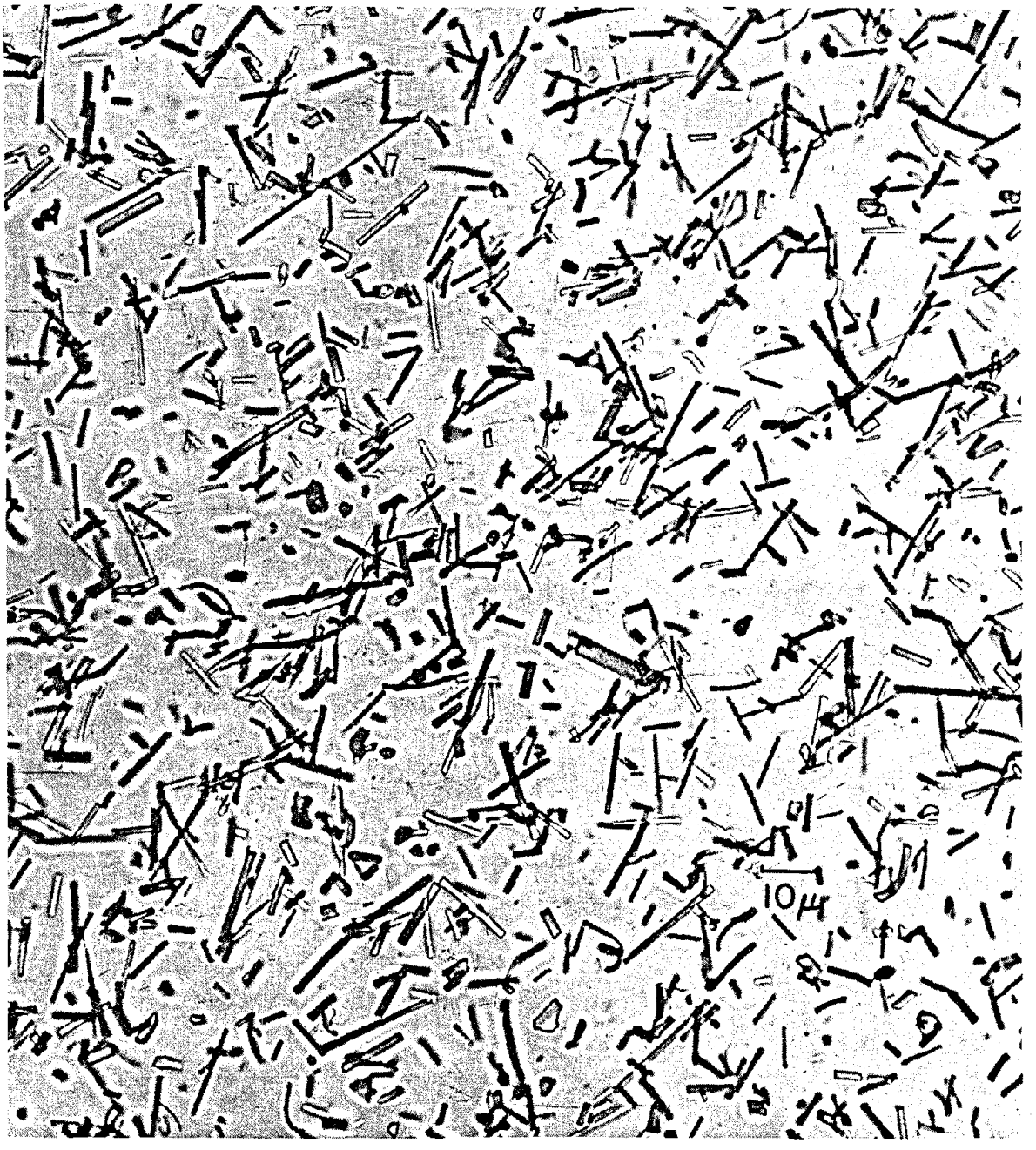

FIGURE 8. CHAMBER 3 FIBERS (800X)

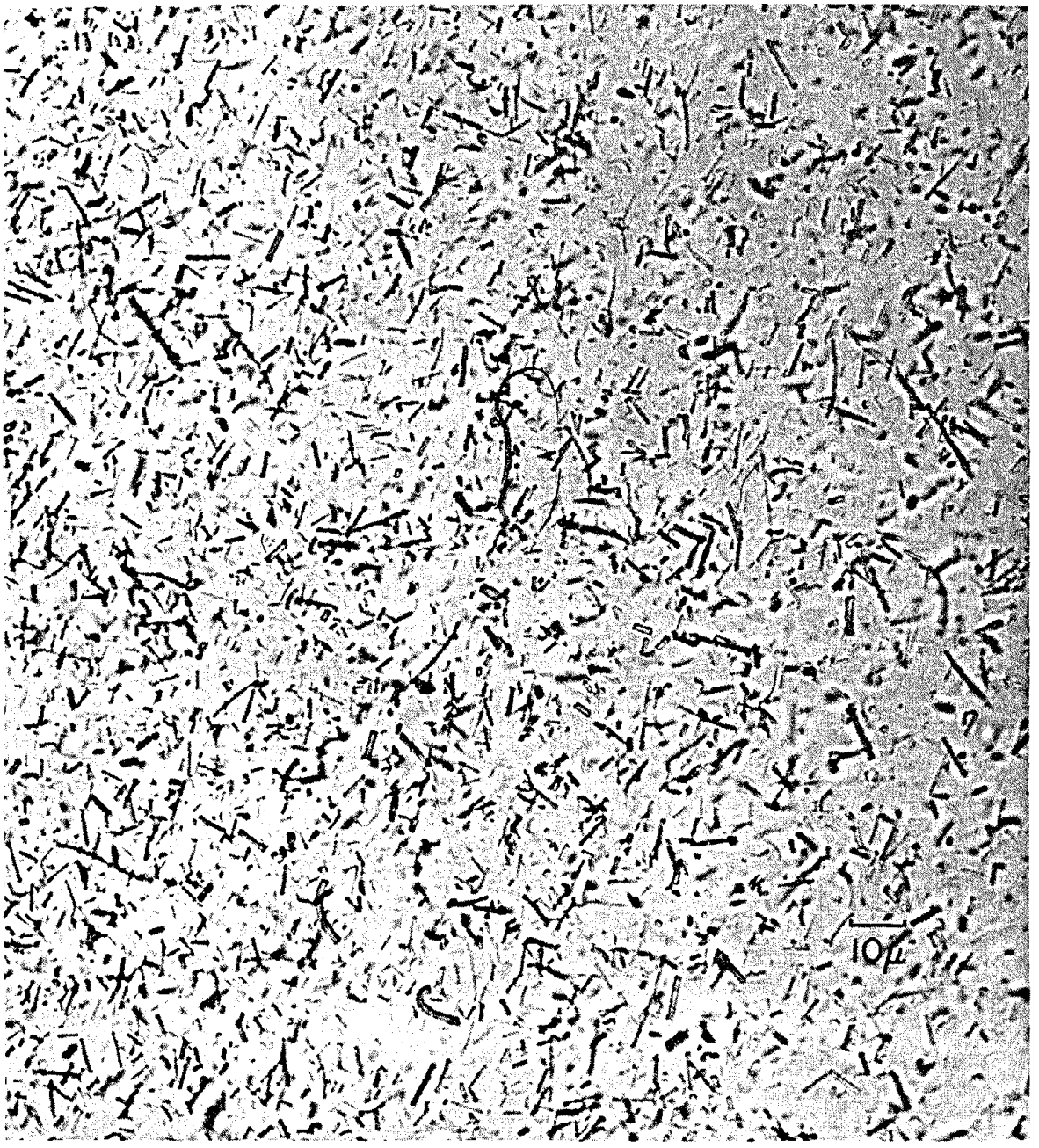

FIGURE 9. CHAMBER 4 FIBERS (800X)

Ultimately, a Bahco-Microparticle classifier* was used to increase the fiber production rate. The Bahco microparticle classifier (shown in Figure 10) is an air centrifuge-elutriator consisting of a rotor assembly driven by an electric motor. The motor and rotor are enclosed in a cast metal housing. The motor operates at 3500 RPM creating a precisely controlled air velocity within the air spiral and sifting chamber of the centrifuge. The sample is introduced into a spiral shaped air current flowing toward the center of the apparatus. The spiral current of air has suitable values of tangential and radial velocities so that a "heavy" portion of the sample is accelerated by the centrifugal force toward the periphery of the whirl. The "light" part of the sample is carried by the air current toward the center of the whirl by means of friction between the air and the powder particle. The size, shape, and weight of the particles determine which direction they take in the air current.

The Bahco successfully removed the oversize fibers from the FG Insulation Fiberglas and the oversize and undersize fibers from the FM Series Air Filter Media fibers. Attempts to classify the fine Tempstran fibers with the Bahco were not satisfactory.

After production started with the Bahco unit, work was undertaken with the larger capacity Donaldson Accucut (TM) Model 812 Air Classifier** with the objective of replacing the Bahco classifier in making the two fiber fractions with binders. In the Majac air classifier, fiber yield was about the same but the production rate was much higher than with the Bahco. Unfortunately, fiber breakage in the Majac reduced the fiber size significantly and the yield was too low.

Trials with the Majac air classifier also were run on the fine fibers which could not be fed into the Bahco. Production rates of about 11 kg of fiber per hour appeared to be possible; however, a single pass did not cut the fibers cleanly and a second pass did not duplicate the quality achieved by the wet separation process used for daily production.

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* Harry W. Dietert Co., Detroit, Michigan

** Majac Division, Donaldson Co., Inc., Minneapolis, Minn.

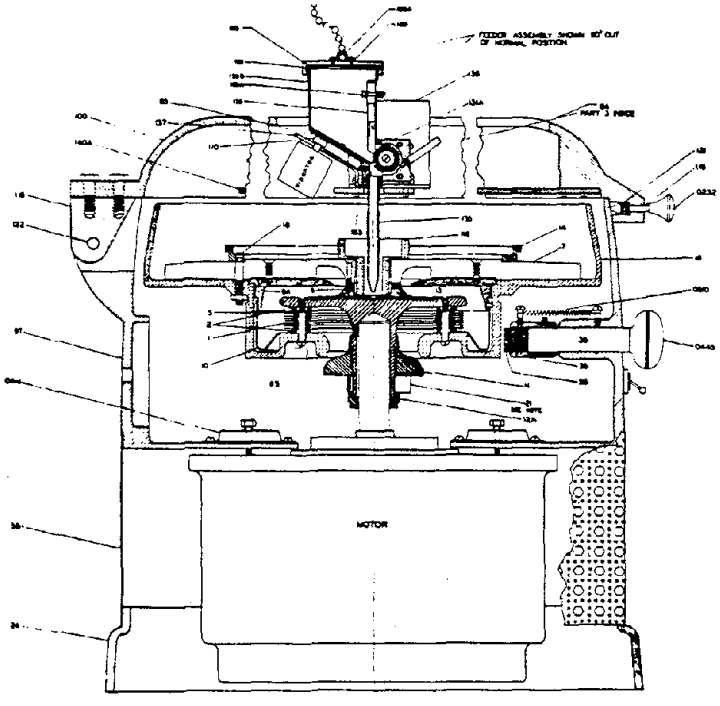

FIGURE 10. THE BAHCO MICROPARTICLE CLASSIFIER USED FOR THE DETERMINATION OF PARTICLE SIZE OF FINE DUST

Feeding the fine fibers also was a problem in the larger classifier.

However, liquid centrifuging was successful with the fine fibers. The centrifuge increased the daily production rate when used on fibers from the sieving and sedimentation tanks. After centrifuging for 1 minute at 1470 rpm, the < 10 μm fibers still were in suspension and the > 10 μm fibers settled. Trial separations were made with propanol, ethyl alcohol, and distilled water. Distilled water was selected for production use.

Table 2 summarizes the classification procedure for each fiber type used in the exposure program.

Fiber Production

Production of fibers was started with the Willy Bleuler mill to provide the daily deliveries of 40 grams each of the two fiber fractions with binders and 10 grams each of the two plain white fibers. Because the Willy Bleuler mill grinds only a 5 to 7 gram batch, studies were continued to find a mill with a larger capacity to reduce production costs.

Milling in a 12 inch diameter rod mill was attempted on the 1 micrometer FM Series Air Filter Media fiber with binder. However, milling with 0.25 to 1 inch diameter steel rods failed to produce significant yields of the required fiber lengths in wet grinds up to 1 hour.

Subsequently, a Planetary mill was evaluated. Batches up to 400 grams were ground in the Planetary mill in the same time that the 5 to 7 gram batches were ground in the Willy Bleuler mill. However, the fibers milled in steel jars were highly contaminated with iron from the mill and balls.

Jars with polypropylene and ceramic liners subsequently were used to reduce contamination of the fibers. The polypropylene liners were not satisfactory for grinding the fibers, but the porcelain liners ground the fibers apparently without contamination. Coating the mill with

TABLE 2. CLASSIFICATION TECHNIQUES TO PRODUCE SIZED FIBERS

	Fiber Fraction	Fiber	Production Method
(1)	4 to 6 micrometer diameter fiber greater than 20 micrometers	4 to 12 micrometer diameter FG Insulation Fiberglas with binder	Ground for 0.5 minute, wet sieved through a 325-mesh sieve, washed twice to remove fines, collected on filter, and sieved to break up cake. Undersized removed by Bahco.
(2)	0.5 to 3.5 micrometer-diameter fiber greater than 10 micrometers long with binder	1 micrometer FM Series Air Filter Media with binder	Ground for 0.5 minute, wet sieved through 325-mesh sieve washed 4 times to remove fines, collected on filter, dried, and sieved to break up agglomerates. Both undersize and oversize fibers removed by Bahco.
(3)	less than 3.5 micrometer diameter fiber greater than 10 micrometers long	1 micrometer Tempstran Code 100/475	Ground for 1 minute, wet sieved through 325-mesh sieve, centrifuged and settled material removed and resuspended, centrifuged again (process repeated 4 times). Fiber collected on filter, dried, and sieved to break up agglomerates.
(4)	less than 3.5 micrometer fiber less 10 micrometers	1 micrometer Tempstran Code 100/475	Suspended material from centrifuge of above separation settled for 24 hours. Settled fraction resuspended and filtered, dried, and sieved to break up agglomerates.

abrasive and impact resistant polyurethane produced the best results, however. Various combinations of grinding media were tried including steel balls, rubber covered steel balls, porcelain balls, and plastic rings and slugs. The steel or porcelain balls produced a 50 to 60 percent yield of the required size fraction in about 1 minute. The other media produced poor yields of usable fibers with 3 to 10 minutes of grinding. Several test grinds were made with polyurethane lined mills and the fibers appeared satisfactory.

However, before changing the grinding procedure to use the higher capacity planetary mills, a series of test grinds was run to compare the fibers made with the planetary mill with the fibers made with the Willy Bleuler mill as follows:

Type of Glass Fiber	Type of Grinder	Weight of Sample, gms *
FG Insulation Fiberglas	Planetary Mill	100
FG Insulation Fiberglas	Willy Bleuler	25
FG Series Air Filter Media with binder	Planetary Mill	90
FG Series Air Filter Media with binder	Willy Bleuler	20
< 10 micrometer Tempstran 100/475	Planetary Mill	80
< 10 micrometer Tempstran 100/475	Willy Bleuler	15
> 10 micrometer Tempstran 100/475	Planetary Mill	80
> 10 micrometer Tempstran 100/475	Willy Bleuler	15

*Weight of two mill grinds

Because the large FG Insulation Fiberglas is the most abrasive fiber, the iron and polyurethane analyses were made only in the FG Insulation Fiberglas with the following results:

Grinder	Contamination, percent	
	Iron	Polyurethane
Planetary Mill	0.1	0
Willy Bleuler Mill	0.3	0

The iron contamination was measured with optical emission spectrography whereas the polyurethane analysis was made by IR. No evidence of urethane was detected with a sensitivity of about 1 percent. Iron contamination was lower in the fibers ground in the planetary mill than in fibers ground in the Willy Bleuler mill.

Tables 3 and 4 provide data comparing length distributions in the four fiber fractions made by the standard classification procedures following grinding in the Willy Bleuler mill or in the planetary mill. The size distributions essentially were equivalent and/or the mass distributions were satisfactory for use in the program by either method of grinding.

Comparisons of the contamination levels and length distributions in the fibers indicated that the products made by grinding in the planetary mill and Willy Bleuler mill were equivalent.

Production of fibers for the exposure program was began in October, 1980, following approval by NIOSH.

Quality Control

Quality of the fibers was characterized at each step of the production and each lot of fiber delivered to the animal facility was examined. If any discrepancy in the fiber size distribution was noted, the lot was rejected and another lot was sent for the inhalation studies.

Daily evaluations were performed with a Lietz optical microscope with a micrometer eyepiece for fiber measurement. Fibers were examined

TABLE 3. COMPARISON OF MASS DISTRIBUTION* IN FIBERS WITH BINDERS

Fiber Length, micrometers	Percent Mass Smaller Than Indicated Length			
	> 20-Micrometer Fiber		> 10-Micrometer Fiber	
	Planetary Mill	Willy Bleuler Mill	Planetary Mill	Willy Bleuler Mill
5.2	--	--	0.37	0.5
6.2	--	--	1.1	2.5
7.4	--	--	3.3	7.5
8.5	--	--	9.6	11.8
9.6	1.0	--	16.6	18.5
10.7	2.6	--	24.0	26.9
11.8	3.1	1.0	34.0	33.1
12.9	6.3	1.5	40.3	36.6
14.0	7.3	3.0	47.3	47.0
15.2	7.8	6.0	49.5	51.9
16.2	14.3	8.5	53.2	58.6
17.3	17.6	9.0	59.1	61.8
18.4	23.2	13.5	62.1	65.3
19.4	28.8	18.0	66.2	69.0
20.6	33.7	19.5	69.5	72.2
21.7	38.3	25.0	71.4	74.2
22.7	42.9	29.5	75.1	77.9
23.8	47.5	34.0	78.4	79.1
25.0	48.5	39.0	79.2	79.5
26.1	50.1	41.0	83.3	79.8
27.2	53.2	46.5	86.3	80.8
28.4	57.8	47.0	87.6	84.0
29.4	61.1	50.5	88.5	85.5
30.6	65.0	55.5	89.5	86.2
31.6	67.2	60.0	90.5	87.0
32.8	73.2	64.5	91.9	88.5
33.8	75.4	70.0	91.9	90.0
35.0	78.6	73.0	93.0	90.7
36.1	80.2	75.5	93.1	91.7
37.2	81.8	77.0	94.1	93.2
38.3	84.0	78.5	94.5	94.0
38.4	84.5	82.0	94.9	94.7
40.3	87.8	83.5	95.2	95.0
41.6	88.3	85.5	96.0	95.0
42.7	88.8	88.5	96.0	95.5
43.8	92.7	90.0	96.7	95.5
44.9	92.7	92.5	96.7	96.0
46.0	93.2	94.0	96.7	96.0
47.0	93.7	95.0	97.5	96.5
48.2	95.3	96.5	98.2	97.0
49.3	95.8	98.0	98.2	97.0
50.4	98.0	98.0	98.6	97.5
51.8	98.0	98.0	99.6	98.5
52.8	99.0	98.0	99.6	98.5
53.7	99.0	99.0	99.6	99.0
54.9	100.0	100.0	100.0	100.0

*Calculated from number distributions determined by counting 100 to 500 fibers.

TABLE 4. COMPARISON OF MASS DISTRIBUTION* IN FIBERS WITHOUT BINDERS

Percent Mass Smaller Than Indicated Length					
> 10-Micrometer Fiber			< 10-Micrometer Fiber		
Fiber Length, micrometers	Planetary Mill	Willy Bleuler Mill	Fiber Length, micrometers	Planetary Mill	Willy Bleuler Mill
4.6	--	0.7	1.96	3.8	5.5
5.0	--	1.4	2.15	10.0	9.9
5.4	--	2.8	2.33	11.3	14.6
5.8	1.3	5.6	2.52	20.0	20.1
6.1	2.6	7.7	2.70	31.3	30.2
6.5	6.6	11.3	2.89	38.8	39.0
6.9	7.9	15.5	3.07	46.3	46.1
7.2	10.2	21.3	3.26	47.5	47.7
7.6	15.5	23.4	3.44	56.3	56.2
8.0	22.1	27.6	3.62	62.5	61.7
8.4	24.7	32.6	3.80	68.8	68.3
8.7	28.7	38.4	4.00	72.5	72.3
9.1	32.3	42.0	4.18	76.3	75.6
9.5	35.9	47.6	4.54	77.5	76.7
9.8	41.3	49.0	4.73	81.3	81.1
10.0	43.9	52.6	4.91	83.8	84.4
11.0	49.4	57.7	5.10	90.0	89.9
12.0	54.0	59.7	5.30	91.0	91.0
12.4	59.3	60.4	5.50	92.5	92.1
12.8	61.9	64.0	5.65	93.7	93.2
13.1	63.2	67.6	6.00	95.2	95.4
13.5	64.5	70.4	6.20	96.5	96.6
13.9	67.1	71.1	6.60	97.7	97.7
14.2	68.4	73.2	7.12	99.0	98.9
14.6	69.7	74.6	9.10	100.0	100.0
15.0	71.0	74.6			
15.3	71.0	76.0			
15.7	72.1	77.4			
16.1	73.7	77.4			
16.4	77.7	79.5			
16.8	77.7	80.2			
17.2	83.0	81.6			
17.6	83.0	83.7			
17.9	85.6	85.8			
18.3	92.2	89.3			
19.5	93.5	89.3			
20.6	94.1	90.0			
21.7	95.4	90.7			
22.8	96.7	91.4			
23.9	98.0	92.8			
25.1	--	93.5			
26.2	--	93.5			
29.5	--	94.2			
31.7	99.3	94.9			
33.9	--	95.6			
38.3	100.0	97.0			
39.4	--	98.4			
40.5	--	98.4			
41.6	--	100.0			

*Calculated from number distributions determined by counting 100 to 500 fibers.

at 100, 500, and 1000X. The fibers were commercial production products, and variations in the diameters were noted early in the program. Classification to reduce the amount of oversize diameter fibers usually was successful, but the fiber diameters were variable. Some lots of fibers were rejected because the diameters did not meet the specifications. Figures 6 - 9 are 800X photographs of several typical lots of glass fiber fractions supplied to the animal laboratory for inhalation exposures.

During the program, fiber counts were made on several lots of production fibers using the Lietz optical microscope or a scanning electron microscope. The fibers were photographed and measured with an optical digital analyzer.

Archive lots were retained on a daily basis throughout the program. At the end of the exposure program, randomly selected samples of fibers were examined. The selected samples were used in the exposure program during the period from November 26, 1980, to December 19, 1980. Approximately 200 to 216 fibers were measured on photographs taken under magnification at 500X, and the mass distributions were calculated.

Data in Table 5, which summarize the measurements shown in Tables 6 - 9, indicate that approximately 91 to 99 percent of each type of fiber by weight was in the required size range. The target was a minimum of 80 percent by mass in the desired size range. Thus, the quality of the fibers was satisfactory.

Tables 10 - 13 give particle size distributions made from SEM photographs of other lots of fiber which were used in the four chambers. Figures 11 - 14 are three-dimensional plots of this data.

TABLE 5. MASS OF FIBERS IN REQUIRED CATEGORY

Group	Fiber	Date Used	Cut Point, micrometers	Percent Mass in Required Size Range
1	4 to 6 micrometer diameter fiber > 20 micrometer long with binder	11/26/80	> 20	97.1
2	0.5 to 3.5 micrometer diameter fiber > 10 micrometer long	12/10/80	> 10	99.4
3	< 3.5 micrometer diameter fiber > 10 micrometer long	12/19/80	> 10	96.5
4	< 3.5 micrometer diameter fiber < 10 micrometer long	12/19/80	< 10	91.1

Micrometers	Cumulative Mass, percent Lot A	Lot B
12.5	0.1	0.2
15.0	0.5	0.5
17.5	0.9	3.6
20.0	2.9	5.4
22.5		7.5
24.0	4.6	8.4
25.0	7.5	11.8
27.5		11.9
30.0	12.2	12.3
32.5		17.6
35.0	18.6	18.5
37.5	19.2	23.5
40.0	23.2	24.8
42.5	23.6	29.4
45.0	24.1	32.9
47.5	36.4	33.3
50.0	40.6	37.7
52.5		41.4
55.0	46.6	47.2
60.0	49.6	48.4
65.0	53.4	51.5
70.0	57.4	56.3
72.5	58.7	64.7
75.0	61.8	76.5
80.0	65.1	88.8
85.0	66.6	
87.5	68.0	94.1
90.0	71.2	
100.0	75.0	
110.0	76.8	100.0
120.0	81.7	
125.0	86.9	
140.0	92.5	
155.0	95.1	
175.0	96.5	
220.0	100.0	

TABLE 7. MASS DISTRIBUTION OF CHAMBER 2 FIBERS.

Micrometers	Cumulative Mass, percent Lot A	Lot B
5.4	0.7	0.4
7.25	1.2	1.6
9.0	4.9	3.5
10.2	6.4	5.5
10.6	11.4	8.6
11.7	12.4	11.1
12.1	14.4	19.4
13.1	19.2	22.0
13.9	21.0	25.3
15.0	28.9	28.0
16.0	34.8	33.7
18.0	35.4	37.7
22.0	41.8	43.2
24.0	47.6	49.0
25.0	48.6	51.6
26.3	51.3	53.8
27.5	54.7	56.2
28.4	55.9	59.7
30.0	59.1	62.2
31.3	63.2	66.8
32.5	71.4	74.3
34.0	76.1	79.8
35.0	82.8	86.5
38.3	88.5	87.4
38.8	91.0	88.2
40.0	92.3	91.2
42.7	93.8	94.8
45.0	96.7	95.9
51.0	98.3	98.4
58.0	100.0	99.2
66.0		100.0

TABLE 8. MASS DISTRIBUTION OF CHAMBER 3 FIBERS.

Micrometers	Cumulative Mass, percent Lot A	Lot B
8.0		1.0
10.0	1.5	3.5
11.0	5.2	
12.0	8.2	6.3
14.0	12.5	10.5
16.0	18.2	15.0
20.0	27.5	21.7
22.0	29.7	
23.0	35.2	26.0
24.0	38.3	30.3
26.0	40.3	36.2
28.0	45.3	40.2
30.0	47.4	42.9
33.0	51.2	48.7
36.0	59.7	54.3
40.0	63.3	59.8
46.0	69.9	66.8
51.0	77.6	72.1
54.0	81.2	74.9
58.0	85.3	78.0
62.0	88.7	80.1
66.0	91.2	82.5
72.0	95.3	86.2
82.0	97.7	89.0
86.0	100.0	92.0
112.0		95.6
124.0		100.0

TABLE 9. MASS DISTRIBUTION OF CHAMBER 4 FIBERS.

Micrometers	Cumulative Mass, percent Lot A	Lot B
1.9	3.8	
2.15	10.1	
2.33	11.3	
2.46		2.8
2.52	20.1	
2.70	31.3	
2.83		7.0
2.89	38.8	
3.07	46.3	
3.20		11.3
3.26	47.5	
3.44	56.2	
3.56		16.9
3.62	62.5	
3.8	68.7	
3.9		22.5
4.0	72.4	
4.2	76.1	
4.3		36.6
4.5	77.3	
4.69		45.0
4.73	81.1	
4.91	83.6	
5.04		54.9
5.1	89.8	
5.3	91.0	
5.4		63.4
5.5	92.3	
5.65	93.5	
5.8		67.6
6.0	94.7	
6.2	97.2	76.1
6.6	98.5	83.1
6.87		84.5
7.2	99.7	87.3
7.6		90.1
8.35		93.0
8.7		94.4
9.0	100.0	95.8
9.82		97.2
12.75		98.6
18.27		100.0

TABLE 10. PARTICLE SIZE DISTRIBUTION OF BULK GLASS FIBERS USED IN CHAMBER 1*.

Length µm	Diameter - µm											
	3.3	5.0	6.7	8.3	10.0	11.7	13.3	15.0	16.7	18.3	20.0	21.6
20		1										
23.3			1									
30			1									
31.6	1											
33.3					1							
36.3				1	1							
40	1		3		1							
43.3				1		1						
46.6				1			1					
50			1		1	1			1			
53.3				1								
56.6							3		1			
60						2	3		1		1	
63.3				1					1			
70			1						3			
73.3				1		1			1		1	
76.6			1					1				
80									1		1	
83.3					2	1		1	1			
86.6					1		1		1			
90					1			1	1			
93.2									1			
96.6					1		2					
100						1	1		1		2	
103.2							1					
106.6					1				2	1		
110									2			
113.2							1					
116.6							1	2	2			
133.2				1								1
139.9				1			2					
143.2					1		2					
149.9						1					1	
163.2							1		1			
166.5							1					
173.2				1					1			
183.2						1						
200									1			
216.5						1						
223.1					1							
229.8						1						
296.4										1		

* 4 to 6 µm diameter > 20 µm long with binder.

TABLE 11. PARTICLE SIZE DISTRIBUTION OF BULK GLASS FIBERS USED IN CHAMBER 2*.

Length µm	Diameter - µm 0.5	1.0	1.5	2.0	2.5	3.0	3.5
3	1	1					
4		5					
5		3					
6		1	4	3			
7	1	1	1	3			
8		3	1	2	1		
9		3	3	1			
10		2	1	1		1	
11			3	3		1	
12		1	1	3			
13		2	1	1		1	
14		1			1		
15		2	1	2			
16		1	1		2		
17		2		1		1	
18		1	1			1	
19		2			1		
20							1
21		2	2	1	1		
22				2			
23		1		1			
24			1	1			
25			2				
30				1			
43				1			
49							1
68						1	
93					1		

* 0.5 to 3.5 µm diameter > 10 µm long with binder.

TABLE 12. PARTICLE SIZE DISTRIBUTION OF BULK GLASS FIBERS USED IN CHAMBER 3*.

Length µm	Diameter -µm 0.5	1.0	1.5	2.0	2.5	3.0
3		1				
3.5		1				
4	3	3				
4.5			1			
5		2	2			
6		2	2	1		
7		1	2			
8		1	3	2		
9			2	2	2	
10			4	1		
11			5	3		
12		1	3	3	1	
13				1	1	2
14		4	1			
15		2	5	1		
16			2	2	1	
17		1		1		
18			1	2		
19			2			
20		2				
24						1
25						1
26	1		1			
27				1		1
29			1			
30				1		
31		1	1	1		
39				2		
42						1
57					1	

* < 3.5 µm diameter > 10 µm long no binder.

TABLE 13. PARTICLE SIZE DISTRIBUTION OF BULK GLASS FIBERS USED IN CHAMBER 4*.

Length µm	Diameter - µm 0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.4
.6		1									
.7		1	1								
.8		3			1						
.9	1	3		1							
1.0		8	7	3							
1.1			1								
1.2		5	6	4	2		1				
1.3											
1.4		6	6			1				1	
1.5			1								
1.6		3	3	5	4	1					
1.7		1			1						
1.8		2	5	4		2	2				
2.0		4	6	5	2	3		2			
2.5		4	1	4		3	1	1	1		
3.0		4	1	5	4	2	2				
3.5		2	2	1		1		1	1		
4.0		2	3	1	2	2	2	1			
4.5		1			2	1					
5.0				2	1						
6.0		1	1	1	1		1				
7.0		1		1	1			1			
8.0			1	1		1				1	
9.0								1			1
.0				1	1						
1.0				1				1			
2.0											
3.0		2									

*< 3.5 µm diameter < 10 µm long no binder.

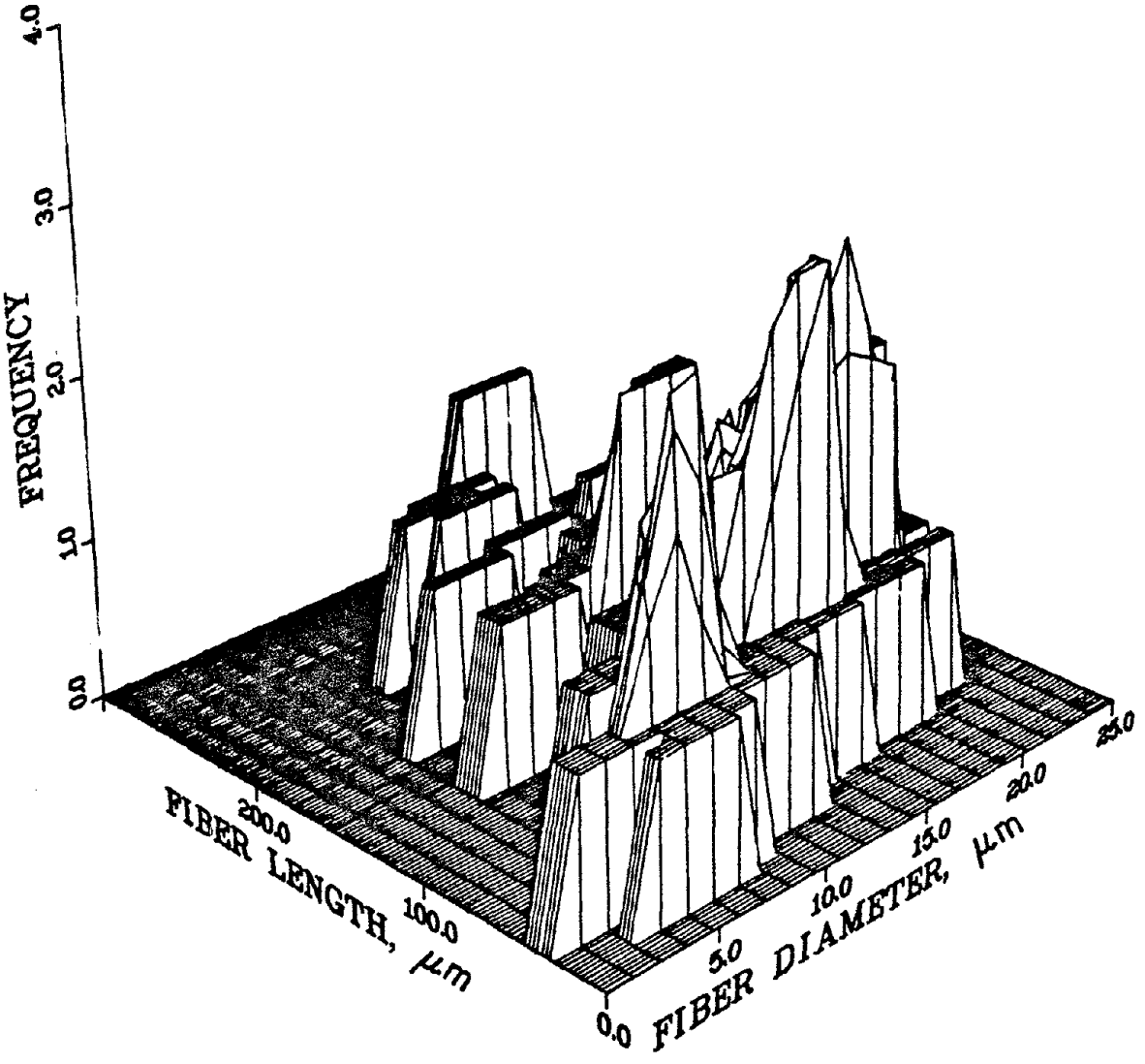

FIGURE 11. SIZE DISTRIBUTION OF GLASS FIBERS USED IN CHAMBER 1.

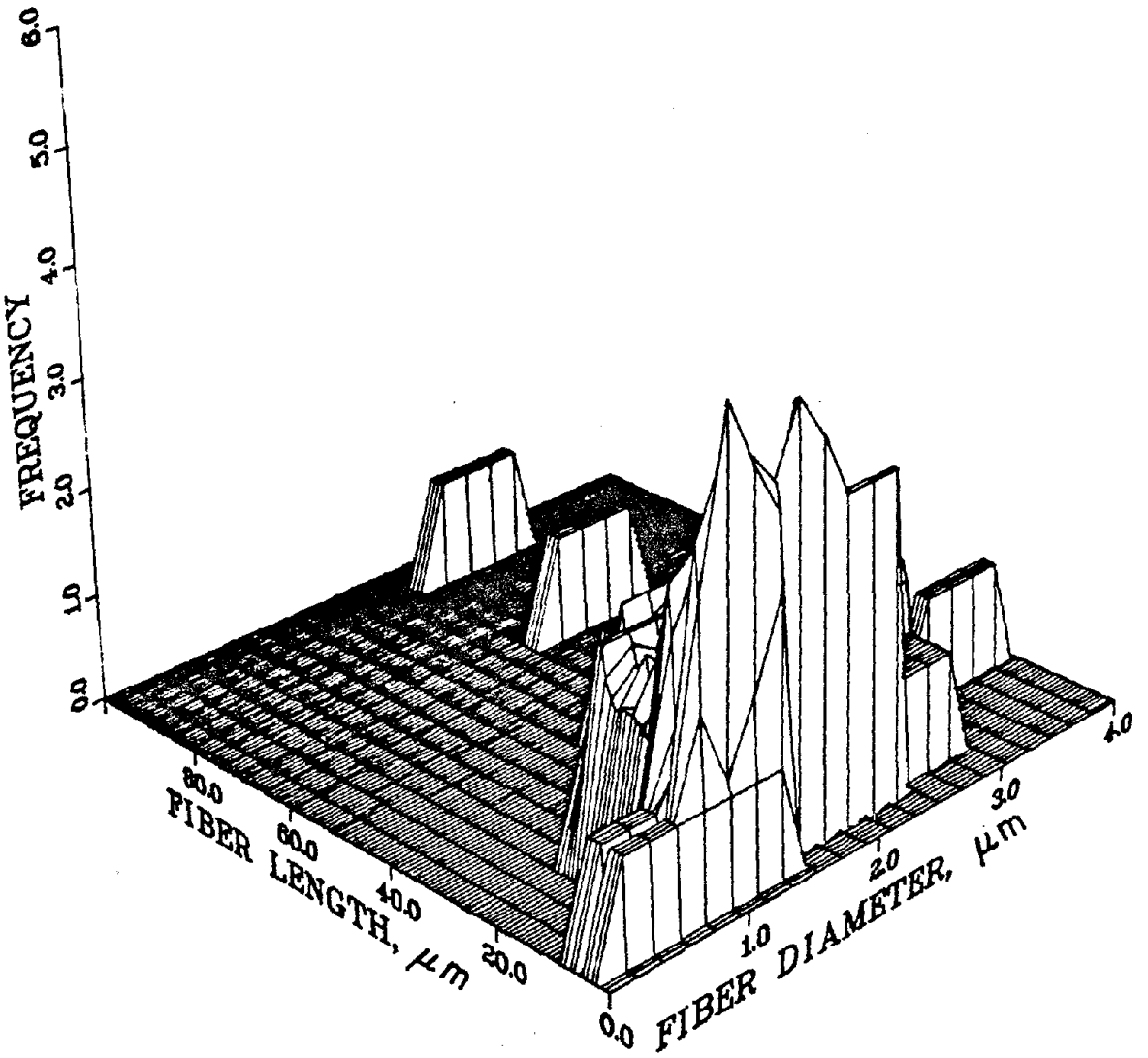

FIGURE 12. SIZE DISTRIBUTION OF GLASS FIBERS USED IN CHAMBER 2.

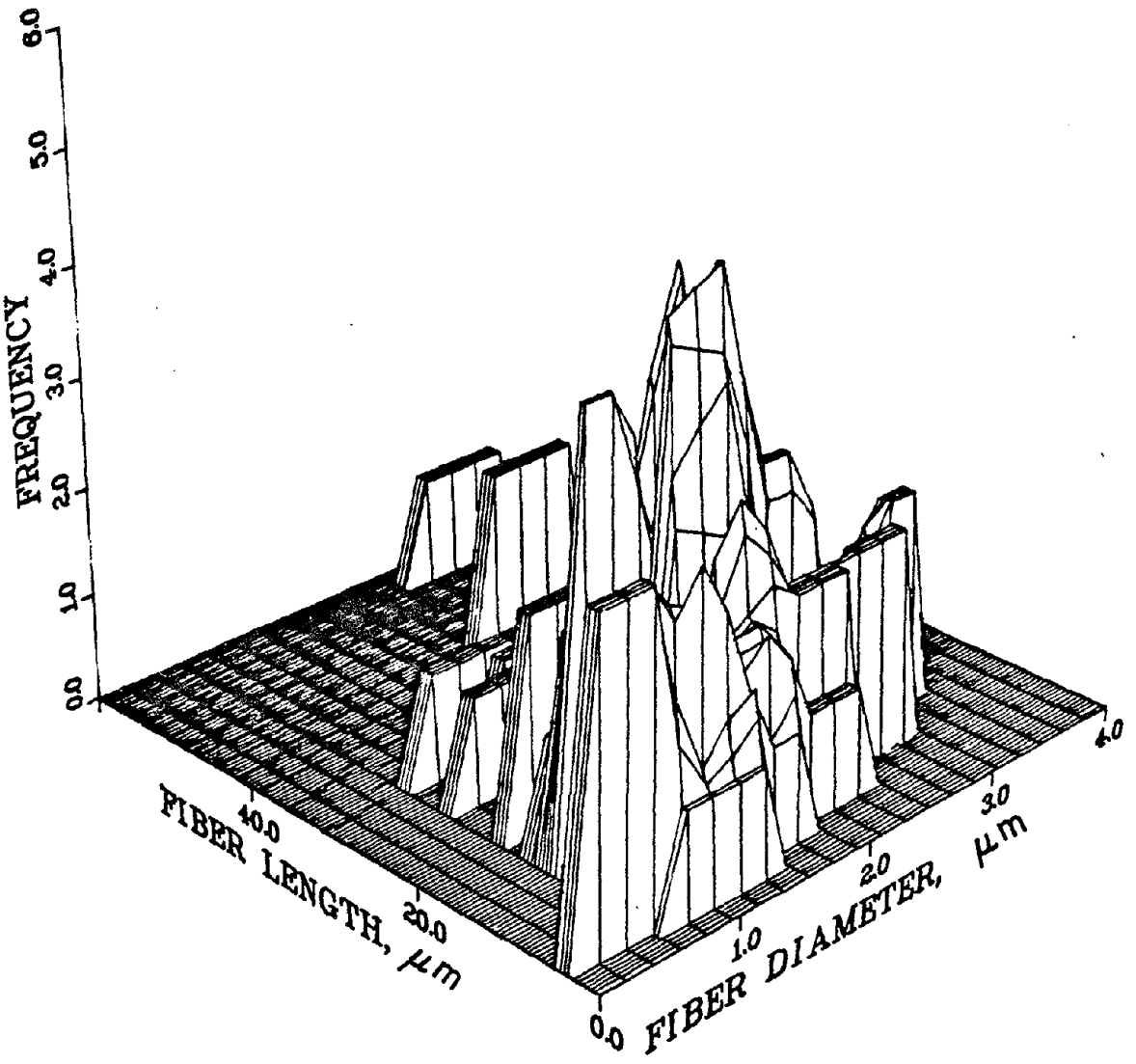

FIGURE 13. SIZE DISTRIBUTION OF GLASS FIBERS USED IN CHAMBER 3.

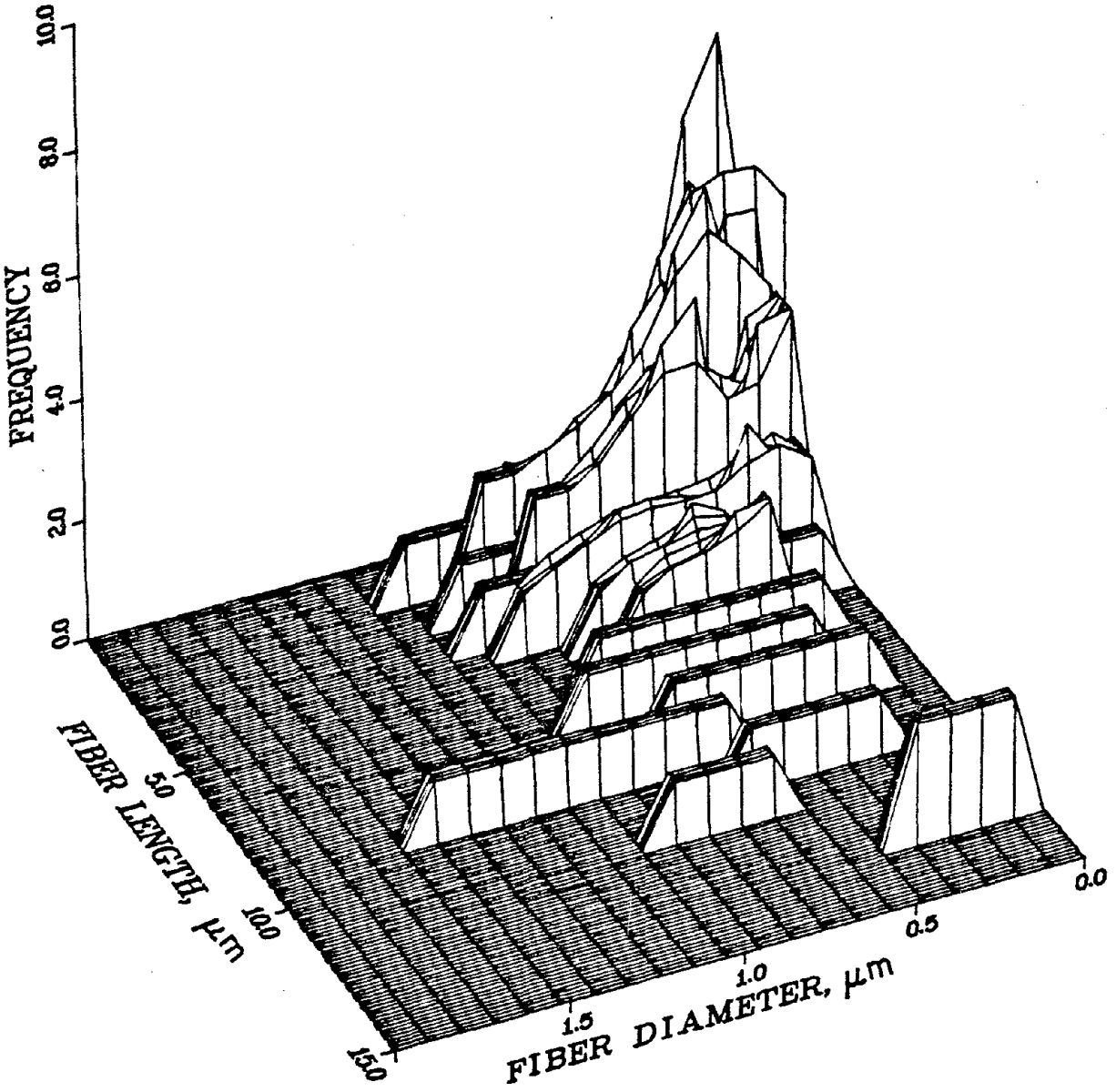

FIGURE 14. SIZE DISTRIBUTION OF GLASS FIBERS USED IN CHAMBER 4.

Fiber Aerosol Generation

Each type of glass fiber was unique in handling characteristics and aerosols ultimately were generated in a manner best suited for each type of fiber. Basically, the generation system consisted of a metering device, a dispersing mechanism, and a delivery system.

Various feeders were considered at the beginning of the program and a bead chain design initially was selected as the best method of providing the required low feed rates. The fibers were dispersed with an air venturi and delivered via a 1/2-inch diameter Tygon tube to the center of the air circulation inlet duct in the cupolas of the chambers. Problems immediately developed in achieving the desired concentrations in the chambers, especially in Chambers 1 and 2 where the higher concentrations of fibers with binders were required. Much of the problem resulted from static charge on the fibers that caused the fibers to deposit on the walls of the delivery tubes and on the walls at the entrance of the cupolas. Feed rates of 7 to 10 times the theoretical rates were necessary to achieve the required concentrations. Radioactive and corona-type static eliminators were installed to reduce the charge on the fibers but the use of static eliminators was discontinued because of possible secondary effects that the radiation, ozone, and ions might have had on the test animals.

The bead chain feeders in Chambers 1 and 2 were replaced with two-fluid atomizers on May 4, 1979. Dispersions of 20 grams of fiber per 100 ml of water were sprayed in short pulses followed by an evaporation period with no significant increase in relative humidity in the chambers.

Wear on the bead chain feeders in Chambers 3 and 4 required increasing operator attention as the study proceeded, and on January 31, 1980, the bead chain feeders were replaced with improved rotary platform feeders. The performance of these feeders was excellent, and the two-fluid atomizer on Chamber 2 subsequently was also replaced with a rotary platform feeder on June 11, 1980, with a reduction in the use of material and need for operator attention. Although the rotary platform feeder also worked on the fiber used in Chamber 1, material requirements were about the same; consequently, the spray system was not changed on Chamber 1.

Bead Chain Feeder

The bead chain feeder design was based on the bead chain meter system described by Marple et al.[32] A venturi aspirator dispersing system was incorporated to avoid loss of fibers in the fluidized granular bed used with the Marple unit.

After several modifications, the design for the fiber aerosol generator was finalized as shown in Figure 15. A bead chain feeds the fibers from the bottom of a conical supply chamber to a venturi aspirator which disperses and fluidizes the fibers. The fluidized fibers are passed through a small cyclone which contains a few 300 to 400 micrometer glass beads or 0.15 cm steel balls to break up or remove agglomerates before passing to the exposure chamber. A 0.3 cm diameter plastic bead chain was used originally; however, it was replaced with a similar metal chain because the plastic chain was too stiff and the end splices failed.

The hopper was vibrated to make the fiber flow into the bead chain reliably. Other approaches, such as mixing the fiber with fine carrier beads, were also tried and discarded. In the fiber bead approach, the carrier beads were collected in the cylcone for reuse. However, metal carrier beads bound in the Teflon lining around the feed tube and the fibers would not mix with glass beads unless the beads were resin coated. The coating on the glass beads deteriorated rapidly in the cylcone. A metal cyclone was used originally and the glass fiber stuck on the metal. Subsequently, the metal cyclone was replaced with a glass cyclone.

Water Spray System

To overcome static charge problems produced by the mechanical methods of feeding the fibers with binders, a system for spraying a water dispersion of fibers was developed for use in Chambers 1 and 2.

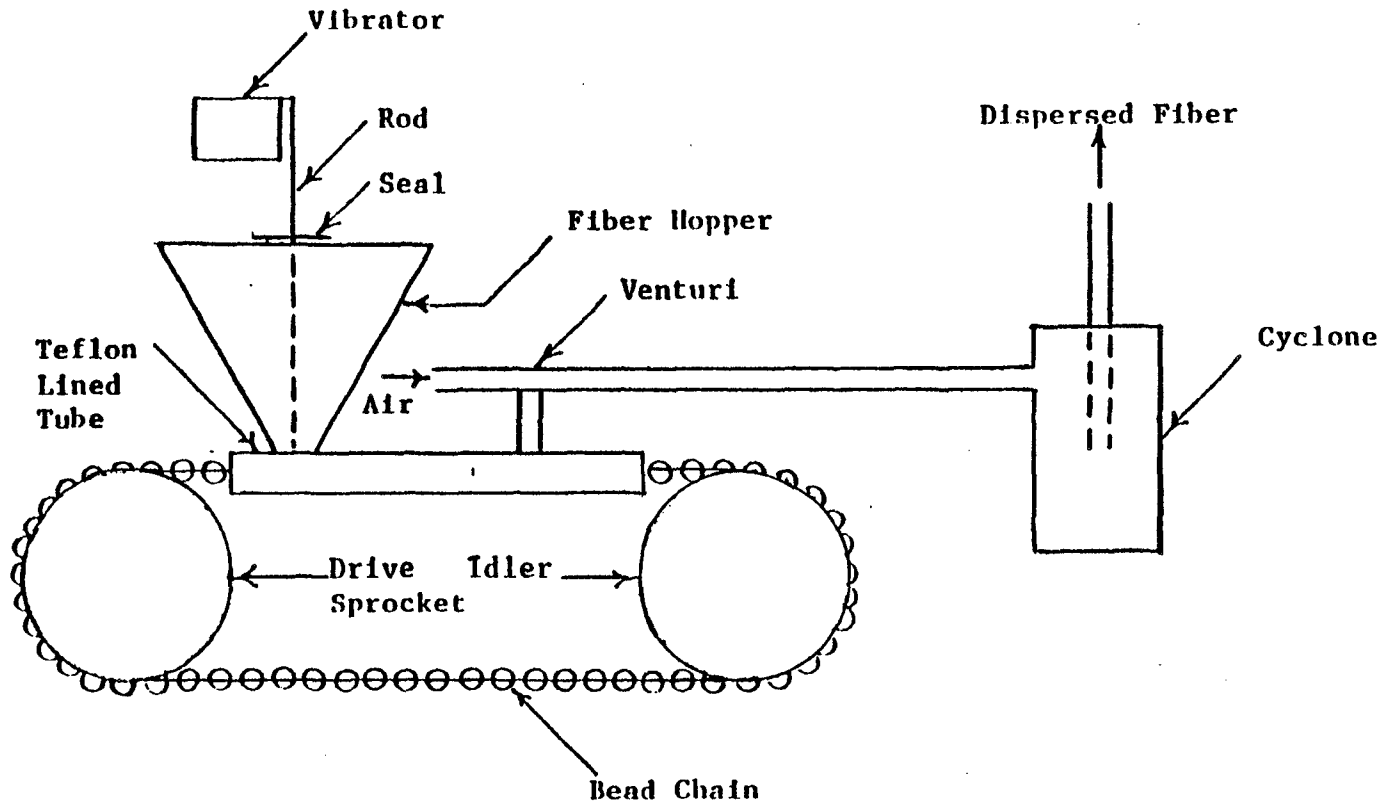

FIGURE 15. AEROSOL GENERATOR

Several spray systems and a nebulizer were tested before selecting a pulsed-type two-fluid atomizer with a cleaning system to prevent plugging of the nozzle.

The atomizer was a Spraying System Company's two-fluid atomizer with a No. 64 air nozzle and No. 1250 fluid body. Each sprayer was equipped with a No. 11829 Clean Out Needle Attachment operated with a solenoid on a cycle timed with the spray pulse. The sprayers operated with a siphon head drawing the fiber dispersion from a 600 ml reservoir below the sprayers. The fiber dispersion was agitated constantly with a magnetic stirrer to keep the fibers in suspension. The sprayers were located in the upper center of the chambers with the nozzles pointed toward the top of the chamber. Initially, the air was circulated with a fan in the top of the chambers to level out the fiber concentration in the chambers, but the use of the fan was discontinued as unnecessary after extensive studies were made of the fiber distribution in the chambers. Fiber concentration in the dispersion, air pressure, liquid flow rate, and pulse rate were adjusted to achieve the desired fiber concentration in the chamber with a minimum amount of water and fiber. Sufficient dilution of the dispersion avoided spraying groups of fibers in individual drops that form agglomerates when the water evaporates. At the same time, the amount of water sprayed was low enough that it did not raise the relative humidity in the exposure chamber more than 2 percent. The required concentrations of 15 mg/m^3 were achieved by spraying a dispersion of about 0.05 grams of fibers per ml of water with about 0.4 ml of Tween 80 dispersing agent per 100 ml of water to suspend the fibers. The sprayer system was operated by a timer that provided seperate control of the spray period from 1 to 10 seconds at 1 to 30 cycles per minute whereas the clean out needle was cycled for 1 second at 1, 2, 4, or 8 times per minute as needed.

Rotary Platform Feeder

By the end of the exposure program, rotary platform feeders such as shown in Figures 16 and 17 were used in Chambers 2, 3, and 4. The feeder consists of a 3 inch diameter by 6 inch cylindrical hopper positioned

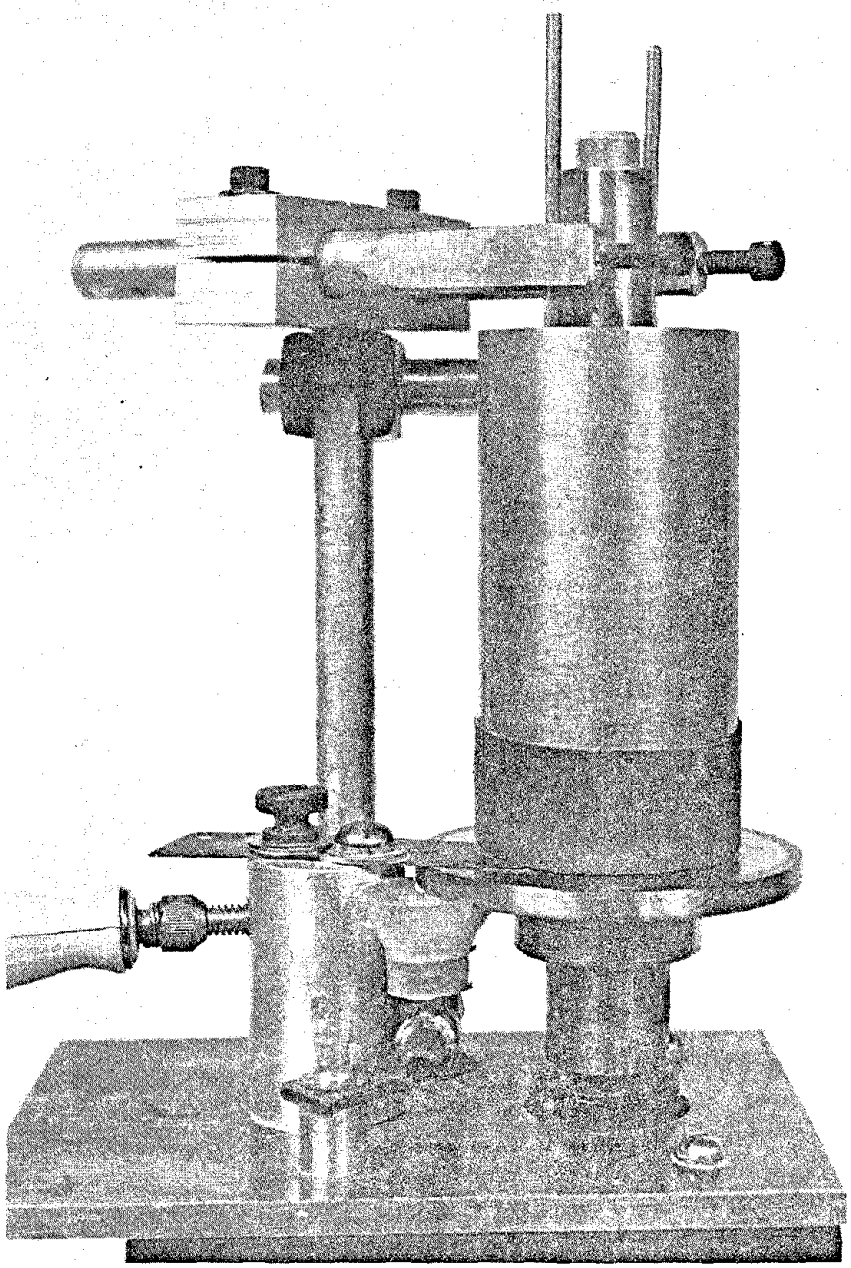

FIGURE 16. ROTARY PLATFORM FEEDER

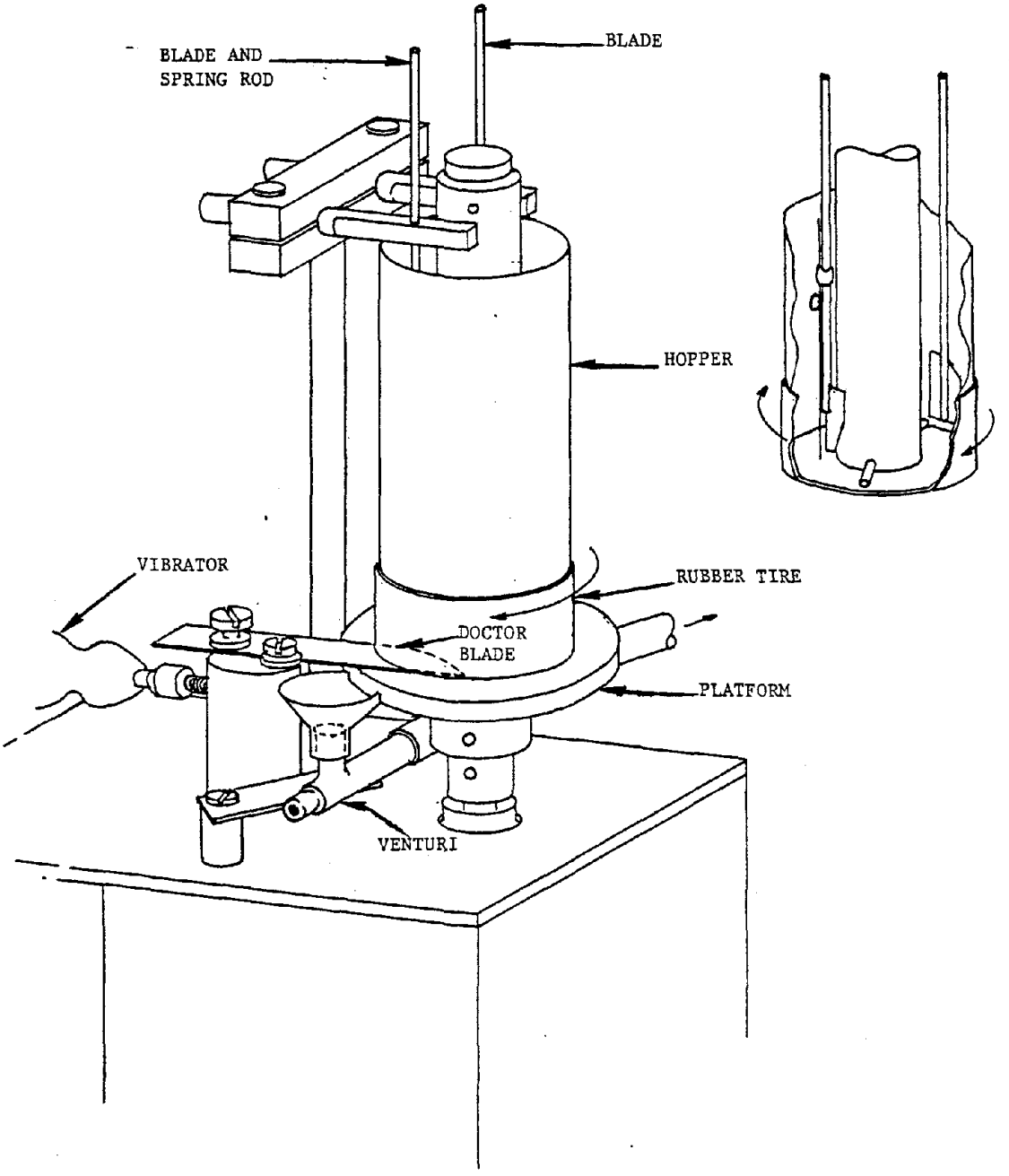

FIGURE 17. DETAILS OF ROTARY PLATFORM FEEDER

above a flat disc-shaped platform. As the cylinder and platform rotate, a thin ribbon of fiber is sliced out of the bottom of the hopper and moves along the edge of a doctor blade that is inserted between the platform and the cylinder. The gap between the hopper and the platform is covered by a rubber tube to prevent leakage of fiber except along the blade. The fiber eventually drops off the edge of the platform into a small funnel where the fiber is aspirated into an air venturi that disperses the fibers and injects the fiber through a 1/2-inch diameter Tygon tube to the inlet of the exposure chamber.

As the feeder rotates, two stirring blades and a spring rod inside the hopper stir the fiber to prevent bridging and move the fiber away from the center post and inner wall of the tube. The doctor blade was vibrated continuously with a small electric vibrator mounted on the doctor blade base.

The feeders were driven with Bodine* Model 533 motors and Bodine* D-C Motor BSH-200 Speed Controls.

Problems

With the bead chain feeders mounted outside the chambers, the required aerosol concentrations of 5 mg/m^3 and 15 mg/m^3 were achieved initially with chain speeds of 1-1/2 beads per minute and 5 beads per minute, respectively. However, the concentration dropped gradually in subsequent tests. Fiber accumulated in the 1/4-inch diameter Tygon tubing between the cyclone and the chamber and gradually slowed the airflow to the point that the aspirator did not pick up all of the fiber from the beads. To correct this problem, the venturi orifice was enlarged to pump more air through the cyclone and Tygon tube, but fiber disposition continued to be a problem.

In all the chambers, 5 to 10 times the calculated amount of fiber was required to achieve the fiber concentration desired in the chambers. Significant charge levels were detected in the chambers with an electrometer probe and large amounts of fiber were deposited on the walls at the entrance to the chamber. Various approaches were tried to stop the deposition including (1) lining the upper portion of the chamber with 10-mil Mylar to build a charge layer that should eventually repel additional charged fiber, (2) passing the

* Made by Bodine Electric Company , Chicago, Illinois 60618

fiber through a tube lined with a 10-millicurie radioactive source to produce ions to neutralize the charge on the fiber, and (3) discharging the fiber at the inlet with ions produced by AC or opposite polarity DC corona from a needle-type ionizer. Although the charge level in the chamber was reduced to zero at times, the fibers with binders still deposited on the walls at the entrance of Chambers 1 and 2.

The feeding problem was especially severe in Chamber 1 where the 4 to 6 micrometer diameter fiber greater than 20 micrometers long was used. Excessively high feed rates were necessary to achieve the desired concentration and the composition of the fiber shifted in the chamber. Static charge apparently deposited the long fibers on the chamber walls in the entrance area. Radioactive and AC and DC corona-type static eliminators were used to neutralize the charge on the fibers but the wall deposition continued. Because the extremely strong radioactive eliminators or high levels of corona that appeared to be necessary might alter the exposure environment, the use of a mechanical-pneumatic feed system was discontinued on Chamber 1 as well as on Chamber 2 where the problem also occurred. The bead chain feeders were replaced with two fluid atomizers mounted inside Chambers 1 and 2. The atomizers were positioned vertically upward and at a level so that the spray fan formed fully before reaching the cupola of the chamber where the fibers were mixed with the fresh air coming into the chamber. Although fiber deposition on the walls in and around the walls of the cupola was significant, the fiber length distribution delivered to the chamber did not shift and the fiber deposition was compensated by increasing the spray rate accordingly. Fiber was recovered from the walls and reprocessed for reuse.

The sprayer systems required frequent operator attention. The fiber delivery rate varied with the siphon height as the level in the feed reservoir dropped during the daily exposure period. The spray period and number of cycles were adjusted frequently each day. The large glass fibers caused extensive wear of the nozzles and clean out needles. Whenever the clean out needles jammed or broke, the large fibers quickly plugged the nozzles.

In contrast, the rotary platform feeders were very reliable and required a minimum amount of operator attention. Rarely, one of the spring stirring rods broke but no other maintenance was required. Speed adjustments

Factors such as moisture content of the fiber as supplied and moisture pickup on the fiber during handling of fibers were considered as possible causes of feed rate variation. Although low moisture content caused problems with static electricity, high moisture content also appeared to cause the fibers to agglomerate in the feeders. These problems were not significant at the normal relative humidity in the exposure area. The fibers were transported and stored in glass jars with the lids tightly closed to maintain their condition in the fiber production operation and to avoid accidental moisture pickup or loss before use.

Exposure Groups

The study involved five groups of animals, including four exposure groups and a control group. The exposures were conducted in 5.4 m^3 chambers with air circulation of 1 m^3/min. Exposure conditions were as follows:

Chamber	Fiber	Concentration, mg/m^3
1	4 to 6 micrometer glass fiber >20 micrometer long with red binder	15
2	0.5 to 3.5 micrometer glass fiber >10 micrometer long with yellow binder	15
3	<3.5-micrometer glass fiber >10 micrometer long	5
4	<3.5-micrometer glass fiber <10 micrometer long	5
5	Control	0

Exposures of rats began in all chambers on March 12, 1979. Exposures of monkeys were delayed until the correct exposure concentrations had been maintained in the chambers for 5 consecutive days. Exposures of the monkeys were initiated at weekly intervals during June and July. Exposure of the last test group started on July 17, 1979. The exposure conditions were approved by NIOSH before the monkeys were put in the chambers.

Exposures of the monkeys were initiated on the following schedule:

Group	Chamber	Starting Date
V	5	6-19-79
IV	4	6-26-79
III	3	7-03-79
I	1	7-10-79
II	2	7-17-79

The temperature in the exposure area and chambers was maintained at 68.8 $\pm$ 1.9° F and the relative humidity at 50 $\pm$ 6 percent throughout the exposure period.

Chamber Monitoring

Aerosol quality was monitored in each chamber at least twice daily by mass samples drawn at 10 ℓ/m and collected on 0.45 micrometer Metricel DM450 filters in 47 mm Gelman holders*. Uniformity of the aerosol was sampled at various locations within the chambers with the mass samplers and with a Sinclair Phoenix photometer. Mass distribution in each chamber also was measured with a cascade impactor once each week. Samples were collected from the chambers with electrostatic samplers of various types. Size distribution in the material collected was examined periodically by observation under 350 to 500 X magnification.

Mass samples were taken with open faced 47 mm Gelman* filter holders which were mounted on 1/4-inch diameter steel tubing so that the samples could be inserted through ports in the front of the chambers on each side of the doors and held in various positions from the front to the rear of the chambers. Air was drawn through the filters with vacuum pumps, and flow was controlled with critical flow orifices. Initially, silver membrane filters were used, but the samples collected on the high density filters created a pressure drop which occasionally affected the critical flow conditions during the 30 minute sampling period. Although the high density filters appeared to be satisfactory for 15 minute sampling periods, a change was made to Metricel DM450 filters

which were satisfactory for 30 minute sampling periods. The filters were moisture conditioned and weighed with a Metler 52 microbalance* under constant humidity conditions in the animal facility. The filters were weighed by a procedure that provided a weighted average precision of about 27 micrograms.** The sampling rates were checked periodically with a wet test meter.*** Table 14 lists the actual flow rate of the sampling orifices.

Before the animal exposures were begun, uniformity of the fiber concentration in the chambers was measured by sampling at various positions along each side of the chamber and over the animal cages in the chambers. Samples were taken at the front, center, and back of the chamber at the level of the upper animal cages and the level of the lower animal cages.

Size distribution of the fibers in each of the exposure chambers was measured at least once a week with a cascade impactor**** shown in Figure 18. The impactor was placed inside the chambers and chamber air was drawn through the impactor with a vacuum pump at a rate of 1 cfm for 30 minutes. Theoretically, the cascade compactor should be capable of measuring the aerodynamic characteristics of a fiber glass aerosol. (See Appendix F for a discussion of inertial characteristics of fibers.) This capability was verified by measuring fibers collected on three successive stages of a well calibrated specially designed Battelle impactor from Chamber 2. Tables 15 through 17 list the measured diameter and length, fiber aspect ratio, and calculated impactions equivalent diameter for each fiber size. The particle size distribution based on impaction equivalent diameters is shown in Figure 19. This plot shows that the cut-off sizes***** for the stages are 6.6 and 3.5 μm as compared to 5.7 and 2.8 μm for spheres with a density of 2.0. The fibers for these chambers were covered with a yellow phenol formaldehyde coating and depending upon the thickness of the coating could have

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* Metler Instrument Corporation, Highstown, New Jersey 08520.

** See Appendix E.

*** GCA Precision Scientifics, Chicago, Illinois.

**** Special Battelle Cascade Impactor

***** Particle diameter for which 50 percent will impact on given stage and 50 percent will pass around to succeeding stage

TABLE 14. ACTUAL FLOW RATE OF SAMPLING ORIFICES

Chamber	Flow Rate CFM	Flow Rate ℓ/m
1	0.354	10.02
2	0.354	10.02
3	0.361	10.22
4	0.358	10.13

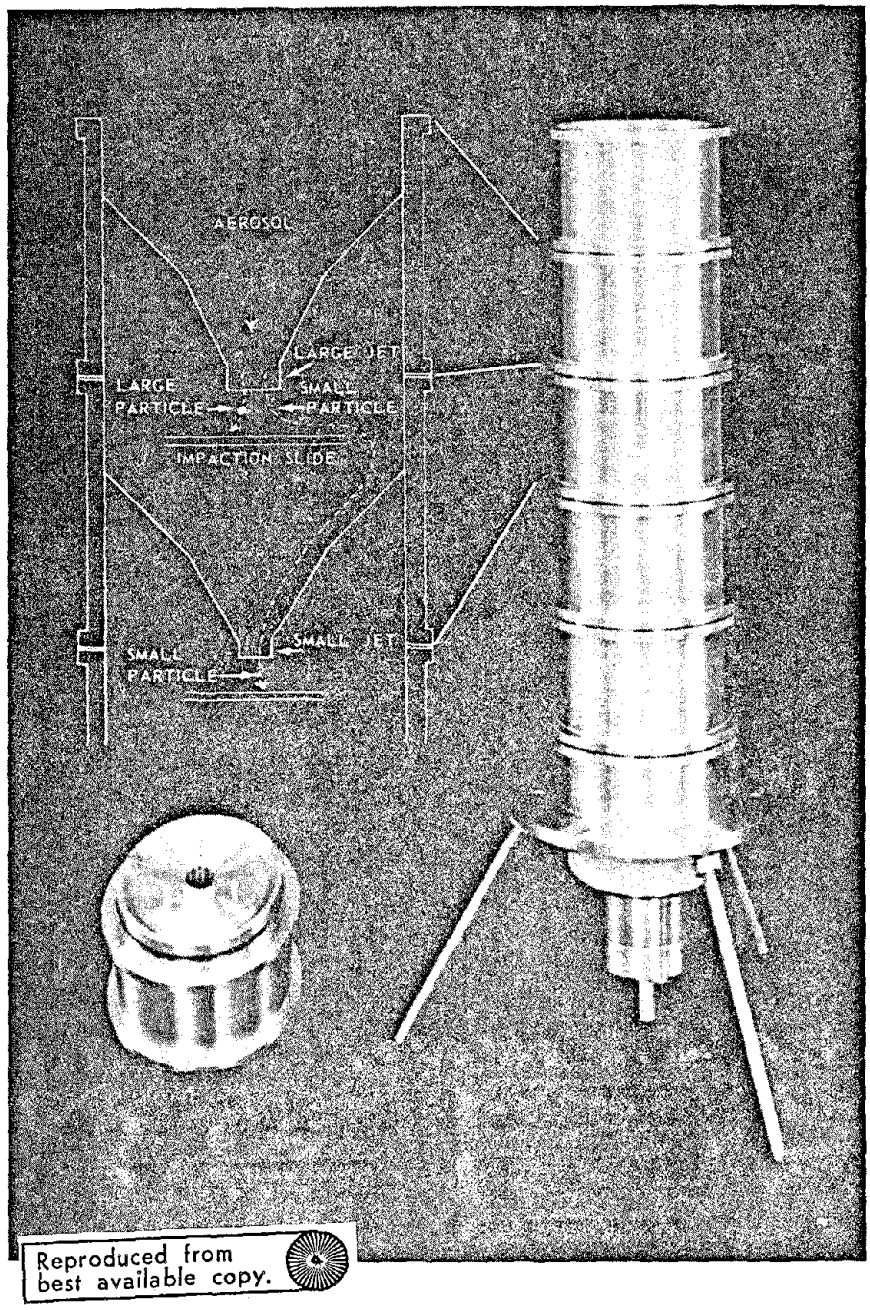

FIGURE 18. PHOTOGRAPH OF CASCADE IMPACTOR

TABLE 15. PARTICLE SIZE DISTRIBUTION OF FIBERS COLLECTED ON STAGE 2 OF CASCADE IMPACTOR FROM CHAMBER 2.*

NO. OF FIBERS	L μm	W μm	β	D_{IE/D_f}	D_{IE} μm
34	3.21	3.21	1	1.5	4.8
16	3.21	1.60	2	1.7	2.7
19	6.42	3.21	2	1.7	5.4
15	6.42	1.6	4	2.2	3.52
32	9.63	3.21	3	2.0	6.4
16	=	1.6	6	2.4	3.84
11	12.84	4.81	3	2.0	9.63
16	=	3.21	4	2.2	7.17
7	=	1.6	8	2.7	4.32
17	16.05	3.21	5	2.3	7.36
3	=	1.6	10	2.9	4.64
1	=	4.81	3.3	2.1	10.08
1	19.26	1.60	12	3.1	4.96
5	=	3.21	6	2.4	7.68
5	=	4.81	4	2.2	10.56
3	22.47	3.21	7	2.6	8.32
4	25.68	3.21	8	2.7	8.64
2	=	1.60	16	3.4	5.44
28	32.10	3.21	10	2.9	9.28
2	32.10	1.60	20	3.8	6.08
3	32.10	4.60	6.7	2.6	12.48
1	35.2	3.21	11	3.0	6.42
6	38.52	3.21	12	3.1	9.92
2	=	1.60	24	4.1	6.56
1	41.73	3.21	13	3.2	10.24
1	44.94	3.21	14	3.3	10.56
1	48.15	1.60	30	4.2	6.72
2	=	3.21	15	3.4	10.88
2	64.2	1.60	40	5.0	8.0
1	80.25	3.20	25	4.2	13.44
1	86.67	3.20	54	5.7	18.24

*0.5 to 3.5 μm glass fibers > 10 μm long with yellow binder

TABLE 16. PARTICLE SIZE DISTRIBUTION OF FIBERS COLLECTED ON STAGE 3 OF CASCADE IMPACTOR FROM CHAMBER 2.*

NO. OF FIBERS	L μm	W μm	β	D_{IE/D_f}	D_{IE} μm
12	3.21	0.6	5	2.3	1.38
38	3.21	1.6	2	1.7	2.72
87	3.21	3.21	1	1.5	4.81
23	6.42	1.6	4	2.2	3.52
8	9.6	0.6	15	3.4	2.04
42	9.6	1.6	6	2.4	3.84
6	9.6	3.21	3	2.0	6.42
15	12.8	1.6	8	2.7	4.32
6	12.8	3.21	4	2.2	7.06
10	16.1	1.6	10	2.9	4.64
5	16.1	3.21	5	2.3	7.38
1	19.2	0.6	30	4.2	2.52
2	19.2	1.6	12	3.1	4.96
1	19.2	3.2	6	2.4	7.68
2	22.4	3.2	7	2.6	8.32
2	25.6	1.6	16	3.4	5.44
4	32.1	3.2	10	2.1	6.72
1	32.1	1.6	20	3.8	6.08
2	38.5	3.2	12	3.1	9.92
2	38.5	1.6	24	4.1	6.56
1	48.1	1.6	30	4.2	6.72
2	48.1	3.2	15	3.4	10.88

*0.5 to 3.5 μm glass fibers > 10 μm long with yellow binder

TABLE 17. PARTICLE SIZE DISTRIBUTION OF FIBERS COLLECTED ON STAGE 4 OF CASCADE IMPACTOR FROM CHAMBER 2.*

NO. OF FIBERS	L μm	W μm	β	D_{IE/D_f}	D_{IE} μm
206	3.21	0.6	5	2.3	1.38
7	=	1.6	2	1.7	2.72
5	=	3.4	1	1.5	4.81
13	6.4	0.6	10	2.9	1.74
6	6.4	1.6	4	2.2	3.52
7	9.6	0.6	15	3.4	2.04
3	9.6	1.6	6	2.4	3.84
12	12.8	0.6	20	3.8	2.28
5	16.1	0.6	25	4.1	2.46
2	19.2	0.6	30	4.2	2.52

*0.5 to 3.5 μm glass fibers > 10 μm long with yellow binder

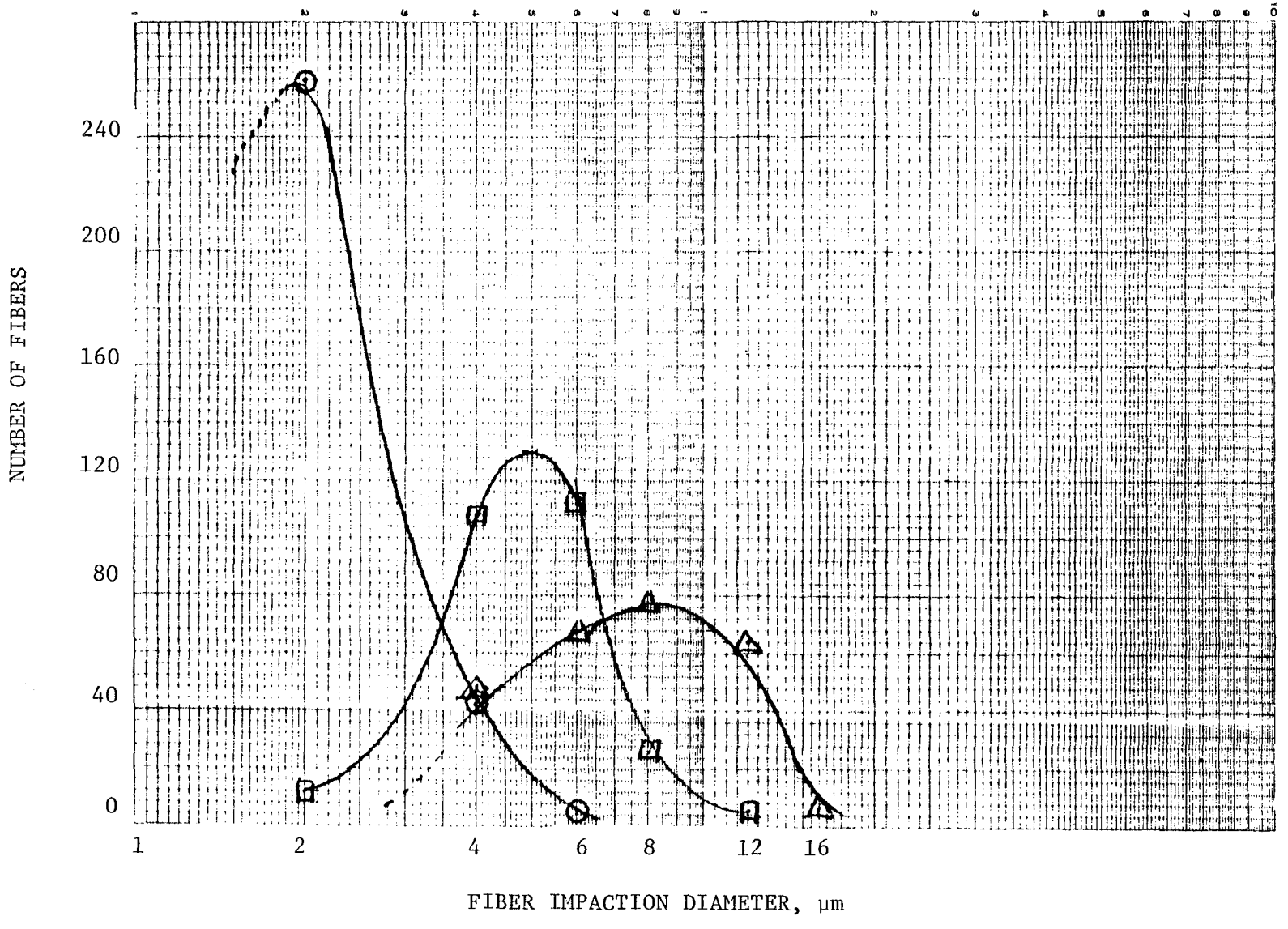

FIGURE 19. PARTICLE SIZE DISTRIBUTION OF GLASS FIBERS OBTAINED WITH A BATTELLE CASCADE IMPACTOR

a lower density. This correlation indicates that a cascade impactor can characterize fibers reasonably well. The major problem with using any type of an instrument to characterize an airborne fiber glass cloud is electrostatics. Total mass collected on the impactor stages were generally less than 10 percent of the mass concentration in the chambers from entrance losses due to the electrical charge on the fiber. Figures 20 through 23 are typical particle size distribution obtained with the cascade impactor. It was found that the impactor could show considerable particle size variation from week to week even though the particle size characteristics of the fiber glass before generation was constant. Some of this variation was due to the accuracy of weighing the impaction stages; however, electrostatics seemed to be the primary cause. The large red fibers which were coated with binder had inertial characteristics so that most of an impactor sample should have collected on the first impaction stage however, none of the extremely large charged fibers failed to reach the impaction surface. Therefore, the only material that deposited on the impactor stages were small fibers, fragments of the layer fibers, and fragments of the binder which were dislocated during powder cloud generation.

To further confirm if the impactor was suitable to characterize power clouds of smaller fiber particle size measurements were made with a scanning electron microscope of bulk powder used in Chamber four.* Similar measurements were made of fibers collected on filters from Chamber four. Table 18 summarizes the particle size measurements. The impaction equivalent diameter and volume of each particle was then calculated. The weight percentage in each size class was then plotted to obtain a cummulative mass distribution as shown in Figure 24. A typical impactor particle size distribution obtained from Chamber four is shown in Figure 23. These figures show that the mass-median impactor equivalent diameter of the filter sample is 1.8 μm and the mass-median impaction diameter taken with the cascade impactor is approximately 1.6 μm. This indicates a close agreement between the impactor and filter samples.

* Microfibers without binder less than 10 μm in length.

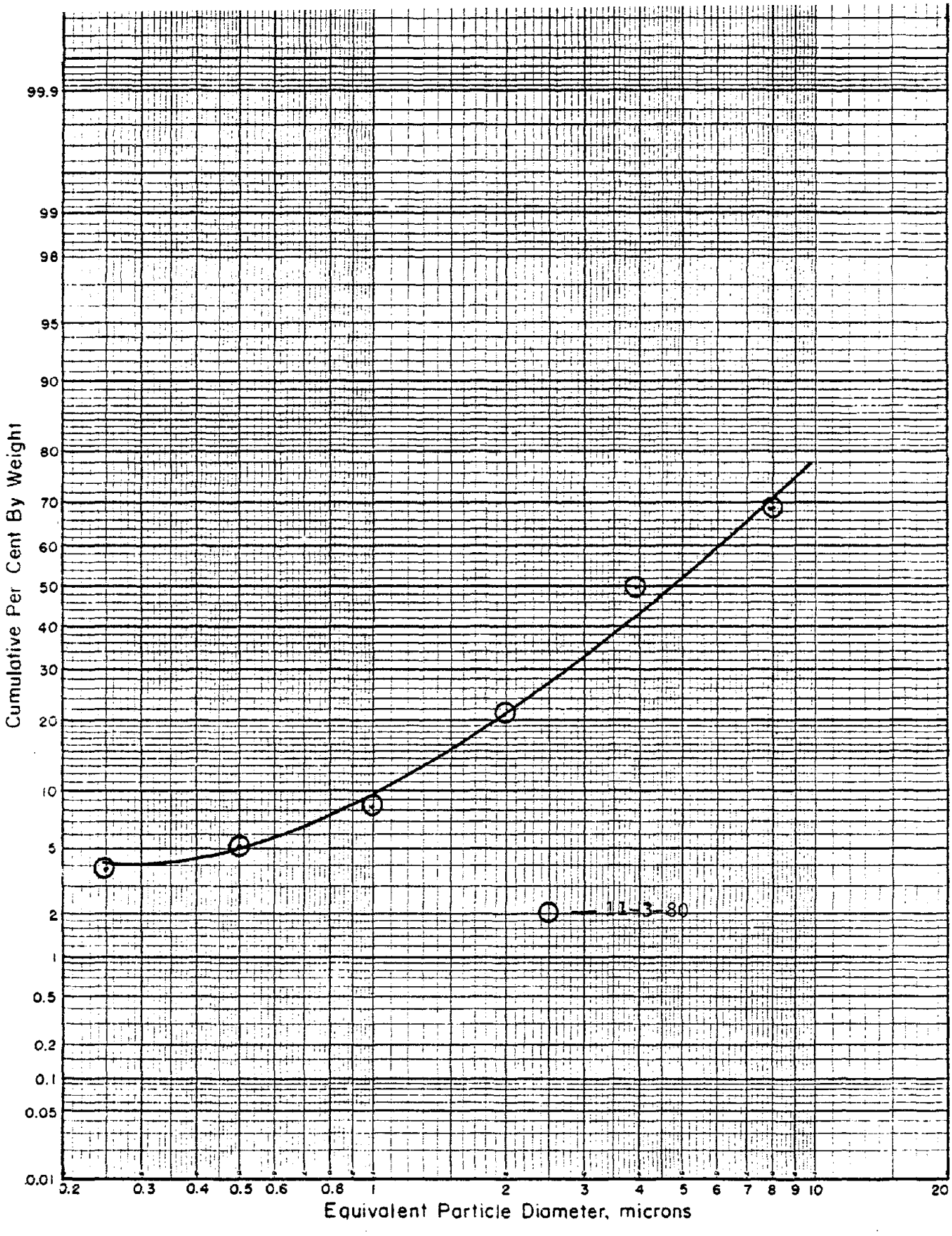

FIGURE 20. PARTICLE SIZE DISTRIBUTION OF FIBERS COLLECTED WITH A CASCADE IMPACTOR FROM CHAMBER 1.

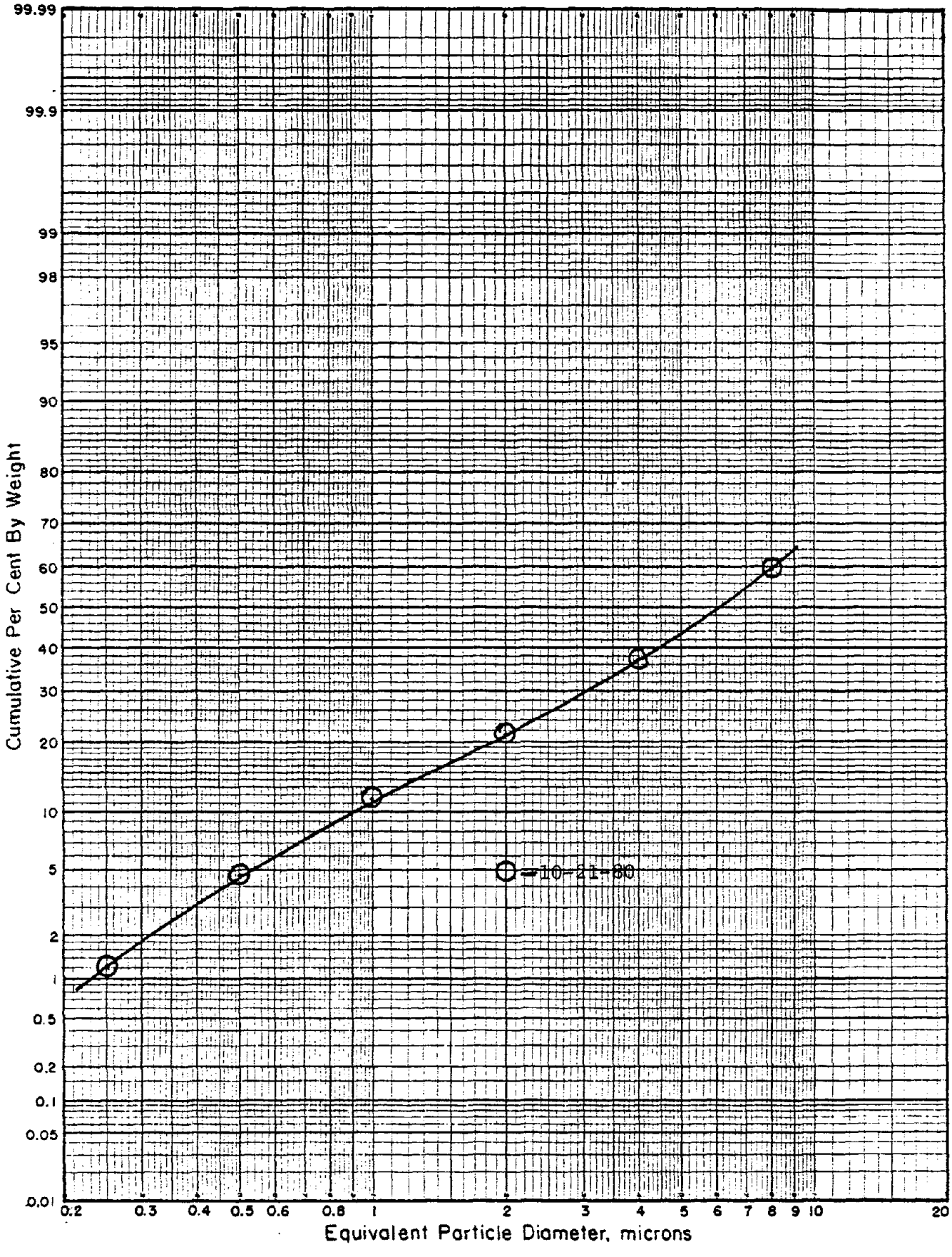

FIGURE 21. PARTICLE SIZE DISTRIBUTION OF FIBERS COLLECTED WITH A CASCADE IMPACTOR FROM CHAMBER 2.

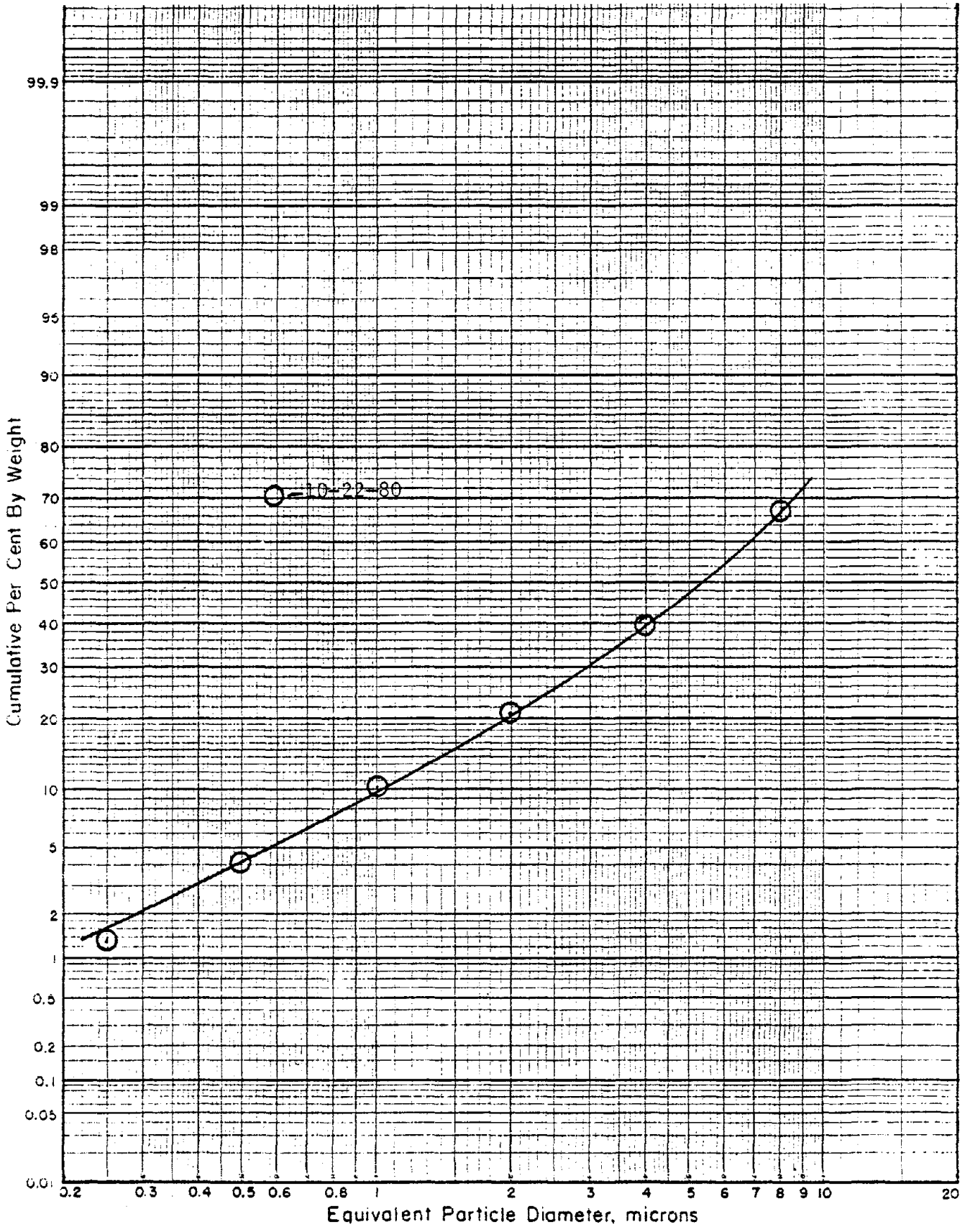

FIGURE 22. PARTICLE SIZE DISTRIBUTION OF FIBERS COLLECTED WITH A CASCADE IMPACTOR FROM CHAMBER 3.

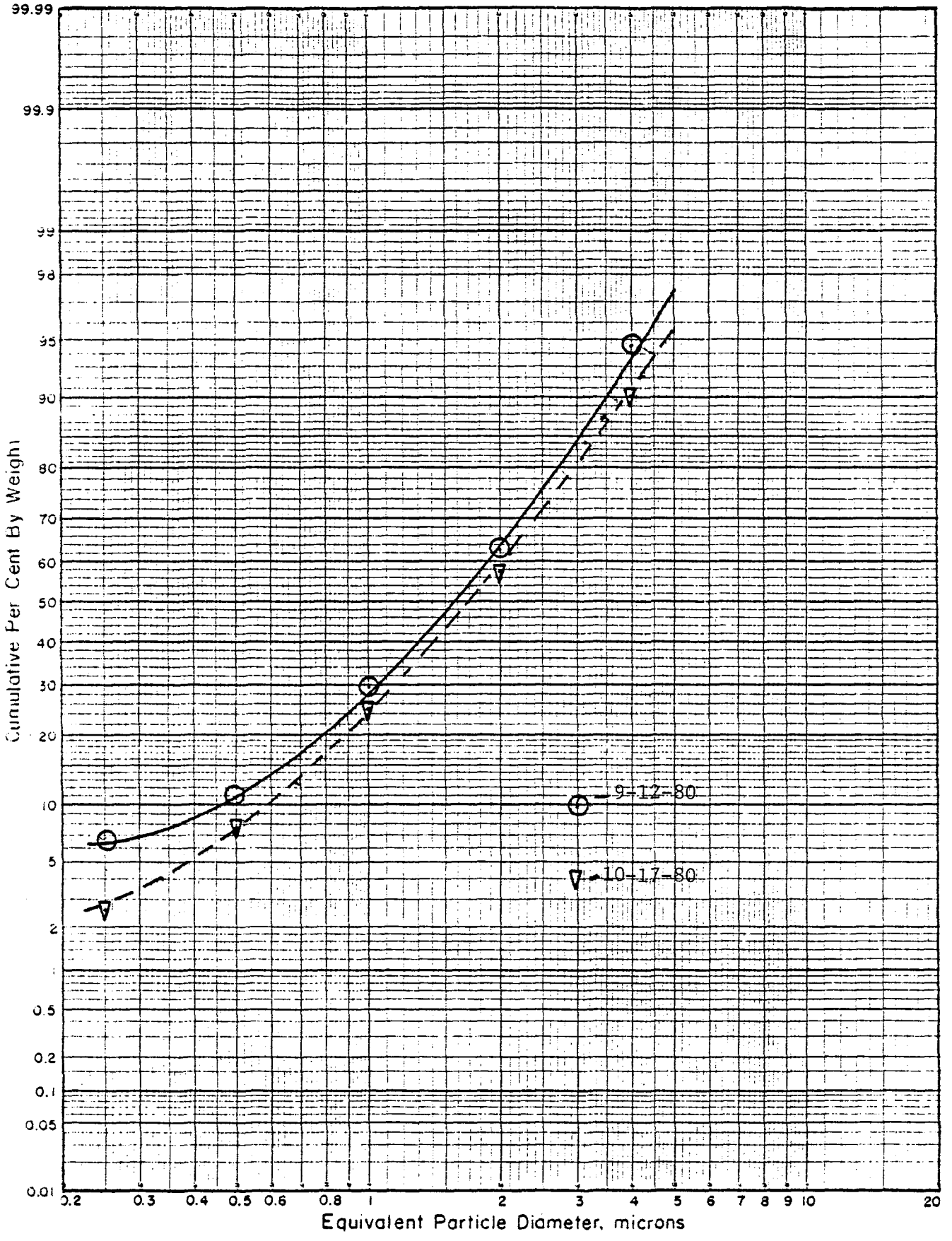

FIGURE 22 PARTICLE SIZE DISTRIBUTION OF FIBERS COLLECTED

TABLE 18. PARTICLE SIZE DISTRIBUTION OF GLASS FIBERS COLLECTED ON FILTER FROM CHAMBER 4.*

D_f μm	L μm	NO.	β	D_{IE/D_f}	D_{IE} μm	Vol. μm^3	Total Volume μm^3
0.17	2	1	12	3.2	0.54	0.06	0.06
0.17	3	1	18	3.7	0.63	0.09	0.09
0.17	4	2	24	4.2	0.71	0.12	0.24
0.17	10	1	60	6.3	1.07	0.30	0.30
0.33	1	1	3	2.1	0.69	0.11	0.11
0.33	2	2	6	2.6	0.86	0.22	0.44
0.33	3	21	9	2.9	0.96	0.33	6.93
0.33	4	20	12	3.2	1.06	0.44	8.80
0.33	5	4	15	3.5	1.16	0.55	2.20
0.33	6	3	18	3.7	1.22	0.66	2.00
0.33	7	3	21	4.0	1.33	0.77	2.31
0.5	10	1	20	4.0	2.00	2.50	2.50
0.5	12	1	24	4.2	2.10	3.00	3.00
0.67	2	3	3	2.1	1.41	0.88	2.69
0.67	3	5	4.5	2.3	1.54	1.35	6.73
0.67	4	8	6	2.6	1.74	1.80	14.36
0.67	5	4	7.5	2.7	1.81	2.24	8.98
0.67	6	4	9	2.9	1.94	2.69	10.77
0.67	7	6	10.5	3.1	2.08	3.14	18.85
0.67	8	3	12	3.2	2.14	3.59	10.77
0.67	9	2	13.5	3.3	2.21	4.04	8.08
1	4	1	4	2.3	2.30	4.00	4.00
1	7	1	7	2.7	2.70	7.00	7.00

*< 3.5 μm in diameter - < 10 μm in length - no binder

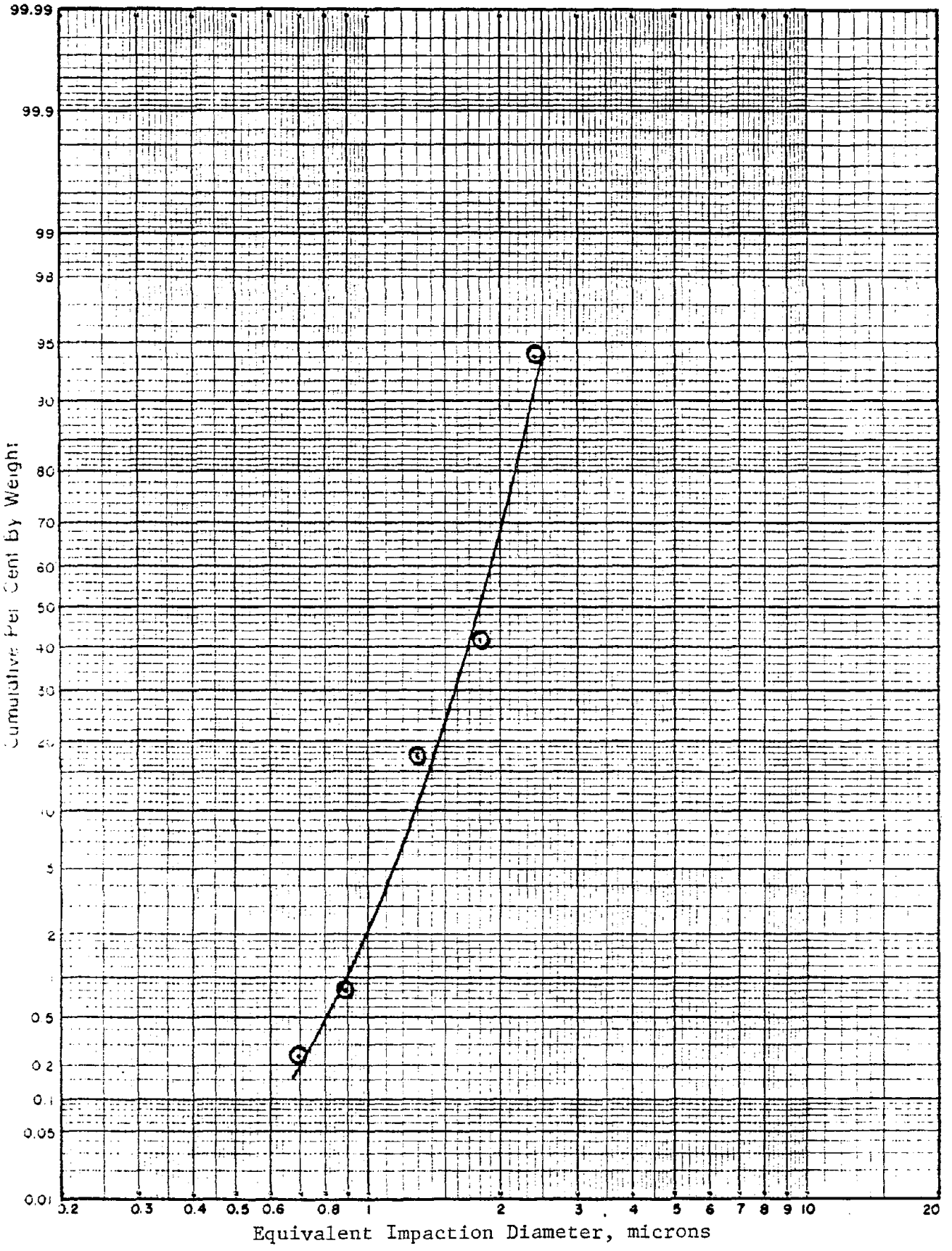

FIGURE 24. IMPACTION EQUIVALENT DIAMETER OF FIBERS COLLECTED ON FILTER FROM CHAMBER 4

A similar technique was used to characterize the fiber distribution obtained from a Chamber 3 filter. Figure 25 is a plot of the resulting equivalent impaction diamter and shows that the mass-median impaction diameter is 5.8 micrometers as compared with 5.3 micrometers obtained with a cascade impactor (Figure 22). The fibers coated with a phenolic binding (Chambers 1 and 2) failed to correlate with the cascade impactor data. It is believed that the larger charged fibers failed to reach the impaction stages of the cascade impactor. This effect was also noted with the uncoated fibers on several occasions as the impactor size distribution could be vastly different within the same fiber batch.

Uniformity of the fiber concentration in Chamber 2 was also examined with a Sinclair Phoenix aerosol and smoke Photometer.* The photometer measurements were made by sampling along the side of the chamber at the level of the upper and middle animal cages. The photometer was used to monitor stability of the concentration only: the output is not linear and considerable work would be required to calibrate the unit for each of the different types of glass fibers. The photometer measurements in Chamber 2 showed the water droplets produced during the atomizing periods and the subsequent evaporation of the water droplets before the next atomizing period. The photometer measurements also confirmed that the fiber concentrations were equivalent on both sides of the chamber and that the concentrations did not vary significantly during monitoring periods up to about 60 minutes.

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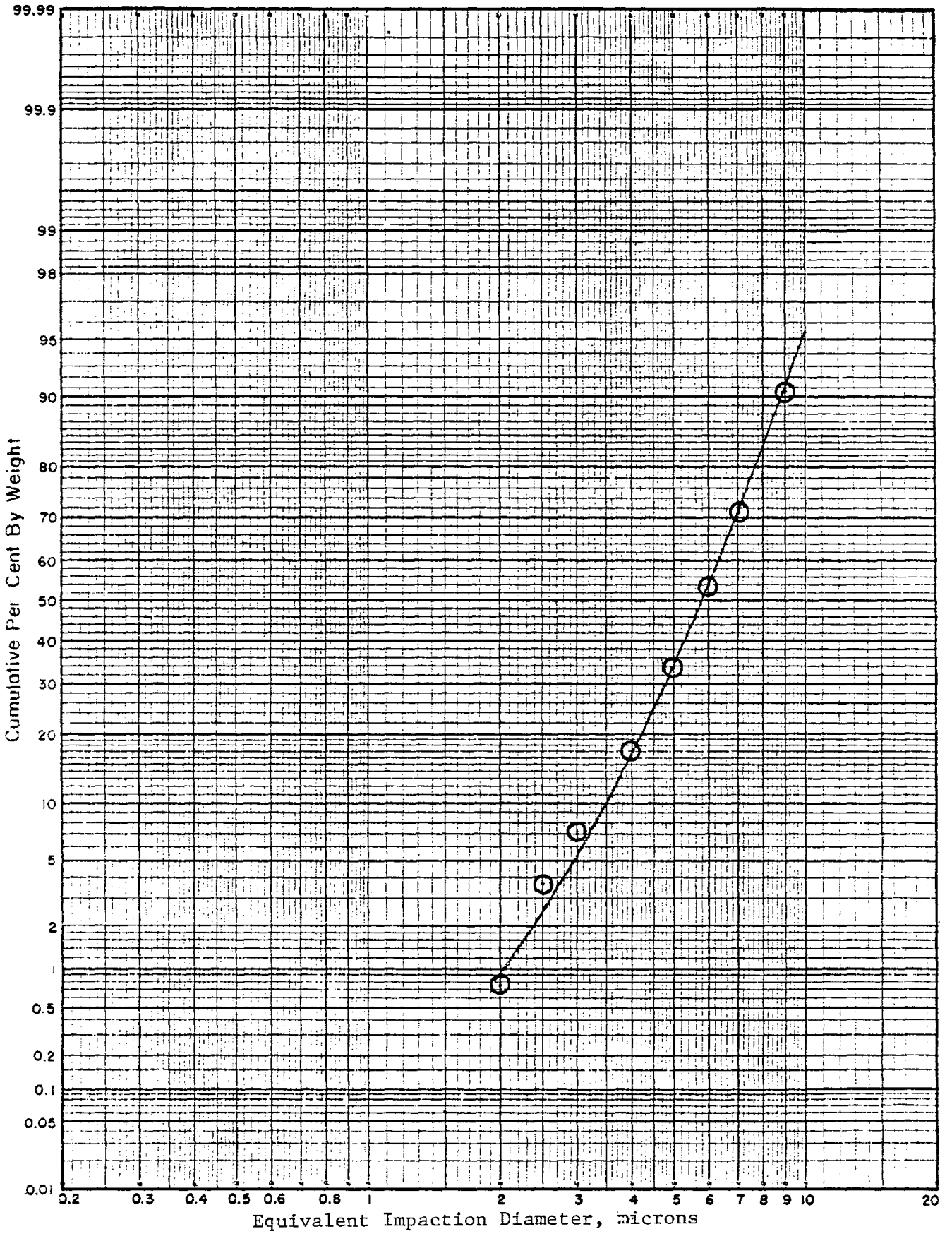
* Model JM-1000 made by Phoenix Precision Instrument Co., Philadelphia, Pa.


99.99
99.9
99
98
95
90
80
70
60
50
40
30
20
10
5
2
1
0.5
0.2
0.1
0.05
0.01
Cumulative Per Cent By Weight
0.2
0.3
0.4
0.5
0.6
0.8
1
2
3
4
5
6
7
8
9
10
20
Equivalent Impaction Diameter, microns

EXPOSURE ENVIRONMENTAL PROCEDURES

Method of Exposure

The animals were exposed for 7 hours per day, 5 days per week, for periods of 72 weeks (monkeys) and 86 weeks (rats), excluding holidays, in Hinners'[33] type chambers which were designed for the health effects research programs conducted at the National Center for Air Pollution Control and the Environmental Protection Agency. These chambers are constructed of stainless steel and are 6 feet square designed with a pyramidal top and bottom with a nominal volume of 5.4 m^3. The doors of the chambers are made of 3/8-inch thick plate glass set in a stainless steel frame and sealed with a neoprene seal. The doors occupy 60 percent of the front side and are held closed with pressure clamps. There are four equally spaced sampling ports in vertical array on each side of the door.

For this study, chambers similar to those shown in Figure 26 were modified to accommodate both rats and monkeys. The interior of the chamber was cleaned daily after each animal exposure with a waterwash ring with high pressure nozzles.

Air was drawn through the chamber by a large blower mounted on the roof of the facility. The air entering each chamber was room air that had been filtered with an absolute filter mounted on the intake to each chamber. The room air had previously been cleaned by an electrostatic precipitator and a bacteriostatic LiCl solution and conditioned to an average 68.8°F and an average 50 percent relative humidity.

At the beginning of the study, a check was made to determine the uniformity of the test-gas concentrations in the Hinners' type exposure chambers. Because a test gas was introduced via the air input metering orifice, it was assumed that its concentrations would be uniform throughout the chamber. This assumption was verified by using methyl chloride as the test gas and monitoring the chamber concentration with an infrared spectrophotometer (MIRAN 1A). A chamber concentration of approximately 400 ppm was used which produced an absorbance reading of 0.39. The chamber was sampled at three levels 12, 24, and 36 inches above the chamber floor. Each level was sampled at 9 points

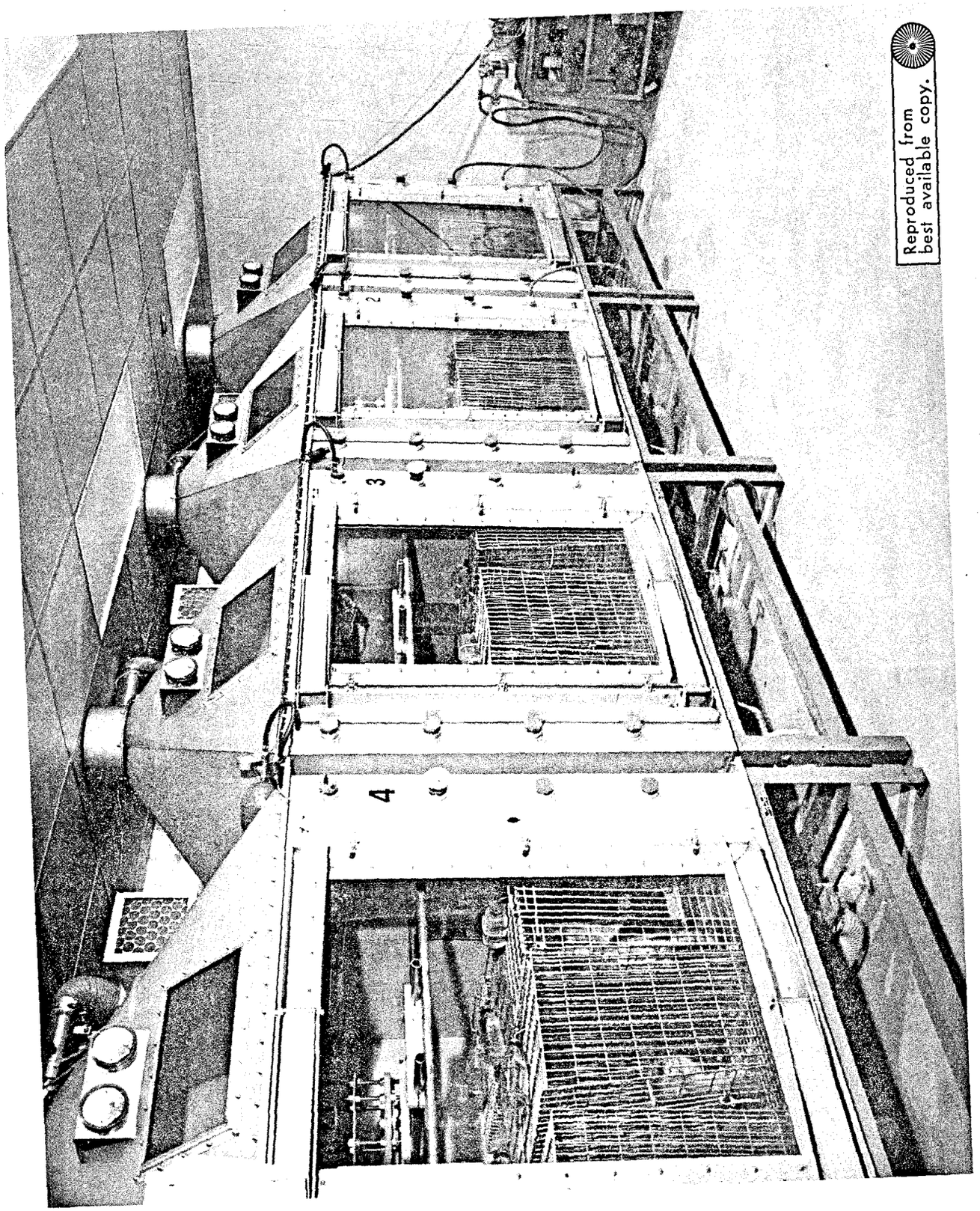


FIGURE 26. PHOTOGRAPH OF ANIMAL INHALATION CHAMBERS

(a 3 x 3 matrix) taken at the front, middle, and back of the chamber at each side at the midline. A total of 27 points was sampled (a 3 x 3 x 3 matrix) and the absorbance reading (0.39) was identical for all points.

To assure randomization of exposure, all cages were rotated from top to bottom and left to right by one position each new exposure day.

Chamber Air Monitoring

The air flow in the exposure chambers was monitored by measuring the pressure drop across an orifice placed in the air inlet as shown in Figure 27.

This orifice was calibrated by means of an ASME Orifice and the theoretical pressure drop across the orifice was calculated. Based upon a flow rate of 1 m^3/min or 35.3 cfm the theoretical change in pressure across the orifice should be 0.19 inches of water. Figure 28 shows the calibration curve obtained.

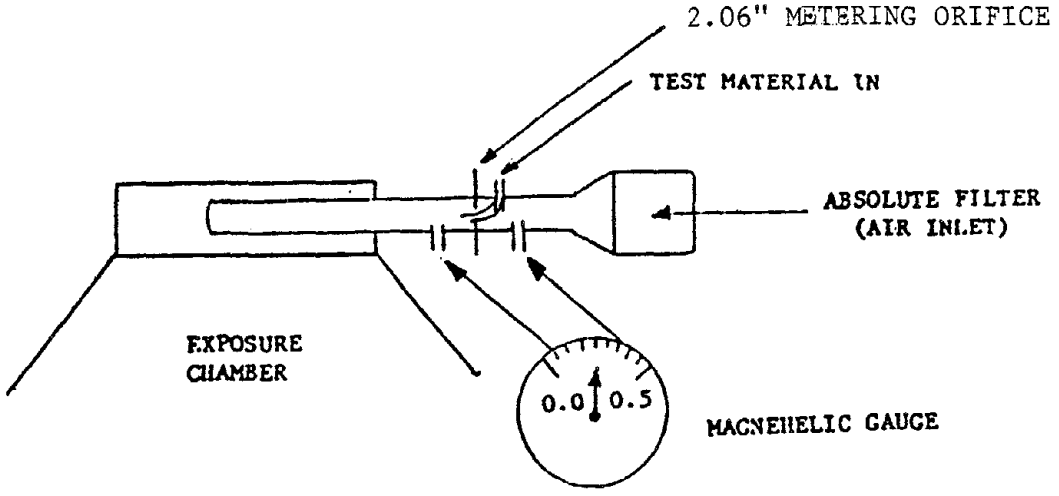


FIGURE 27. SCHEMATIC OF AIR MONITORING SYSTEM

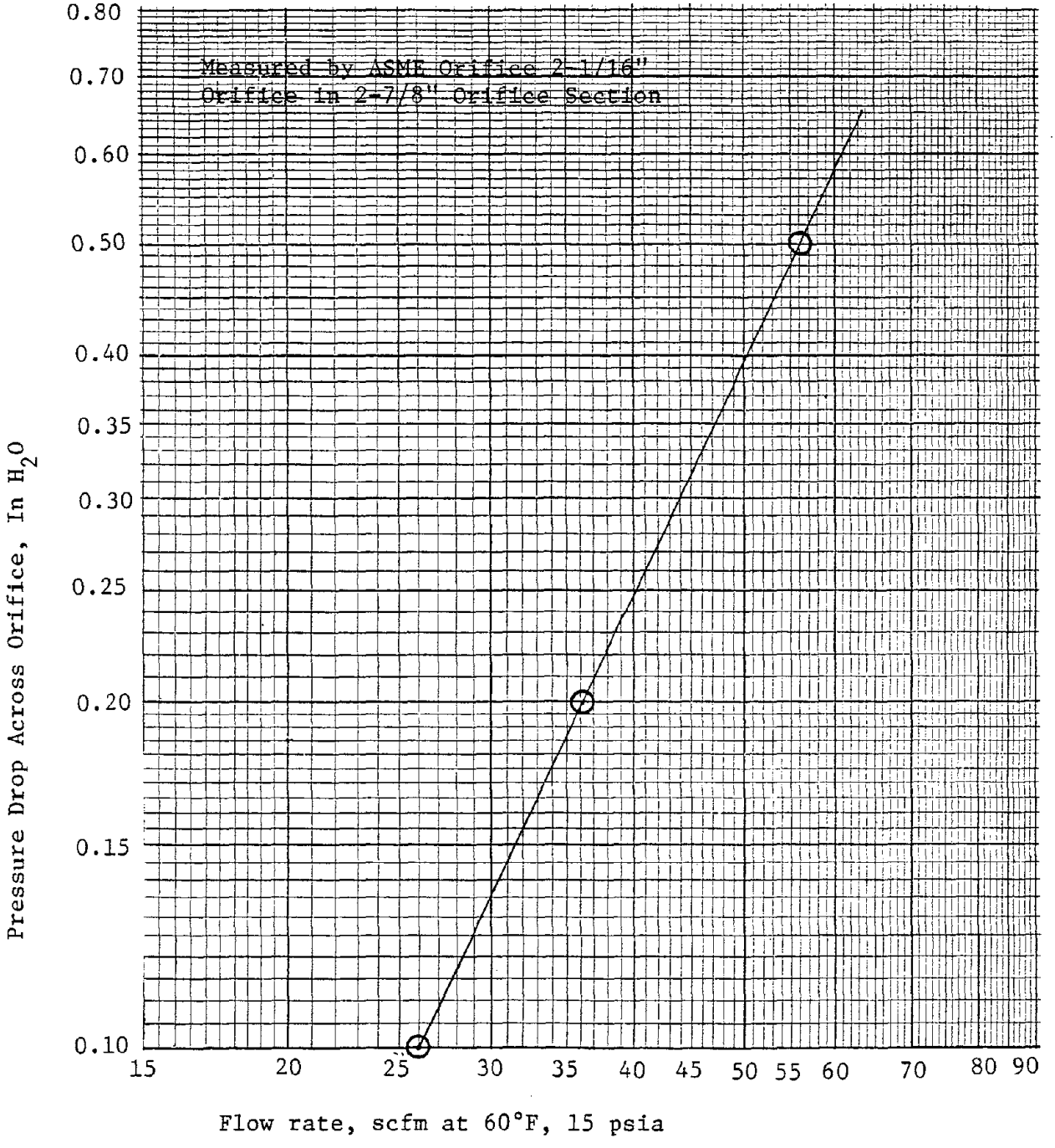


FIGURE 28. CHAMBER AIR FLOW CALIBRATION

RESULTS

EXPOSURE ENVIRONMENT RESULTS

Temperature and Relative Humidity

Throughout this study, only slight variations of relative humidity or temperature were detected for the inhalation chambers. Actual readings varied somewhat, but in accordance with the room environment. The exposure and holding rooms were monitored to determine changes from the desired temperature of 70 $\pm$ 2°F and the desired relative humidity of 45 $\pm$ 5 percent. These measurements were originally made with separate temperature and hygrometer instruments, mounted in each chamber. As the study progressed, the instruments in the interior of the various chambers did not always agree exactly due to a build up of glass fibers on the hygrometer element. The average temperature throughout the study was 68.8 $\pm$ 1.9°F and the relative humidity 50.0 $\pm$ 6.4 percent. The actual records are maintained by the Battelle Quality Assurance Unit of the Biological Sciences Department.

Ammonia Level

During the exposure period, a test was made to determine the ammonia level within a chamber that was fully loaded with test animals. The measurement, which was taken at the end of an exposure period, showed that the ammonia level was approximately 0.2 ppm.

Size Characteristics of Glass Fibers

Besides the measurement of the fiber glass clouds with a cascade impactor (which was previously discussed), samples were collected on absolute filters and subsequent particle size measurements made of photo micrographs taken of these collections.

Figures 29 - 32 are scanning electron micrographs of filters used to obtain mass concentration of the powder cloud in the four chambers. Tables 19 - 22 summarize the particle size measurements of 200 fibers made from these and similar micrographs. Figures 33 - 36 are three-dimensional plots of these data. These figures indicate that the mass of the fibers was within the given specifications.

Filter samples were also given to Dr. Lloyd Stetler (NIOSH-Cincinnati) for particle size analysis. The filter samples were ashed at 100 watts for two hours in a low temperature asher. The residue from each filter was then added to 200 ml of filtered, deionized water. Five drops of Aerosol OT were added to each suspension which was then allowed to stand for 10 minutes. The suspensions were then stirred magnetically for 2 minutes and filtered through a 25 mm diameter, 0.1 μm pore size Nuclepore filter. The filters were mounted on carbon planchets with colloidal graphite and then analyzed in the SEM using a LeMart Scientific Model B-10 image analysis system. Analyses were performed at a magnification of 1000X.

Tables J-1 through J-4 summarize the particle size measurements which were obtained for fibers with aspect ratios of 5:1 and greater. Figures J-1 through J-4 are three-dimensional plots of these data. The results obtained with the automatic counter agree quite well with the manual measurements.

Exposure Concentrations

The protocol specifies that concentration measurements should be made twice a day. However, because of the potentially large variations in concentrations, an attempt was made to make at least four measurements when operational time permitted. Table 23 summarizes the concentrations for the initial time period in which only rats were exposed and the following six quarters in which both rats and monkeys were exposed. In addition, the table shows the overall exposure concentrations for both rats and monkeys. Appendix D shows the average daily chamber concentration.

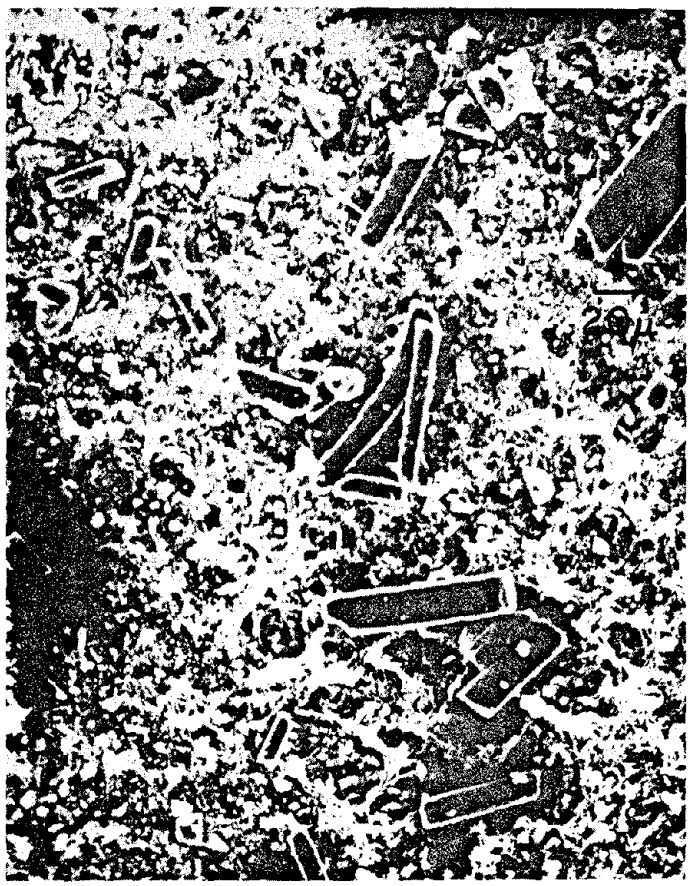


FIGURE 29. SEM PHOTOGRAPH OF GLASS FIBERS COLLECTED FROM CHAMBER 1 (300X)

FIGURE 30. SEM PHOTOGRAPH OF GLASS FIBERS FROM CHAMBER 2 (1000X)

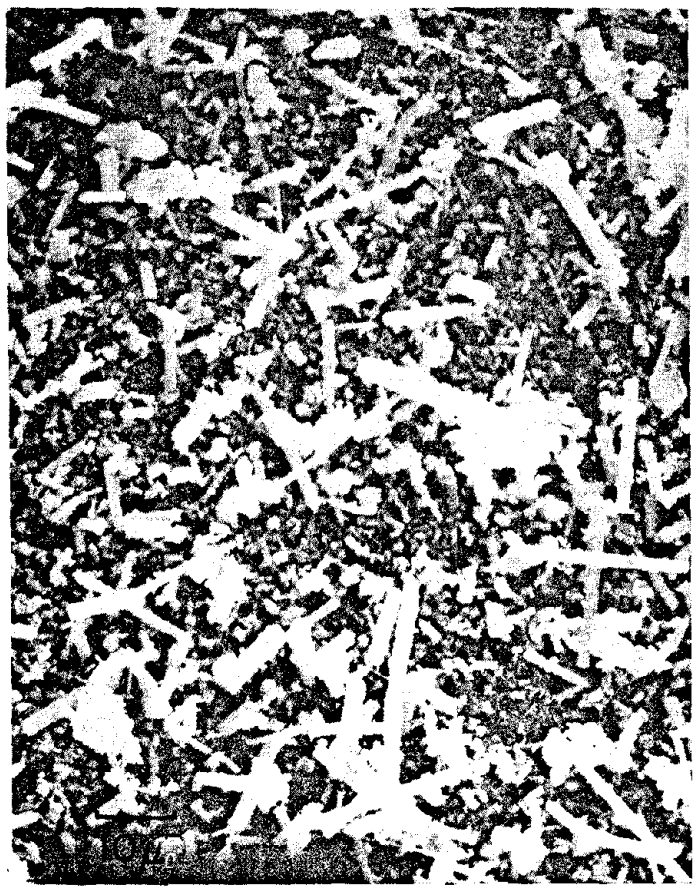


FIGURE 31. SEM PHOTOGRAPH OF GLASS FIBERS FROM CHAMBER 3 (1000X)

FIGURE 32. SEM PHOTOGRAPH OF GLASS FIBERS FROM CHAMBER 4 (3000X)

TABLE 19. PARTICLE SIZE DISTRIBUTION OF GLASS FIBERS COLLECTED ON FILTER FROM CHAMBER 1*.

Length µm	Diameter - µm									
	3.33	5.0	6.67	8.33	10.0	11.67	13.33	15.0	16.67	18.33
16.7	1									
20			1							
21.7	1									
23.3			3							
26.7			2	1						
28.3	1									
30	1	1	1	4	5					
33.3			5	1	3					
36.7			1		7	3				
40		1		4	4	1	2			
43.3			4	2			1			
45			1							
46.7			2	1	2	2	2			
50		1	1	1	2	2	1		1	
53.3					1	1				
56.7			1	1	1		1			
60				1	1			1		
61.7					1					
63.3						1				
66.7			1	2		3				1
70					1				1	
73.3					1					1
76.7					2				2	
78.3						1				
80						1				
83.3		1				2	2			
90									1	
93.3					1					
96.7					1				1	
100				1	1				2	
103.3				1						
110				1						
123.3							1			
173.3							1			

* 4 to 6 µm diameter > 20 µm long with binder.

TABLE 20. PARTICLE SIZE DISTRIBUTION OF GLASS FIBERS COLLECTED ON FILTER FROM CHAMBER 2*.

Length	Diameter - μm												
μm	0.25	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	6.0
4		1	2										
5	2	1	2										
6		2	3	1	1								
7		1	2	1	2								
8		1	7	2	5								
9		2	2				1						
10		2	5	4	3		1						
11			2	3	5	1	1						
12			1	2	6								
13			3	2	1	3							
14			1	1	4		1						
15						1	3		1				
16				1	1	2			1				
17				1	2	1	1	1	1				
18			1		5	1		1	2				
19			1				2	1	1				
20			2	1	1	3	3				1		
21					1			1	1				
22					2	1	4						
23					1	1							
24			2		2								
25						2	1	1	1				
26					1	2	2	2					
27					1		1						
28			1		1	1				1			
29										1			
30				1		1							
31			1						1				
32					1	1							
33			1		1		2		2		1		
34											1		
35					1								
36					1				1				
37					1								
38								1					
39							1			1			
41							2						
42											1		
43									1				
49								1					
51												1	
54											1		
56					1								
59						1							
60					1								
63													1
73									1				
93									1				

* 0.5 to 3.5 μm diameter > 10 μm long with binder.

TABLE 21. PARTICLE SIZE DISTRIBUTION OF GLASS FIBERS COLLECTED ON FILTER FROM CHAMBER 3*.

Length µm	Diameter - µm								
	0.25	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0
3		1	14						
3.5			1						
4	1	1	16						
5		1	10	3					
5.5			1						
6		1	13	4	2				
7			8	1	4				
8		2	8	9	1				
9			9	3	2				
10			2	1	4	2	1		
11			1	3	2				
12			2		1				
13			1	1	2	1			
14			3	1			1		
15		1	4		2	1	1		
16			1	1					
17	1		2	3	2				1
19				1	2				
20				1	1	1		1	
21			1	2					
22				3	1				
23			1		3				
24					1		1		
25						1		1	
26					1		1		
27					2				
28					2				
31						1			
32			1		1				
36					1				
37							1		
39			1						
65			1						

* < 3.5 µm diameter >10 µm long no binder.

TABLE 22. PARTICLE SIZE DISTRIBUTION OF GLASS FIBERS COLLECTED ON FILTER FROM CHAMBER 4*.

Length µm	Diameter - µm									
	.08	.17	.33	.5	.67	.83	1.0	1.2	1.3	1.5
1.0		3	9							
1.3		2	3							
1.7	1	1	1	1						
2.0		2	5	3	4					
2.3		3	3	1	1					
2.7	1	1	16	1	8					
3.0		2	6		3					
3.3			10		6	1	1			
3.7		2	7	1	1					
4.0		2	7		6					
4.3			1		1	1	1			
4.7			2		3	1				
5.0			3	1	4			1	1	
5.3					1	1				
5.7			1		2					
6.0			2		3					
6.3				1						
6.7			3		6		2			
7.0			1	1	1					
7.3					1		1			1
7.7					2	1			3	
8.3			1			1				
8.7					1					
9.0			1		1					
9.3							2			
9.7		1		1	3					
14.3			1			1				
16.3							1			

* < 3.5 µm diameter < 10 µm longer no binder.

TABLE 23. AVERAGE CHAMBER CONCENTRATIONS

QUARTER		CHAMBER 1	2	3	4
1 Rats Only	Date	3-12-79 to 7-9-79	3-12-79 to 7-16-79	3-12-79 to 7-2-79	3-12-79 to 6-
	Concentration mg/m^3	9.43 ± 6.44	10.84 ± 7.47	3.71 ± 2.08	4.80 ±
	Exposure Days	64.5	86.4	77.1	74.2
2 Rats & Monkeys	Date	7-10-79 to 10-9-79	7-17-79 to 10-16-79	7-3-79 to 10-2-79	6-26-79 to 9-
	Concentration mg/m^3	12.39 ± 4.17	14.04 ± 4.76	4.52 ± 1.96	4.85 ±
	Exposure Days	64.6	64.7	63.9	63.7
3 Rats & Monkeys	Date	10-10-79 to 1-9-80	10-17-79 to 1-16-80	10-3-79 to 1-2-80	9-26-79 to 12
	Concentration mg/m^3	15.24 ± 4.55	15.73 ± 7.70	4.77 ± 2.84	4.06 ±
	Exposure Days	59.7	59.6	59.7	60.4
4 Rats & Monkeys	Date	1-10-80 to 4-9-80	1-17-80 to 4-16-80	1-3-80 to 4-2-80	12-26-79 to 3-
	Concentration mg/m^3	13.57 ± 4.36	16.23 ± 4.62	4.71 ± 1.66	4.77 ±
	Exposure Days	64.3	64.2	64.2	62.2
5 Rats & Monkeys	Date	4-10-80 to 7-9-80	4-17-80 to 7-16-80	4-3-80 to 7-2-80	3-26-80 to 6-
	Concentration mg/m^3	14.33 ± 4.19	15.51 ± 2.75	5.13 ± 1.46	4.55 ±
	Exposure Days	63.1	63.1	64.0	67.0
6 Rats & Monkeys	Date	7-10-80 to 10-9-80	7-17-80 to 10-16-80	7-3-80 to 10-2-80	6-26-80 to 9-
	Concentration mg/m^3	16.23 ± 3.23	15.46 ± 2.45	5.60 ± 0.88	5.34 ±
	Exposure Days	64.5	64.1	64.2	64.8
7 Rats & Monkeys	Date	10-10-80 to 1-14-81	10-17-80 to 1-17-81	10-3-80 to 1-1-81	9-26-80 to 12-
	Concentration mg/m^3	16.56 ± 2.20	16.77 ± 2.06	5.50 ± 0.72	5.10 ± 0
	Exposure Days	60.9	60.0	59.0	61.0
TOTAL RAT EXPOSURE	Concentration mg/m^3	13.96 ± 4.16	14.94 ± 4.55	4.85 ± 1.66	4.78 ± 1
	Exposure Days	441.5	462.0	452.0	453.1
TOTAL MONKEY EXPOSURE	Concentration mg/m^3	14.72 ± 3.78	15.62 ± 4.06	5.04 ± 1.58	4.78 ± 1
	Exposure Days	377.0	375.6	374.9	378.9

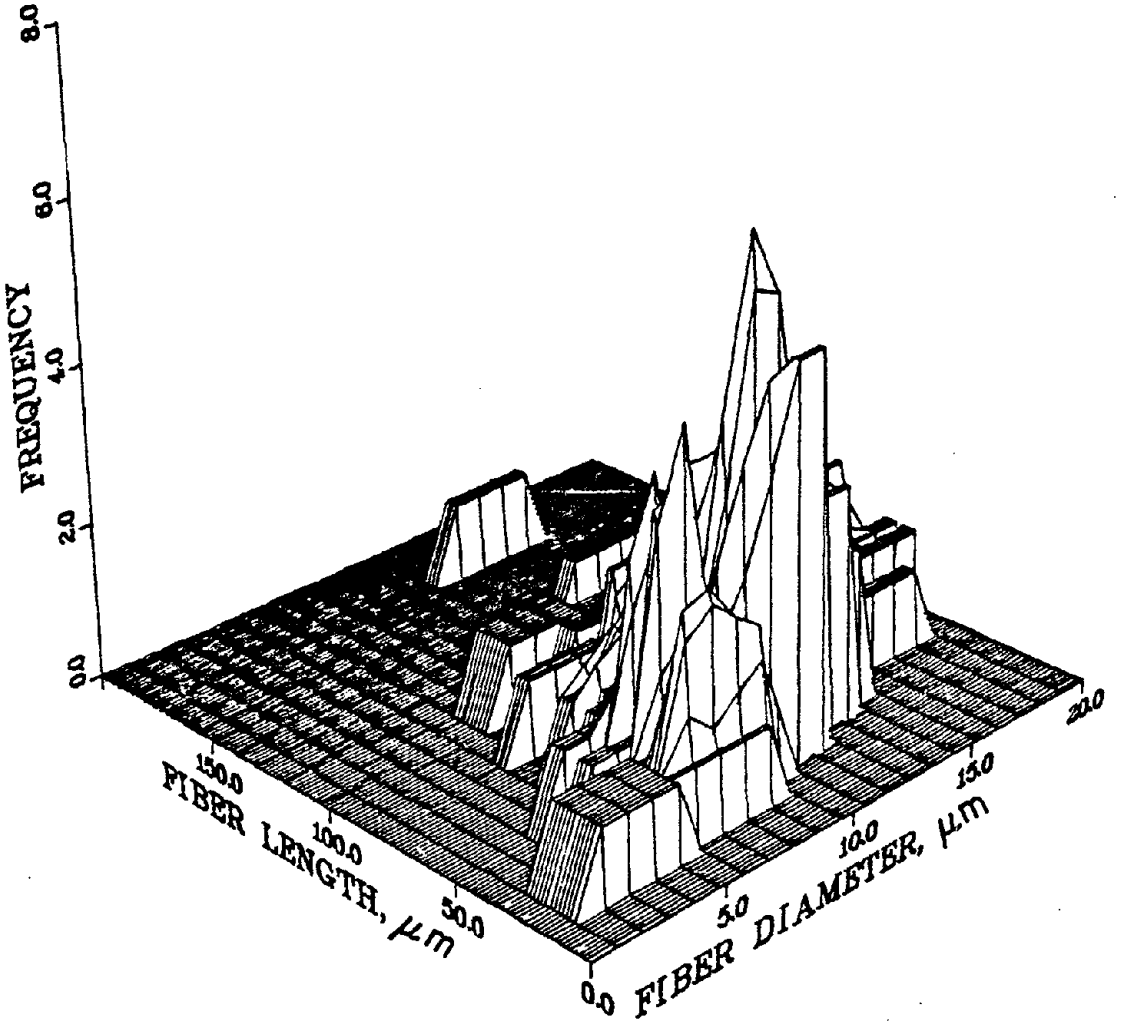


FIGURE 33. SIZE DISTRIBUTION OF GLASS FIBERS COLLECTED ON FILTER FROM CHAMBER 1.

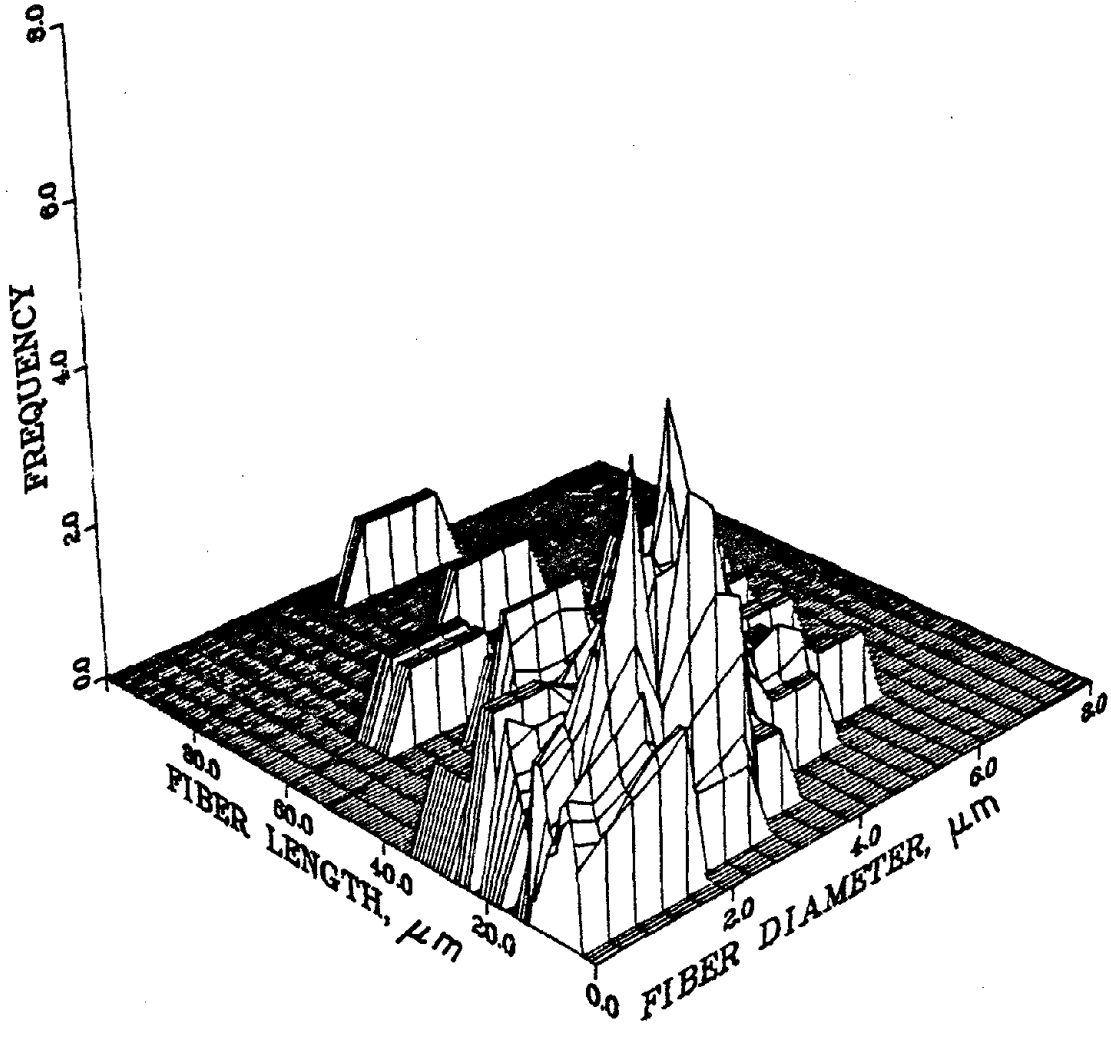


FIGURE 34. SIZE DISTRIBUTION OF GLASS FIBERS COLLECTED ON FILTER FROM CHAMBER 2.

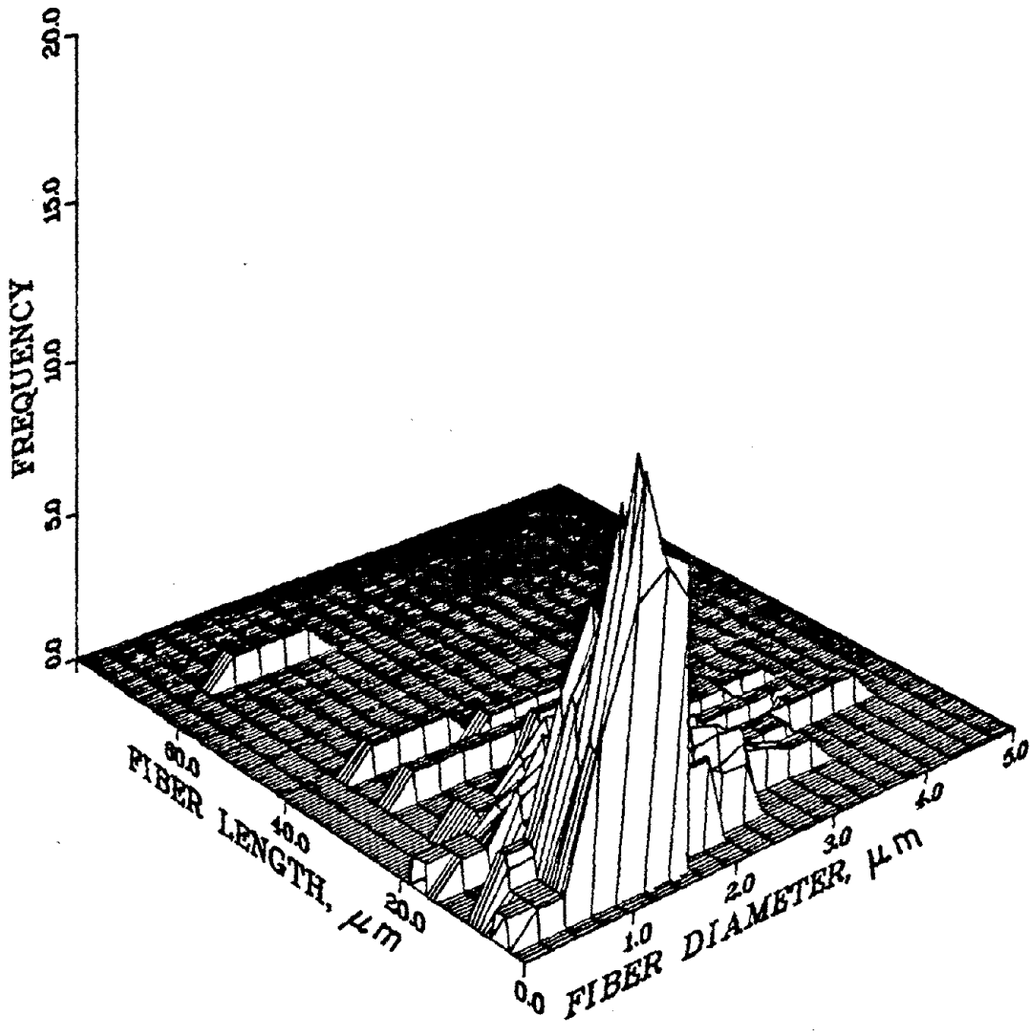


FIGURE 35. SIZE DISTRIBUTION OF GLASS FIBERS COLLECTED ON FILTER FROM CHAMBER 3.

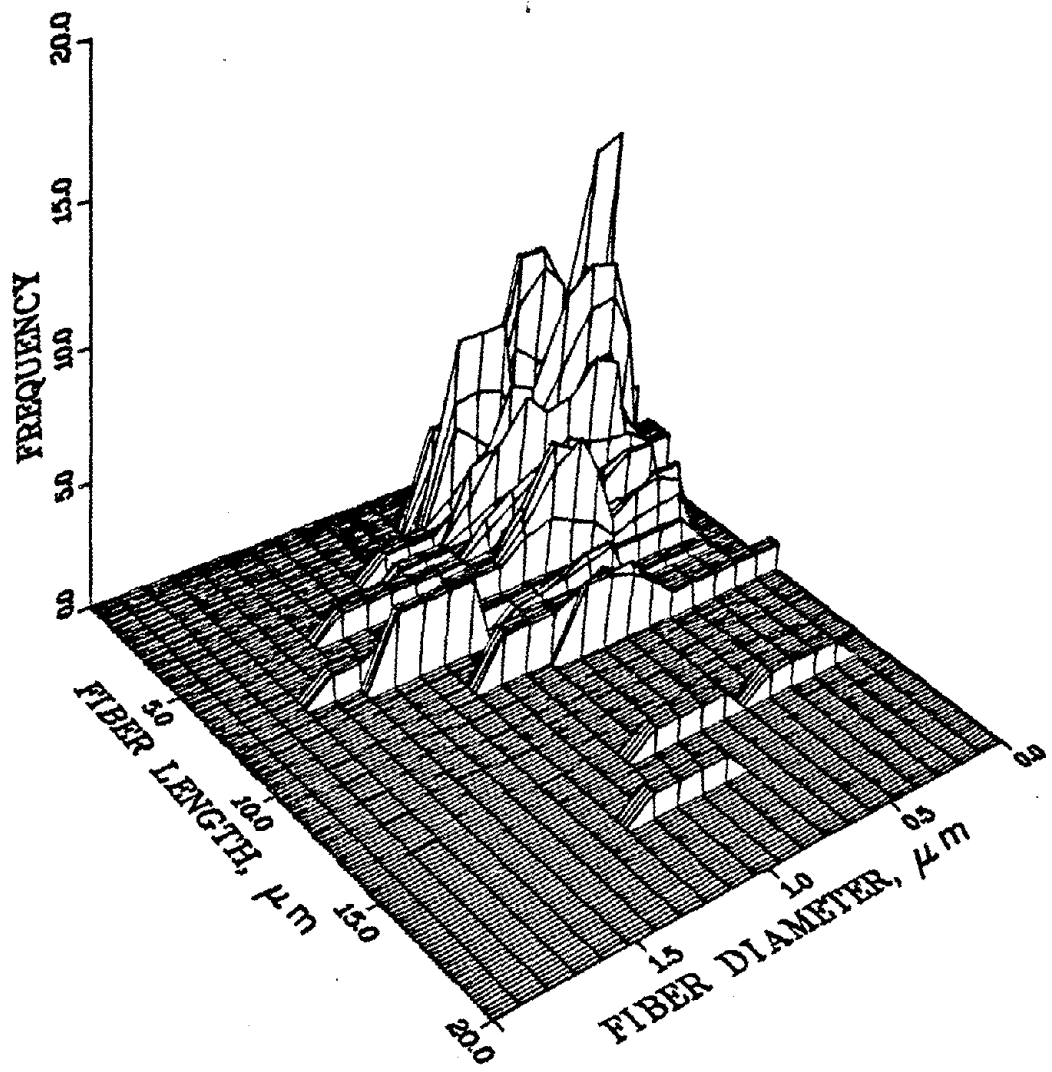


FIGURE 36. SIZE DISTRIBUTION OF GLASS FIBERS COLLECTED ON FILTER FROM CHAMBER 4.

EXPERIMENTAL ANIMAL RESULTS

Ophthalmic Examination Results

The pretest ophthalmic examinations were performed on monkeys number CM801A through CM816A, CM825A through CM831A and CM867A on February 22, 1979, and on monkeys number CM817A through CM820A, CM822A through CM824A, CM832A through CM846A, CM849A through CM858A, CM860A through CM866A and CM868A on February 23, 1979. At the time of the pretest examination, monkey number CM809A from the F01 group was noted to have lost some of its right eyelid allowing an excessive amount of palpebral conjunctiva to be exposed, and monkey CM829A had a scratch spanning the width of the cornea (top to bottom) with a resultant corneal opacity. No other ocular abnormalities were noted at the pretest eye examination.

The postexposure eye examinations for the F01 group were done on January 15, 1981 (CM839A, CM851A, and CM823A), and January 16, 1981 (CM809A, CM802A, CM865A, CM849A, CM856A, CM843A, CM855A, CM817A and CM858A); the F02 group on January 20, 1981 (CM846A, CM862A, CM864A, and CM834A), January 21, 1981 (CM810A, CM838A, CM840A and CM837A), and January 22, 1981 (CM854A, CM808A and CM813A); the F03 group on January 9, 1981 (CM850A, CM803A, and CM822A), January 12, 1981 (CM835A, CM815A, CM824A, and CM814A) and January 14, 1981 (CM836A, CM833A, CM841A, and CM825A); the F04 group on December 30, 1980 (CM801A and CM807A), December 31, 1980 (CM818A, CM828A, CM812A, CM867A and CM857A), and January 5, 1981 (CM819A, CM830A, CM831A, CM842A and CM832A); and the F05 group postexposure eye examinations were done on December 22, 1980 (CM820A, CM844A, CM805A, CM868A and CM861A) and December 23, 1980 (CM845A, CM860A, CM816A, CM806A, CM829A, CM852A, and CM853A). Postexposure eye examinations were not done on monkey CM811A from the F02 group nor monkey CM863A from the F03 group as both of these animals died before study termination. The only ocular abnormality noted in the monkeys at the postexposure examination was an opaque corneal scar spanning the cornea (top to bottom) on monkey number CM829A where the scratch and scar had previously been. No lesions attributable to fiber exposure were seen in the monkeys.

Discussion of Clinical Observations

With the exceptions of monkey number CM811A who died early with a syndrome analagous to diabetes mellitus (see pathology discussion for details) and monkey number CM863A who was sacrificed in a moribund condition of undetermined cause (also see pathology discussion for details), the monkeys remained in good health throughout the study. Clinical abnormalities noted by the observing technicians were largely minor problems commonly seen in caged primates or problems that resulted from the handling procedures necessary for this study. None of the clinical abnormalities observed in the monkeys was considered to be the result of exposure to the fibrous glass test material.

Some clinical abnormalities were observed commonly in the monkeys, i.e., traumatic lesions, hairloss, nasal discharge or dried exudate in a nostril, varying periods of reduced appetite, and pigmentary alterations. Other abnormalities, such as coughing, wheezing, lumps, and distended abdomens occurred less often. Some abnormalities such as diarrhea, blood in stool, vomiting, and cloudy urine did occur but were very rare.

Traumatic lesions were by far the most commonly noted clinical abnormalities. These lesions included lacerations sustained from a bite from a neighboring monkey (they were in close proximity when in the exposure chambers); lacerations caused by having a finger, toe or tail pinched in the cage when moving from holding room to chamber or vice versa; traumatic lesions that occurred when the monkeys were caught for blood collection and TB testing; or the actual handling and procedures of blood collection and TB testing. Virtually every monkey in the study had a traumatic lesion at some time. Most were very minor, but some did require sutures and monkey number CM832A from the F04 group fractured the radius and ulna of its left arm when an animal technician tried to remove it from its cage.

Another very commonly occurring clinical abnormality in these monkeys was hairloss. It is not uncommon for caged primates to entertain themselves by plucking hair from their body. These monkeys engaged in this pastime frequently. Ten of twelve monkeys in the F01 group, ten of twelve

in F02, eight of twelve in F03, eleven of twelve in F04, and ten of twelve in F05 manifested some hairloss during the months of the study.

Sneezing, nasal discharge, and dried exudate in the nostrils, when considered as a class of clinical observations, occurred in eight of twelve monkeys in F01, ten of twelve in F02, eleven of twelve in F03, nine of twelve in F04, and eight of twelve in F05. This did not progress to anything more profound, nor did it have any apparent effect on the overall condition of the monkeys. The condition occurred in all treatments and the control group with similar frequency. Thus, no significance was attributed to these observations.

Sixty-five percent of the monkeys in this study manifested a reduction in their appetites for some brief period or periods of time. This was true of the monkeys in all groups and occurred at various times during the study period. Such behavior is not uncommon for caged primates, and no particular significance was attached to it.

Thirty-five percent of the monkeys, representing all five groups, had some sort of pigmentary change during the course of the study. These changed ranged from red spots on the face to blue areas on the abdomen to brown spots on the forehead. Many of these pigmentary changes occurred following the healing of a traumatic lesion. As with the other observed abnormalities, they were considered inconsequential.

Besides these commonly observed abnormalities, a number of clinical abnormalities were noted sporadically in these animals with no apparent group or time correlation. Nine of the monkeys had a rough haircoat for some part of the study period, fourteen developed a lump or a cyst (most of these were small swellings that were located beside the nose and were caused by a chronic infection of the canine tooth root), ten monkeys vomited on at least one occasion during study (most of these were in close association with administration of anesthesia for pulmonary function testing), five had a bout of diarrhea, eight had a distended abdomen (soon after eating), and nine had at least one occasion of no stool at all. In addition, nine of the monkeys had periods of coughing and/or wheezing shortly after pulmonary function testing, although this condition was transient. A few other observations were noted sporadically (five ocular discharge, two swollen eyes, five

rashes, two slightly dehydrated and one cloudy urine), but none of these lesions was of any consequence. Seven of the monkeys were observed to be thin and/or weak during the study. Two of these seven were CM811A and CM863A, the two early death animals. The other five completed the study and were considered to be naturally thin animals.

When all of the observed clinical abnormalities are considered, there was nothing seen in the monkeys that could be attributed to fiber exposure and, in fact, most of the observed abnormalities were commonly associated with caged primates. The fact that the protocol requirements of this study necessitated frequent moving and handling of the animals led to greatly increased opportunity for trauma and stress manifestations.

As was the case with the monkeys, the rats did not manifest any clinical signs that could be attributed to exposure to the fibrous glass test material. There were some clinical abnormalities that occurred commonly in the rats of all test groups and the control group. The signs and lesions associated with chronic respiratory disease, such as porphyrin pigmented nasal and ocular discharge and a small area of hairloss with exposed skin at the canthus of both eyes, were seen in most of the animals in every exposure group at some time during the study. The incidence of nasal and/or ocular discharge ranged from 80 to 85 percent among the groups (treatment and control) and the incidence of hairloss at the canthus ranged from 51 to 61 percent. The duration of these signs was from 2 to 3 days to 3 or 3 months.

Another commonly observed clinical abnormality was trauma. Such things as bruised tails, cuts and abrasions of the tail, and cuts on the feet that were caused by being accidentally caught in the cage door occurred in animals from all exposure groups. In the F01 group 24 percent of the animals, 19 percent in F02, 21 percent in F03, 14 percent in F04, and 22 percent in F05 had some sort of traumatic lesion at some time during the study. These lesions generally healed unenventfully and had no apparent impact on the study conclusions.

Late in the study the rats began to have a higher incidence of tumors (commonly in the abdomen and usually the spleen). Incidences ranged from 29 to 40 percent. The occurrence was evenly spread across exposure

groups and controls and was about what would be expected of aging Fischer 344 rats as a result of the Fischer rat leukemia syndrome. Another clinical abnormality that is coincidental with this syndrome and was commonly observed was general paleness. Paleness was observed in 8 to 14 percent of the animals across the exposure groups and controls.

Other commonly occurring clinical abnormalities were eye lesions (i.e. cataract and/or cloudy cornea) in 7 to 14 percent within the exposure and control groups, rough haircoat in 5 to 26 percent from group to group, some alopecia (2 to 14 percent), and some thinness or loss of body condition (4 to 14 percent).

In addition, other abnormalities were noted sporadically and with no apparent correlation to exposure level. Such abnormalities as malocclusion, head tilt, prolapsed vagina, dehydrated, yellowish discharge from the urogenital tract, diarrhea, depression, and bloating were occasionally noted.

As with the monkeys, none of the observed clinical abnormalities were considered to be associated with fiber exposure. Most of the abnormalities are associated with long term confinement of aging rats. The necessity for frequent handling of the rats contributed to the incidence of trauma and other stress-related conditions.

Hematology and Clinical Chemistry

Monkeys

Table 24 shows group means and standard deviations for each group. The baseline mean is the average of two baseline values for each parameter. Results for individual animals are shown in Tables 25 through 29.

There were no changes in mean values for hematology or clinical chemistry parameters that were outside the expected range nor were there any biologically significant variations from control values. There were occasional fluctuations in individual values for a given parameter which is expected but there was no evidence that such changes were related to fiberglass exposure.

There were several changes in the two animals that died spontaneously (i.e., 811A, F02, and 863A, F03). Both monkeys were mildly anemic. Monkey 811A had a mild regenerative anemia at baseline as judged by erythrocyte parameters and reticulocytes. In addition, the BUN was slightly elevated and the IP markedly reduced. No cause of death was determined for monkey 811A. Amyloidosis of pancreatic islets was observed in monkey 863A, was associated with a severe elevation in serum glucose, and was the apparent cause of death. Cholesterol and LDH were mildly elevated in this animal and sodium was mildly depressed.

Rats

Tables 30 and 31 show group means and standard deviations for each group. There were no changes in mean values for any exposure group that indicated an effect resulting from fiberglass exposure. There were occasional mild aberrations, for example, those that occurred in erythrocyte parameters in males from Group F04. The decreases noted resulted from moderately depressed values in two rats in which mononuclear cell leukemia occurred with attendant bone marrow suppression. Mean values were

TABLE 24. MEAN VALUES FOR HEMATOLOGY AND CLINICAL CHEMISTRY PARAMETERS: BASELINE AND TERMINAL VALUES BY GROUP.

	Dose Group	F01					F02					F03				
		Baseline	1 S.D.		Terminal	1 S.D.	Baseline	1 S.D.		Terminal	1 S.D.	Baseline	1 S.D.		Terminal	1 S.D.
HEMATOLOGY	HCT (%)	40.8	3.9		43.3	4.9	38.6	2.9		42.9	4.5	41.1	4.0		46.2	5.0
	HGB (gm/dl)	12.7	1.2		12.6	1.4	12.2	0.9		12.6	1.1	13.0	1.4		13.8	1.6
	RBC (10^6/CUMM)	6.60	0.56		6.27	0.68	6.20	0.58		6.12	0.61	6.50	0.61		6.44	0.57
	WBC (10^3/CUMM)	14.2	4.8		13.4	2.8	14.3	3.8		11.9	3.1	14.4	4.4		13.4	3.2
	RET (% RBC)	0.7	0.6		0.5	0.2	1.0	1.1		0.5	0.2	0.6	0.3		0.5	0.2
	Platelets (10^3/CUMM)	256	65		450	83	231	54		392	82	248	50		433	78
	Diff. % Neut. I	0.1	0.3		0.2	0.4	0.4	0.9		0.1	0.3	0.2	0.4		0	0
	Neut. M	36	13		33	13	37	11		39	15	39	12		35	12
	Lympho.	58	12		58	14	57	9		52	13	56	13		58	12
	Eosino.	5.8	4.3		5.5	3.5	4.8	4.4		6.8	5.3	4.8	4.0		4.1	2.4
	Baso.	0.2	0.6		0	0	0.3	0.6		0.3	0.6	0.2	0.4		0.2	0.6
	Mono.	0	0		2.3	1.5	0.1	0.4		1.5	1.6	0.2	0.4		2.4	1.2
	MCV	62	3.5		70	3.2	63	2.5		70	2.5	64	4.4		72	4.4
	NRBC/100 WBC															
BLOOD CHEMISTRY	BUN (mg/dl)	17	3.8		17	3.1	18	4.1		20	8.3	18	2.5		21	3.0
	Glucose (mg/dl)	99	26		92	17	110	34		79	17	106	22		99	22
	Creatinine (mg/dl)	1.4	0.2		1.6	0.2	1.4	0.2		1.4	0.2	1.5	0.2		1.7	0.2
	Inorganic Phosphorus (mg/dl)	5.3	1.4		3.5	0.7	5.3	1.3		4.7	1.4	5.2	1.1		3.3	0.8
	Calcium (meq/L)	5.6	0.5		5.4	0.6	5.7	0.60		5.4	0.3	5.8	0.4		5.3	0.6
	Total Bilirubin (mg/dl)	0.14	0.14		0.37	0.07	0.14	0.13		0.49	0.16	0.09	0.09		0.27	0.05
	Cholesterol (mg/dl)	119	20		134	24	107	21		138	30	116	26		122	21
	LDH (I.U./L)	315	114		205	92	278	128		158	62	292	217		180	86
	SGOT (I.U./L)	30	9.8		24	7.7	31	16.5		24	7.0	42	37.8		34	12.1
	Sodium (meq/L)	162	8.7		162	5.9	161	7.7		156	5.6	163	5.9		160	3.7
	Potassium (meq/L)	5.8	0.9		6.0	0.5	5.7	0.9		5.6	0.5	6.0	0.8		5.9	0.5

TABLE 24. (CONTINUED)

	Dose Group	F04					F05									
		Baseline	1 S.D.		Terminal	1 S.D.	Baseline	1 S.D.		Terminal	1 S.D.	Baseline	1 S.D.		Terminal	1 S.D.
HEMATOLOGY	HCT (%)	40.5	2.4		44.2	3.0	39.2	3.4		44.2	2.6					
	HGB (mg/dl)	12.8	0.6		12.9	1.0	12.2	1.0		12.9	0.7					
	RBC (10^6/CUMM)	6.54	0.45		6.18	0.39	6.21	0.51		6.74	0.32					
	WBC (10^3/CUMM)	15.8	4.9		12.0	4.0	14.0	2.9		13.2	2.8					
	RET (% RBC)	0.6	0.4		0.5	0.2	0.7	0.6		0.5	0.3					
	Platelets (10^3/CUMM)	240	54		446	100	304	77		451	85					
	Diff. % Neut. I	0.0	0.2		0.2	0.4	0.2	0.5		0	0					
	Diff. % Neut. M	37	11		33	13	36	11		28	14					
	Diff. % Lympho.	57	13		60	13	59	10		64	13					
	Diff. % Eosino.	4.6	5.0		5.1	3.7	4.6	4.2		3.6	3.6					
	Diff. % Baso.	0.0	0.2		0	0	0.0	0.2		0.2	0.6					
	Diff. % Mono.	0.6	1.0		2.0	1.5	0	0		2.5	1.4					
	MCV	62	3.3		71	3.8	64	3.2		66	2.8					
	NRBC/100 WBC															
BLOOD CHEMISTRY	BUN (mg/dl)	18	3.8		17	2.9	18	3.3		17	2.9					
	Glucose (mg/dl)	101	26		81	20	100	26		98	19					
	Creatinine (mg/dl)	1.4	0.2		1.4	0.3	1.4	0.2		1.4	0.2					
	Inorganic Phosphorus (mg/dl)	5.6	1.1		4.2	0.7	5.3	1.2		5.2	1.2					
	Calcium (meq/L)	5.8	0.4		5.3	0.4	5.7	0.3		5.2	0.2					
	Total Bilirubin (mg/dl)	0.15	0.07		0.38	0.10	0.20	0.21		0.46	0.15					
	Cholesterol (mg/dl)	113	20		130	24	124	27		151	31					
	LDH (I.U./L)	272	107		218	86	328	175		274	94					
	SGOT (I.U./L)	34	13.6		24	6.9	37	18		31	5.2					
	Sodium (meq/L)	162	5.9		160	6.2	164	5.3		160	4.4					
	Potassium (meq/L)	5.9	0.7		5.4	0.7	6.2	0.8		5.6	0.4					

TABLE 25. BASELINE AND TERMINAL VALUES FOR HEMATOLOGIES AND SERUM CHEMISTRY PARAMETERS: 15 mg/m^3 - F01

	Animal Number	M809A			M802A			M865A			M849A			M856A		
	Pathology Number	804467			804468			804469			804470			804471		
		Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
		2/12/79	2/21/79	1/14/81	2/12/79	2/21/79	1/14/81	2/12/79	2/21/79	1/14/81	2/12/79	2/21/79	1/14/81	2/12/79	2/21/79	1/14/81
HEMATOLOGY	HCT (%)	49	50	50	44	43	46	45	41	46	39	38	42	40	38	40
	HGB (gm/dl)	15.2	15.0	14.4	13.6	13.9	13.6	12.9	13.2	13.2	12.6	12.4	12.6	11.6	11.9	11.5
	RBC (10^6/CUMM)	7.59	7.26	6.70	6.89	6.03	6.39	6.68	6.36	6.25	6.54	6.35	5.93	6.20	6.17	5.68
	WBC (10^3/CUMM)	14.4	13.7	11.5	15.1	13.7	15.9	19.0	13.2	15.4	11.8	12.6	9.3	10.5	6.9	14.4
	RET (% RBC)	1.8	0.5	0.4	0.2	0.5	0.7	1.1	0.3	1.0	0.9	0.4	0.3	0.1	0.7	0.7
	Platelets (10^3/CUMM)	180	225	439	330	290	476	280	300	555	332	190	445	240	262	426
	Diff. % Neut. I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	Diff. % Neut. M	18	24	26	38	39	42	32	23	23	45	28	30	64	45	57
	Diff. % Lympho.	76	70	67	60	55	46	58	68	66	39	55	55	35	54	33
	Diff. % Eosino.	6	6	6	2	6	7	10	9	9	16	17	12	1	1	7
	Diff. % Baso.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Diff. % Mono.	0	0	1	0	0	6	0	0	2	0	0	3	0	0	2
	MCV	66	69	74	65	63	72	68	64	73	60	59	71	65	63	70
	NRBC/100 WBC															
BLOOD CHEMISTRY	BUN (mg/dl)	22	18	17	19	18	16	17	14	15	18	14	20	18	17	18
	Glucose (mg/dl)	79	104	83	122	79	83	68	58	86	126	121	126	107	77	84
	Creatinine (mg/dl)	2.1	1.7	1.8	1.6	1.7	2.1	1.2	1.2	1.4	1.1	1.3	1.5	1.3	1.3	1.8
	Inorganic Phosphorus (mg/dl)	4.3	5.9	3.2	5.5	8.3	4.1	4.2	5.4	3.6	4.8	8.1	3.7	3.8	4.9	2.1
	Calcium (meq/L)	6.3	6.2	5.7	5.5	6.0	5.7	5.1	5.0	5.4	5.2	5.2	5.7	5.3	5.4	5.4
	Total Bilirubin (mg/dl)	0.13	0.26	0.49	0.10	0.09	0.39	0.10	0.13	0.38	0.10	0.09	0.38	0.10	0.08	0.30
	Cholesterol (mg/dl)	132	136	134	113	137	148	96	114	119	85	93	102	114	147	151
	LDH (I.U./L)	214	418	132	442	216	150	458	401	218	356	264	173	288	205	176
	SGOT (I.U./L)	25	43	19	46	31	28	52	34	23	25	22	17	38	21	23
	Sodium (meq/L)	179	162	163	167	162	169	166	156	163	161	151	158	165	156	160
	Potassium (meq/L)	7.2	5.6	5.5	5.6	5.4	5.9	6.3	5.7	5.6	5.5	5.5	7.2	6.0	5.1	6.0

TABLE 25. (CONTINUED)

		Animal Number	M843A			M855A			M851A			M823A			M839A		
		Pathology Number	804472			804473			804475			804476			804477		
			Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
			2/12/79	2/21/79	1/14/81	2/12/79	2/21/79	1/14/81	2/13/79	2/22/79	1/14/81	2/13/79	2/22/79	1/14/81	2/13/79	2/21/79	1/14/81
HEMATOLOGY		HCT (%)	39	36	36	39	39	43	44	43	43	38	35	42	37	35	35
		HGB (gm/dl)	11.3	10.9	10.7	11.6	12.3	12.5	13.2	13.3	12.5	12.4	11.3	12.1	11.3	11.6	10.3
		RBC (10^6/CUMM)	5.90	5.60	5.16	6.66	6.77	6.38	7.42	7.20	6.72	6.80	6.20	6.55	5.95	5.88	5.01
		WBC (10^3/CUMM)	12.4	12.9	10.9	15.6	11.8	16.3	18.1	24.6	16.5	27.4	22.4	15.8	13.6	17.2	10.5
		RET (% RBC)	1.7	0.8	0.4	0.3	0.3	0.3	1.7	0.3	0.7	2.1	1.6	0.7	0.5	0.6	0.5
		Platelets (10^3/CUMM)	188	152	280	295	230	479	155	178	332	310	328	424	222	218	493
	Diff. %	Neut. I	0	0	0	0	0	0	0	0	1	1	1	1	0	1	0
	Diff. %	Neut. M	25	28	19	53	41	33	20	20	23	53	52	51	19	30	17
	Diff. %	Lympho.	69	66	75	44	58	65	69	74	68	42	39	42	77	67	79
	Diff. %	Eosino.	6	6	4	3	1	1	11	6	8	4	8	3	3	2	1
	Diff. %	Baso.	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	Diff. %	Mono.	0	0	2	0	0	1	0	0	0	0	0	3	0	0	3
		MCV	66	64	71	59	57	68	60	61	64	56	57	64	62	60	70
		NRBC/100 WBC															
BLOOD CHEMISTRY		BUN (mg/dl)	16	14	15	20	16	19	15	12	10	16	14	20	15	12	17
		Glucose (mg/dl)	83	151	117	100	115	95	123	118	112	110	122	88	62	65	69
		Creatinine (mg/dl)	1.4	1.4	1.5	1.5	1.6	1.8	1.5	1.2	1.6	1.5	1.6	1.6	1.7	1.6	1.5
		Inorganic Phosphorus (mg/dl)	5.4	7.3	4.6	3.7	3.1	3.2	5.5	7.0	4.4	3.9	5.6	2.9	4.2	4.0	2.5
		Calcium (meq/L)	5.6	5.1	5.5	5.5	5.4	5.9	6.0	5.6	5.6	5.9	4.8	5.6	5.8	6.0	5.1
		Total Billrubin (mg/dl)	0.05	0.09	0.48	0.66	0.17	0.30	0.43	0.13	0.44	0.07	0.01	0.28	0.01	0.06	0.32
		Cholesterol (mg/dl)	125	122	154	132	143	169	83	78	80	129	121	147	136	133	140
		LDH (I.U./L)	380	474	165	579	384	105	418	187	149	130	282	432	202	204	222
		SGOT (I.U./L)	28	32	28	43	23	13	47	19	17	32	25	38	21	19	26
		Sodium (meq/L)	175	154	168	162	152	160	170	167	174	171	150	152	162	155	157
		Potassium (meq/L)	7.1	4.6	5.9	7.7	4.7	6.2	7.5	6.0	6.2	5.5	4.5	5.9	6.3	5.3	5.9

TABLE 25. (CONTINUED)

		Animal Number	M817A			M858A											
		Pathology Number	804491			804510											
			Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
			2/13/79	2/22/79	1/14/81	2/14/79	2/23/79	1/14/81									
HEMATOLOGY		HCT (%)	41	38	43	43	42	51									
		HGB (gm/dl)	12.6	12.1	12.2	13.4	13.6	15.2									
		RBC (10^6/CUMM)	7.40	6.91	6.84	6.17	6.06	6.37									
		WBC (10^3/CUMM)	12.1	7.0	8.9	13.4	15.3	14.2									
		RET (% RBC)	0.7	1.1	0.6	0.3	0.5	0.6									
		Platelets (10^3/CUMM)	265	358	498	162	185	362									
	Diff. %	Neut. I	1	0	0	0	0	0									
		Neut. M	56	51	36	33	27	33									
		Lympho.	39	40	58	65	70	59									
		Eosino.	4	9	4	1	3	5									
		Baso.	0	0	0	0	0	0									
		Mono.	0	0	2	1	0	3									
		MCV	56	56	63	70	69	79									
		NRBC/100 WBC															
BLOOD CHEMISTRY		BUN (mg/dl)	17	18	17	25	26	22									
		Glucose (mg/dl)	115	85	88	90	117	98									
		Creatinine (mg/dl)	1.5	1.7	1.4	1.8	1.6	2.1									
		Inorganic Phosphorus (mg/dl)	5.6	5.4	4.9	6.2	4.2	4.3									
		Calcium (meq/L)	5.7	5.4	5.0	6.1	5.9	6.0									
		Total Bilirubin (mg/dl)	0.08	0.02	0.27	0.16	0.13	0.36									
		Cholesterol (mg/dl)	78	84	97	135	116	158									
		LDH (I.U./L)	112	107	427	267	156	166									
		SGOT (I.U./L)	21	15	34	26	18	30									
		Sodium (meq/L)	164	167	161	162	158	165									
		Potassium (meq/L)	5.2	6.5	6.0	6.4	5.9	6.3									

TABLE 26. BASELINE AND TERMINAL VALUES FOR HEMATOLOGIES AND SERUM CHEMISTRY PARAMETERS: 15 mg/m^3 - FO2

		Animal Number	M810A			M838A			M840A			M837A			M864A		
		Pathology Number	804478			804479			804480			804481			804482		
			Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
			2/13/79	2/23/79	1/19/81	2/21/79	3/23/79	1/19/81	2/13/79	2/22/79	1/19/81	2/13/79	2/22/79	1/19/81	2/13/79	2/22/79	1/19/81
HEMATOLOGY		HCT (%)	40	36	46	40	42	42	45	42	46	38	39	44	40	39	46
		HGB (gm/dl)	12.3	11.9	13.5	13.0	13.0	13.0	13.4	12.7	12.8	12.7	13.1	13.0	12.9	13.0	13.9
		RBC (10^6/CUMM)	6.30	5.80	6.44	6.33	6.33	5.75	7.65	6.88	6.67	6.30	6.17	6.01	6.55	6.23	6.31
		WBC (10^3/CUMM)	11.5	11.9	8.5	10.9	13.4	12.2	19.3	17.0	15.9	12.7	13.3	12.3	9.7	9.3	11.5
		RET (% RBC)	0.4	0.2	0.4	0.6	0.7	0.4	0.4	1.0	0.5	1.4	0.6	0.8	0.6	0.2	0.5
		Platelets (10^3/CUMM)	260	268	494	195	235	407	222	320	427	130	172	339	202	210	442
	Diff. %	Neut. I	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Diff. %	Neut. M	50	55	29	53	37	71	32	33	35	37	53	58	15	19	26
	Diff. %	Lympho.	42	43	57	47	58	26	64	62	52	62	47	36	70	67	55
	Diff. %	Eosino.	5	2	14	0	3	1	4	4	10	1	0	4	13	13	15
	Diff. %	Baso.	0	0	0	0	0	1	0	1	0	0	0	0	2	1	1
	Diff. %	Mono.	0	0	0	0	2	1	0	0	3	0	0	2	0	0	3
		MCV	63	63	72	63	66	74	59	61	69	61	63	74	61	63	73
		NRBC/100 WBC															
BLOOD CHEMISTRY		BUN (mg/dl)	22	30+	23	18	19	22	18	11	17	14	14	15	22	16	18
		Glucose (mg/dl)	79	105	98	113	120	77	78	131	80	80	99	71	74	78	101
		Creatinine (mg/dl)	1.6	1.7	1.7	1.7	1.5	1.4	1.3	1.4	1.4	1.5	1.4	1.6	1.2	1.1	1.6
		Inorganic Phosphorus (mg/dl)	3.6	5.0	6.5	4.0	6.6	3.3	4.8	6.3	4.5	4.2	5.3	5.6	5.0	6.8	5.8
		Calcium (meq/L)	6.1	5.6	5.6	5.8	5.2	5.0	6.1	4.7	5.4	5.5	5.4	5.5	5.9	5.3	5.9
		Total Bilirubin (mg/dl)	0.06	0.29	0.48	0.21	0.16	0.46	0.13	0.06	0.44	0.16	0.11	0.45	0.08	0.02	0.75
		Cholesterol (mg/dl)	117	113	164	99	142	150	125	106	141	90	98	144	149	159	197
		LDH (I.U./L)	170	403	263	265	231	225	215	283	104	379	184	120	319	267	117
		SGOT (I.U./L)	21	165*	26	38	27	39	34	29	27	27	17	18	34	24	18
		Sodium (meq/L)	167	158	159	157	157	150	165	147	157	162	153	158	159	151	164
		Potassium (meq/L)	6.0	4.7	5.0	5.5	5.0	5.2	5.7	3.9	5.4	5.8	4.7	5.3	6.1	5.8	6.3

+Other data omitted (hematology not performed same day): BUN: 25, Glucose: 126, Creatinine: 1.6, Inorganic Phosphorus: 6.2, Calcium: 5.7, Total Bilirubin: 0.23, Cholesterol: 131, LDH: 436, SGOT: 42, Sodium: 162, Potassium: 6.5.

*Omitted; out of range of other values, not used in determining mean and standard deviation. High value possibly due to animal being bled two days in a row.

TABLE 26. (CONTINUED)

	Animal Number	M854A			M808A			M813A			M811A			M862A		
	Pathology Number	804483			804484			804485			804486			804487		
		Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
		2/13/79	2/22/79	1/19/81	2/13/79	2/22/79	1/19/81	2/13/79	2/22/79	1/19/81	2/13/79	2/22/79	3/10/81	2/13/79	2/22/79	1/19/81
HEMATOLOGY	HCT (%)	40	39	44	41	39	41	41	39	49	35	34	32	39	35	46
	HGB (gm/dl)	12.9	12.1	12.6	12.7	12.3	12.1	12.8	12.5	14.1	10.5	10.6	10.1	12.0	10.9	13.1
	RBC (10^6/CUMM)	6.92	6.48	6.65	6.39	6.13	5.90	6.76	6.36	6.83	5.15	5.07	4.75	6.19	5.53	6.72
	WBC (10^3/CUMM)	14.3	15.2	9.9	12.1	10.9	8.9	22.8	15.0	15.2	12.3	10.8	8.6	16.5	15.4	17.7
	RET (% RBC)	0.3	0.0	0.5	0.5	0.6	0.7	0.8	0.4	0.6	5.1	3.2	0.4	0.3	0.9	0.4
	Platelets (10^3/CUMM)	235	370	356	250	205	526	242	212	421	260	182	400	190	248	219
	Diff. % Neut. I	2	2	0	0	0	0	0	0	0	0	2	0	1	0	0
	Diff. % Neut. M	41	44	28	45	44	51	45	38	39	28	35	32	25	30	15
	Diff. % Lympho.	56	54	66	52	51	40	47	49	50	72	62	62	64	60	72
	Diff. % Eosino.	1	0	5	3	5	7	7	13	11	0	1	1	10	8	11
	Diff. % Baso.	0	0	0	0	0	0	1	0	0	0	0	0	0	2	2
	Diff. % Mono.	0	0	1	0	0	2	0	0	0	0	0	5	0	0	0
	MCV	58	60	66	65	64	70	61	61	71	68	68	67	63	64	69
	NRBC/100 WBC															
BLOOD CHEMISTRY	BUN (mg/dl)	18	14	15	15	15	14	19	16	18	24	17	45	18	18	17
	Glucose (mg/dl)	187	195	73	86	96	81	173	89	81	96	136	107	117	95	54
	Creatinine (mg/dl)	1.6	1.6	1.5	1.7	1.6	1.4	1.3	1.3	1.7	1.5	1.4	1.0	1.4	1.2	1.1
	Inorganic Phosphorus (mg/dl)	6.1	8.2	4.6	5.9	5.3	4.3	4.9	4.7	5.6	4.1	7.3	1.1	3.8	4.8	5.3
	Calcium (meq/L)	5.9	5.5	5.5	6.9	6.3	5.2	5.7	5.1	5.8	6.4	5.3	5.2	5.3	5.3	5.9
	Total Bilirubin (mg/dl)	0.63	0.14	0.52	0.14	0.10	0.38	0.14	0.00	0.61	0.04	0.02	0.14	0.13	0.08	0.72
	Cholesterol (mg/dl)	109	99	150	119	119	134	87	80	118	98	108	80	91	91	133
	LDH (I.U./L)	786	329	111	110	186	87	261	144	113	273	261	257	269	282	134
	SGOT (I.U./L)	100	35	19	22	19	13	38	20	23	27	27	27	25	21	20
	Sodium (meq/L)	174	157	155	178	168	153	163	157	162	172	155	144	160	159	157
	Potassium (meq/L)	7.3	5.2	5.5	7.4	6.9	5.1	5.8	5.4	5.8	7.3	4.9	5.6	6.0	5.9	6.1

TABLE 26. (CONTINUED)

	Animal Number	M846A			M834A											
	Pathology Number	804488			804489											
		Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
		2/13/79	2/22/79	1/19/81	2/13/79	2/22/79	1/19/81									
HEMATOLOGY	HCT (%)	36	32	39	39	36	40									
	HGB (gm/dl)	11.3	10.3	11.4	11.6	11.2	11.6									
	RBC (10^6/CUMM)	5.90	5.32	5.55	6.18	5.76	5.80									
	WBC (10^3/CUMM)	21.6	21.1	13.0	14.1	11.7	8.8									
	RET (% RBC)	1.7	0.8	0.5	1.3	1.4	0.8									
	Platelets (10^3/CUMM)	148	230	319	240	322	356									
	Diff. % Neut. I	0	0	1	0	0	0									
	Diff. % Neut. M	38	22	41	36	35	40									
	Diff. % Lympho.	51	73	55	60	62	60									
	Diff. % Eosino.	11	4	2	4	3	0									
	Diff. % Baso.	0	1	0	0	0	0									
	Diff. % Mono.	0	0	1	0	0	0									
	MCV	61	61	70	63	63	70									
	NRBC/100 WBC															
BLOOD CHEMISTRY	BUN (mg/dl)	23	16	18	19	14	17									
	Glucose (mg/dl)	71	117	52	107	122	71									
	Creatinine (mg/dl)	1.3	1.3	1.2	1.7	1.7	1.5									
	Inorganic Phosphorus (mg/dl)	3.5	7.4	4.5	4.2	5.9	5.8									
	Calcium (meq/L)	7.0	4.8	5.1	6.1	5.2	5.5									
	Total Bilirubin (mg/dl)	0.25	0.13	0.45	0.15	0.05	0.48									
	Cholesterol (mg/dl)	73	82	100	103	103	148									
	LDH (I.U./L)	300	291	172	212	256	198									
	SGOT (I.U./L)	45	32	25	29	27	32									
	Sodium (meq/L)	170	154	156	168	156	162									
	Potassium (meq/L)	6.9	4.6	6.3	5.5	5.2	6.1									

TABLE 27. BASELINE AND TERMINAL VALUES FOR HEMATOLOGIES AND SERUM CHEMISTRY PARAMETERS: 5 mg/m^3 - F03

		Animal Number	M833A			M836A			M841A			M825A			M835A		
		Pathology Number	804474			804490			804492			804493			804494		
			Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
			2/13/79	2/22/79	1/5/81	2/13/79	2/22/79	1/5/81	2/13/79	2/22/79	1/5/81	2/13/79	2/22/79	1/5/81	2/21/79	3/23/79	1/5/81
HEMATOLOGY		HCT (%)	45	41	51	52	48	52	38	35	39	43	42	53	44	47	52
		HGB (gm/dl)	13.9	13.0	15.2	16.0	15.4	15.6	11.8	11.1	11.7	13.6	13.7	15.9	14.8	15.0	15.8
		RBC (10^6/CUMM)	7.59	6.84	7.41	7.53	6.89	6.73	6.03	5.59	5.50	6.48	6.47	7.02	7.40	7.68	7.18
		WBC (10^3/CUMM)	13.4	11.6	14.2	21.6	22.3	14.8	18.2	15.5	11.2	11.0	9.2	16.6	12.1	16.0	12.3
		RET (% RBC)	0.4	0.4	0.5	1.4	0.2	0.6	1.1	0.6	0.6	0.6	0.6	0.3	0.7	1.0	1.0
		Platelets (10^3/CUMM)	220	308	576	225	222	436	185	260	378	235	265	466	195	220	275
	Diff. %	Neut. I	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0
		Neut. M	53	46	50	59	39	52	23	40	20	37	37	44	30	29	33
		Lympho.	45	50	46	30	51	41	65	53	71	60	62	51	62	61	64
		Eosino.	2	4	1	11	9	3	12	7	6	2	0	3	7	10	1
		Baso.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Mono.	0	0	3	0	0	4	0	0	3	0	0	2	1	0	2
		MCV	59	60	69	70	70	77	63	63	71	66	65	75	60	63	72
		NRBC/100 WBC															
BLOOD CHEMISTRY		BUN (mg/dl)	30	22	22	21	16	19	18	14	21	21	20	24	14	18	23
		Glucose (mg/dl)	76	136	78	136	105	132	120	92	76	76	71	94	105	135	76
		Creatinine (mg/dl)	1.5	1.3	1.6	2.1	1.7	1.6	1.5	1.3	1.7	1.7	1.7	1.9	1.6	1.4	2.0
		Inorganic Phosphorus (mg/dl)	5.0	6.3	3.5	4.9	6.5	2.3	5.1	6.9	1.9	3.0	4.2	2.8	5.4	7.6	3.7
		Calcium (meq/L)	7.0	4.7	3.4	6.4	5.9	5.5	5.7	5.3	3.7	5.7	5.6	5.9	5.6	5.3	5.6
		Total Bilirubin (mg/dl)	0.12	0.04	0.32	0.15	0.07	0.24	0.09	0.00	0.19	0.07	0.06	0.30	0.18	0.09	0.35
		Cholesterol (mg/dl)	137	101	126	92	105	115	136	146	149	132	141	140	154	175	158
		LDH (I.U./L)	275	315	202	902	334	180	149	401	133	179	115	155	260	196	220
		SGOT (I.U./L)	19	23	17	50	31	28	24	35	26	23	20	35	29	22	35
		Sodium (meq/L)	178	151	161	170	165	161	163	154	153	167	158	160	155	160	159
		Potassium (meq/L)	6.1	4.0	6.2	7.0	5.7	5.7	5.6	4.5	5.8	6.1	5.6	6.6	5.4	5.7	5.1

TABLE 27. (CONTINUED)

		Animal Number	M815A			M824A			M814A			M863A			M850A		
		Pathology Number	804495			804496			804497			804498			804499		
			Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
			2/14/79	2/23/79	1/5/81	2/14/79	2/23/79	1/5/81	2/14/79	2/23/79	1/5/81	2/14/79	2/23/79	3/3/80*	2/14/79	2/23/79	1/5/81
HEMATOLOGY		HCT (%)	41	40	40	41	41	46	38	39	48	36	35	25	44	43	49
		HGB (gm/dl)	12.7	12.4	12.0	12.5	12.9	13.6	11.7	12.6	14.0	11.3	11.0	8.4	14.0	14.4	14.7
		RBC (10^6/CUMM)	6.26	6.01	5.51	6.69	6.67	6.76	6.22	6.46	6.76	5.65	5.27	3.89	6.02	6.15	6.18
		WBC (10^3/CUMM)	20.0	14.4	14.5	14.0	13.6	12.4	9.7	8.2	10.8	12.5	18.4	8.2	19.2	18.7	20.1
		RET (% RBC)	0.3	0.6	0.5	0.4	0.5	0.3	0.3	0.3	0.7	0.7	0.8	0.7	0.2	0.5	0.5
		Platelets (10^3/CUMM)	252	242	410	200	195	345	295	262	479	205	250	312	302	380	558
	Diff. %	Neut. I	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0
	Diff. %	Neut. M	23	24	22	53	42	34	67	45	48	32	37	46	29	50	32
	Diff. %	Lympho.	74	75	73	47	55	62	30	52	46	63	61	48	59	45	55
	Diff. %	Eosino.	2	0	2	0	3	3	2	2	6	5	1	0	11	5	9
	Diff. %	Baso.	1	1	0	0	0	0	0	1	0	0	0	0	0	0	2
	Diff. %	Mono.	0	0	3	0	0	1	1	0	0	0	1	3	1	0	2
		MCV	67	67	73	62	62	68	62	61	71	65	66	65	73	71	79
		NRBC/100 WBC															
BLOOD CHEMISTRY		BUN (mg/dl)	23	22	25	16	17	20	17	16	23	17	17	47	21	16	16
		Glucose (mg/dl)	109	109	140	103	122	95	79	124	120	141	144	499	84	117	81
		Creatinine (mg/dl)	1.7	1.6	1.9	1.7	1.5	5.7	1.3	1.3	1.5	1.4	1.2	0.4	1.5	1.2	1.5
		Inorganic Phosphorus (mg/dl)	5.0	5.0	3.9	4.9	5.2	3.7	4.0	4.0	3.9	6.1	5.5	3.9	5.3	6.6	3.3
		Calcium (meq/L)	6.7	5.9	5.0	6.1	6.0	5.7	5.1	5.4	5.8	5.8	6.0	4.9	6.3	6.5	5.1
		Total Bilirubin (mg/dl)	0.11	0.12	0.25	0.02	0.01	0.35	0.00	0.02	0.23	0.15	0.02	0.46	0.19	0.08	0.29
		Cholesterol (mg/dl)	112	94	104	95	94	114	85	82	96	131	114	325	132	130	113
		LDH (I.U./L)	220	260	162	202	193	126	373	143	133	246	177	559	455	180	130
		SGOT (I.U./L)	32	39	35	30	32	46	22	18	19	38	21	205	68	31	28
		Sodium (meq/L)	172	160	154	165	159	160	161	156	166	164	156	135	165	161	158
		Potassium (meq/L)	7.0	5.5	5.4	6.5	5.8	5.8	6.0	5.0	6.6	5.8	6.0	6.0	7.2	6.5	5.9
		*Not used in calculating means & standard deviations; animal died with diabetes															

TABLE 27. (CONTINUED)

		Animal Number	M803A			M822A											
		Pathology Number	804500			804501											
			Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
			2/14/79	2/23/79	1/5/81	2/14/79	2/23/79	1/5/81									
HEMATOLOGY		HCT (%)	40	38	43	42	41	43									
		HGB (gm/dl)	12.4	12.1	12.8	12.5	13.1	13.2									
		RBC (10^6/CUMM)	6.78	6.45	6.29	6.41	6.54	6.12									
		WBC (10^3/CUMM)	18.0	10.7	11.0	14.3	9.8	14.7									
		RET (% RBC)	0.2	0.6	0.5	0.1	0.7	0.3									
		Platelets (10^3/CUMM)	255	270	455	230	180	459									
	Diff. %	Neut. I	0	0	0	0	0	0									
		Neut. M	37	23	19	24	43	48									
		Lympho.	59	77	75	69	55	43									
		Eosino.	3	0	2	7	1	6									
		Baso.	0	0	0	0	1	0									
		Mono.	1	0	4	0	0	3									
		MCV	60	59	69	66	63	71									
		NRBC/100 WBC															
BLOOD CHEMISTRY		BUN (mg/dl)	19	16	24	19	15	19									
		Glucose (mg/dl)	84	77	92	112	102	98									
		Creatinine (mg/dl)	1.5	1.4	1.8	1.6	1.6	1.7									
		Inorganic Phosphorus (mg/dl)	4.3	3.6	3.0	6.4	5.4	3.4									
		Calcium (meq/L)	6.1	5.3	5.5	6.1	6.3	5.7									
		Total Bilirubin (mg/dl)	0.09	0.03	0.27	0.39	0.07	0.27									
		Cholesterol (mg/dl)	136	107	141	127	114	120									
		LDH (I.U./L)	205	705	168	781	125	150									
		SGOT (I.U./L)	24	175	26	135	62	64									
		Sodium (meq/L)	170	156	160	178	165	163									
		Potassium (meq/L)	6.3	4.7	5.6	8.0	7.3	6.2									

TABLE 28. BASELINE AND TERMINAL VALUES FOR HEMATOLOGIES AND SERUM CHEMISTRY PARAMETERS: 5 mg/m^3 - F04

		Animal Number	M801A			M819A			M830A			M831A			M842A		
		Pathology Number	804466			804502			804503			804504			804505		
			Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
			2/21/79	3/8/79	12/29/80	2/14/79	2/23/79	12/29/80	2/14/79	2/23/79	12/29/80	2/14/79	2/23/79	12/29/80	2/14/79	2/23/79	12/29/80
HEMATOLOGY		HCT (%)	41	41	46	44	42	46	42	38	43	43	40	46	39	39	45
		HGB (gm/dl)	13.4	12.5	13.3	13.8	13.4	13.1	13.5	12.2	12.3	13.5	12.8	14.0	12.3	12.5	12.9
		RBC (10^6/CUMM)	6.92	6.57	6.41	7.51	7.14	6.81	7.07	6.46	6.00	6.46	6.07	6.17	6.40	6.46	6.44
		WBC (10^3/CUMM)	9.9	9.3	9.8	28.9	26.1	19.2	13.7	13.3	10.0	18.3	16.8	14.2	17.0	15.6	11.1
		RET (% RBC)	0.3	0.4	0.1	0.3	0.8	0.2	0.1	0.9	0.7	1.0	1.0	0.8	1.4	0.4	0.4
		Platelets (10^3/CUMM)	310	402	479	265	212	384	285	195	397	242	392	703	180	250	442
	Diff. %	Neut. I	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		Neut. M	34	41	31	24	38	17	17	37	26	40	36	41	27	31	27
		Lympho.	60	52	60	73	59	74	81	63	73	43	50	54	62	55	59
		Eosino.	3	7	7	2	3	6	2	0	1	15	13	5	1	14	14
		Baso.	3	0	0	0	0	0	0	0	0	0	1	0	0	0	0
		Mono.	0	0	2	0	0	3	0	0	0	2	0	0	0	0	0
		MCV	60	63	72	60	59	67	60	59	72	66	66	75	61	60	70
		NRBC/100 WBC															
BLOOD CHEMISTRY		BUN (mg/dl)	17	17	17	24	20	21	16	17	15	15	16	14	16	14	21
		Glucose (mg/dl)	99	73	80	83	114	67	82	97	63	71	99	75	116	97	119
		Creatinine (mg/dl)	1.3	1.3	1.3	1.5	1.4	1.6	1.4	1.4	1.3	1.3	1.1	1.3	1.6	1.5	1.9
		Inorganic Phosphorus (mg/dl)	4.2	6.9	4.0	5.2	5.1	5.2	8.1	6.0	4.8	6.1	6.0	4.9	6.7	5.3	2.9
		Calcium (meq/L)	6.1	6.1	5.4	6.3	6.0	6.0	6.6	6.1	5.3	6.1	5.6	5.6	6.3	5.7	5.3
		Total Bilirubin (mg/dl)	0.16	0.12	0.39	0.16	0.08	0.31	0.11	0.30	0.34	0.13	0.08	0.38	0.18	0.14	0.35
		Cholesterol (mg/dl)	126	132	140	102	95	106	106	97	100	104	84	116	126	117	142
		LDH (I.U./L)	233	227	333	265	116	181	165	326	148	213	310	153	283	129	168
		SGOT (I.U./L)	29	26	35	37	31	34	23	44	16	31	44	18	30	18	21
		Sodium (meq/L)	153	155	162	169	161	174	172	160	158	167	156	158	171	165	167
		Potassium (meq/L)	5.7	6.0	4.9	7.0	6.4	6.5	6.7	6.6	5.2	7.2	5.7	5.7	6.6	5.6	6.2

TABLE 28. (CONTINUED)

	Animal Number	M832A			M818A			M828A			M812A			M867A		
	Pathology Number	804506			804507			804508			804509			804511		
		Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
		2/22/79	3/8/79	12/29/80	2/14/79	2/23/79	12/29/80	2/14/79	2/23/79	12/29/80	2/14/79	2/23/79	12/29/80	2/14/79	2/23/79	12/29/80
HEMATOLOGY	HCT (%)	39	44	43	40	38	44	38	36	40	42	42	43	41	42	43
	HGB (gm/dl)	12.5	13.4	12.2	12.5	12.5	13.1	12.3	11.8	12.2	12.5	13.3	12.5	13.4	13.8	13.0
	RBC (10^6/CUMM)	6.53	7.20	6.34	6.27	6.01	5.99	6.13	5.82	5.61	6.58	6.66	6.01	6.36	6.52	5.68
	WBC (10^3/CUMM)	12.7	19.3	11.3	17.2	12.6	12.8	15.2	17.7	8.4	11.6	15.5	9.4	18.8	15.5	18.2
	RET (% RBC)	1.7	0.7	0.6	0.4	0.9	0.8	0.2	0.5	0.6	0.2	0.1	0.4	0.4	0.5	0.4
	Platelets (10^3/CUMM)	235	242	363	225	222	411	240	290	419	292	315	569	165	205	416
	Diff. % Neut. I	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1
	Diff. % Neut. M	37	24	24	48	25	28	36	25	15	41	54	44	57	41	61
	Diff. % Lympho.	57	71	72	20	73	65	53	60	75	53	44	44	40	58	32
	Diff. % Eosino.	6	5	2	1	2	3	9	15	5	5	2	10	0	1	4
	Diff. % Baso.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Diff. % Mono.	0	0	2	1	0	3	2	0	5	1	0	2	3	0	2
	MCV	60	62	67	65	64	73	62	62	72	65	64	71	65	65	75
	NRBC/100 WBC															
BLOOD CHEMISTRY	BUN (mg/dl)	21	19	20	19	14	15	16	17	17	16	11	15	16	15	15
	Glucose (mg/dl)	75	68	77	153	147	117	82	107	82	94	168	71	88	88	61
	Creatinine (mg/dl)	1.4	1.4	1.4	1.6	1.4	1.1	1.2	1.3	1.1	1.4	1.6	1.3	1.5	1.4	1.3
	Inorganic Phosphorus (mg/dl)	4.9	4.8	3.5	7.1	7.8	4.7	6.0	3.6	3.7	5.3	6.1	4.3	4.9	6.0	5.2
	Calcium (meq/L)	5.2	5.9	5.1	6.0	5.5	5.1	5.6	5.5	4.9	5.8	5.4	5.1	6.2	6.2	5.7
	Total Bilirubin (mg/dl)	0.12	0.08	0.35	0.13	0.18	0.58	0.09	0.08	0.57	0.10	0.07	0.49	0.14	0.35	0.32
	Cholesterol (mg/dl)	99	115	123	125	121	121	108	96	136	178	147	182	90	98	105
	LDH (I.U./L)	292	134	156	308	384	316	104	176	163	373	452	400	385	317	328
	SGOT (I.U./L)	40	24	21	35	35	34	21	23	19	40	67	32	36	51	30
	Sodium (meq/L)	159	156	160	173	156	154	162	156	153	165	153	158	167	165	153
	Potassium (meq/L)	5.9	5.5	4.8	6.0	4.4	4.9	5.9	4.6	5.2	6.0	5.0	5.5	5.7	6.0	4.1

TABLE 28. (CONTINUED)

Animal Number			M807A			M857A													
Pathology Number			804512			804513													
			Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	dase II	Terminal	Base I	Base II	Terminal
			2/14/79	2/23/79	12/29/80	2/14/79	2/23/79	12/29/80									
HEMATOLOGY		HCT (%)	43	42	46	39	35	40									
		HGB (gm/dl)	12.9	13.1	13.0	12.0	11.6	11.5									
		RBC (10^6/CUMM)	7.11	7.11	6.83	6.74	6.06	5.91									
		WBC (10^3/CUMM)	16.8	14.4	9.2	6.7	6.3	5.4									
		RET (% RBC)	1.3	0.7	0.4	0.1	0.1	0.3									
		Platelets (10^3/CUMM)	260	295	502	230	175	391									
	Diff. %	Neut. I	0	0	1	0	0	0									
		Neut. M	41	53	34	35	55	42									
		Lympho.	48	45	57	64	45	56									
		Eosino.	8	2	5	0	0	1									
		Baso.	0	0	0	0	0	0									
		Mono.	3	0	3	1	0	1									
		MCV	61	60	67	58	58	68									
		NRBC/100 WBC															
BLOOD CHEMISTRY		BUN (mg/dl)	16	13	18	23	16	15									
		Glucose (mg/dl)	115	103	78	75	100	65									
		Creatinine (mg/dl)	1.5	1.4	1.2	1.8	1.4	1.6									
		Inorganic Phosphorus (mg/dl)	4.8	4.7	3.5	5.2	4.7	3.9									
		Calcium (meq/L)	5.7	5.6	4.9	5.9	5.3	4.9									
		Total Bilirubin (mg/dl)	0.11	0.22	0.26	0.26	0.24	0.32									
		Cholesterol (mg/dl)	122	113	131	119	100	140									
		LDH (I.U./L)	446	425	178	281	215	266									
		SGOT (I.U./L)	34	67	21	21	19	18									
		Sodium (meq/L)	162	160	159	166	152	162									
		Potassium (meq/L)	6.5	5.6	5.5	5.9	4.6	5.4									

TABLE 29. BASELINE AND TERMINAL VALUES FOR HEMATOLOGIES AND SERUM CHEMISTRY PARAMETERS: CONTROL - F05

	Animal Number	M845A			M860A			M820A			M816A			M806A		
	Pathology Number	804514			804515			804516			804517			804518		
		Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
		2/12/79	2/21/79	12/22/80	2/12/79	2/21/79	12/22/80	2/12/79	2/21/79	12/22/80	2/12/79	2/21/79	12/22/80	2/12/79	2/21/79	12/22/80
HEMATOLOGY	HCT (%)	45	41	47	39	38	41	41	37	46	37	38	40	48	43	44
	HGB (gm/dl)	13.5	13.1	13.7	11.7	11.9	11.7	12.5	12.0	13.4	11.3	12.0	12.0	13.4	13.7	12.8
	RBC (10^6/CUMM)	6.40	6.31	6.75	5.97	5.95	6.08	6.45	6.35	7.11	5.71	5.97	6.24	7.18	7.16	6.94
	WBC (10^3/CUMM)	12.6	13.9	18.2	13.4	16.0	12.0	7.9	9.2	9.7	14.3	14.2	11.0	13.7	11.4	10.1
	RET (% RBC)	0.4	0.6	1.1	0.4	1.0	0.2	0.3	0.1	0.7	1.8	0.3	0.8	0.2	0.2	0.3
	Platelets (10^3/CUMM)	342	500	348	290	228	368	232	250	447	342	422	566	322	355	474
	Diff. % Neut. I	0	0	0	0	1	0	0	0	0	0	1	0	0	1	0
	Diff. % Neut. M	49	49	63	28	28	44	29	42	17	32	30	32	26	43	32
	Diff. % Lympho.	48	49	32	60	65	46	61	47	79	68	67	66	74	56	61
	Diff. % Eosino.	3	2	3	12	6	6	10	11	1	0	2	1	0	0	1
	Diff. % Baso.	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
	Diff. % Mono.	0	0	2	0	0	3	0	0	3	0	0	1	0	0	6
	MCV	70	66	69	65	65	68	64	59	65	66	64	64	67	61	63
	NRBC/100 WBC															
BLOOD CHEMISTRY	BUN (mg/dl)	22	17	24	21	20	19	13	11	13	14	16	13	17	18	18
	Glucose (mg/dl)	64	72	82	62	64	77	102	126	127	112	126	100	79	97	64
	Creatinine (mg/dl)	1.5	1.5	1.3	1.2	1.3	1.4	1.4	1.6	1.7	1.1	1.4	1.3	1.5	1.7	1.6
	Inorganic Phosphorus (mg/dl)	4.0	4.0	3.2	4.2	6.1	4.1	4.8	5.4	6.6	4.2	4.9	3.7	5.7	5.6	4.0
	Calcium (meq/L)	5.3	5.4	5.2	5.5	5.9	5.0	5.8	5.7	5.6	5.4	6.2	5.1	5.9	6.6	5.3
	Total Bilirubin (mg/dl)	0.10	0.17	0.69	0.10	0.13	0.44	0.10	0.14	0.32	0.22	0.39	0.63	0.10	0.17	0.53
	Cholesterol (mg/dl)	91	109	104	119	142	124	125	128	161	168	208	216	130	151	157
	LDH (I.U./L)	420	352	412	160	159	214	300	585	265	256	187	259	269	235	417
	SGOT (I.U./L)	36	26	35	28	26	28	37	65	31	29	25	28	26	26	30
	Sodium (meq/L)	164	155	153	162	166	164	166	159	164	158	163	154	166	166	157
	Potassium (meq/L)	6.5	5.3	5.9	6.2	6.6	6.1	5.9	6.1	6.3	5.3	5.4	5.0	6.8	6.4	5.6

TABLE 29. (CONTINUED)

		Animal Number	M829A			M852A			M853A			M844A			M805A		
		Pathology Number	804519			804520			804521			804522			804523		
			Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
			2/12/79	2/21/79	12/22/80	2/12/79	2/21/79	12/22/80	2/12/79	2/21/79	12/22/80	2/12/79	2/21/79	12/22/80	2/12/79	2/21/79	12/22/80
HEMATOLOGY		HCT (%)	39	37	44	43	39	46	37	34	42	39	35	48	40	37	44
		HGB (gm/dl)	11.7	11.7	12.7	13.2	13.1	13.2	10.9	10.4	12.8	11.5	11.1	14.0	12.6	12.0	12.5
		RBC (10^6/CUMM)	6.35	6.22	6.70	6.67	6.46	6.86	6.01	5.59	6.87	5.54	5.26	6.81	6.88	6.44	7.10
		WBC (10^3/CUMM)	17.0	15.4	15.4	20.4	17.0	18.3	13.3	15.0	14.6	17.1	11.0	12.0	15.5	14.2	12.4
		RET (% RBC)	0.3	0.4	0.4	1.3	0.6	0.3	0.3	1.3	0.6	0.4	0.6	0.1	1.2	0.5	0.5
		Platelets (10^3/CUMM)	172	280	582	238	288	424	418	302	411	295	298	557	238	255	350
	Diff. %	Neut. I	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		Neut. M	23	25	19	30	24	25	41	24	13	54	28	28	46	38	22
		Lympho.	74	67	69	65	65	68	48	71	73	46	64	63	53	62	70
		Eosino.	3	8	7	4	11	5	11	5	13	0	8	8	1	0	5
		Baso.	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0
		Mono.	0	0	3	0	0	2	0	0	1	0	0	1	0	0	3
		MCV	63	60	66	65	61	67	62	61	62	70	67	70	59	58	62
		NRBC/100 WBC															
BLOOD CHEMISTRY		BUN (mg/dl)	18	21	17	18	18	16	25	21	15	19	17	16	21	16	18
		Glucose (mg/dl)	86	114	113	127	113	91	87	179	89	102	113	91	113	87	117
		Creatinine (mg/dl)	1.2	1.3	1.3	1.2	1.3	1.2	1.5	1.4	1.6	1.4	1.5	1.7	1.5	1.4	1.5
		Inorganic Phosphorus (mg/dl)	5.5	5.4	7.1	4.9	6.5	5.0	3.9	9.0	5.3	4.9	6.2	6.1	5.3	5.2	5.7
		Calcium (meq/L)	5.6	6.0	5.1	5.5	5.3	5.0	5.6	5.3	5.1	6.0	6.0	5.6	5.6	6.0	5.1
		Total Bilirubin (mg/dl)	0.10	0.16	0.40	0.50	0.16	0.34	0.10	0.06	0.60	0.06	0.13	0.40	0.10	0.19	0.26
		Cholesterol (mg/dl)	110	107	130	117	133	170	93	102	122	117	134	167	91	96	126
		LDH (I.U./L)	199	143	338	900	369	242	363	263	347	368	257	175	319	210	240
		SGOT (I.U./L)	27	27	41	81	40	34	30	30	33	35	25	22	55	35	31
		Sodium (meq/L)	170	162	162	164	161	159	172	156	157	172	161	168	171	166	162
		Potassium (meq/L)	6.7	6.1	6.0	6.4	4.8	5.0	7.1	5.1	5.4	7.0	4.4	5.8	6.9	6.1	5.3

TABLE 29. (CONTINUED)

		Animal Number	M868A			M861A											
		Pathology Number	804524			804525											
			Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal	Base I	Base II	Terminal
			2/12/79	2/21/79	12/22/80	2/12/79	2/21/79	12/22/80									
HEMATOLOGY		HCT (%)	36	35	42	43	39	47									
		HGB (gm/dl)	10.9	11.2	12.5	13.4	13.0	13.7									
		RBC (10^6/CUMM)	5.58	5.61	6.48	6.65	6.30	6.90									
		WBC (10^3/CUMM)	15.2	8.0	12.8	15.4	15.5	11.9									
		RET (% RBC)	0.7	0.3	0.3	1.9	1.9	1.0									
		Platelets (10^3/CUMM)	255	222	381	355	405	504									
	Diff. %	Neut. I	2	0	0	0	0	0									
		Neut. M	41	34	20	44	64	21									
		Lympho.	51	60	67	56	34	73									
		Eosino.	6	5	10	0	2	4									
		Baso.	0	1	0	0	0	0									
		Mono.	0	0	3	0	0	2									
		MCV	65	63	65	65	63	69									
		NRBC/100 WBC															
BLOOD CHEMISTRY		BUN (mg/dl)	14	15	16	22	20	17									
		Glucose (mg/dl)	81	87	106	111	103	115									
		Creatinine (mg/dl)	1.5	1.4	1.4	1.8	1.7	1.5									
		Inorganic Phosphorus (mg/dl)	3.8	6.9	6.0	4.4	6.3	6.1									
		Calcium (meq/L)	5.5	5.4	5.2	5.9	6.1	5.2									
		Total Bilirubin (mg/dl)	0.10	0.11	0.31	0.35	1.03	0.67									
		Cholesterol (mg/dl)	88	141	168	134	136	170									
		LDH (I.U./L)	259	259	286	362	670	96									
		SGOT (I.U./L)	26	24	34	40	88	23									
		Sodium (meq/L)	169	163	162	172	155	161									
		Potassium (meq/L)	6.6	5.9	5.2	6.6	7.5	5.7									

TABLE 30. GROUP MEAN VALUES FOR HEMATOLOGIES AND CLINICAL CHEMISTRY PARAMETERS IN MALE RATS

	Dose Group	F01		F02		F03		F04		F05	
		Mean	1 S. D.	Mean	1 S. D.	Mean	1 S. D.	Mean	1 S. D.	Mean	1 S. D.
HEMATOLOGY	HCT (%)	48	5.9	49	4.1	49	4.4	44	8.0	50	6.1
	HGB (G%)	15.9	2.2	16.1	1.5	15.9	1.3	14.5	2.3	16.2	1.9
	RBC (10^6 CUMM)	9.00	1.56	9.06	0.84	8.86	1.27	8.13	1.53	9.12	1.15
	RET (% RBC)	1.8	1.9	1.8	0.6	2.4	1.4	2.0	0.9	1.2	0.5
	Platelets (10^3/CUMM)	503	90	498	72	515	108	574	158	506	124
	WBC (10^3/CUMM)	4.2	1.3	5.1	1.1	4.6	1.1	7.9	6.0	5.9	1.9
	DIFF. % Neut. I	0.4	1.3	0.0	0.0	0.0	0.0	0.2	0.7	0.0	0.0
	DIFF. % Neut. M	53	5.7	47	9.1	47	7.0	50	13.6	56	14.3
	DIFF. % Lympho.	45	5.3	50	9.7	50	7.7	48	13.4	42	14.2
	DIFF. % Eosino.	1.2	1.0	2.2	1.9	3.1	4.4	1.5	1.5	1.1	0.9
	DIFF. % Baso.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	DIFF. % Mono.	0.6	0.7	0.4	0.5	0.2	0.5	0.4	0.5	0.0	0.0
	MCV	53	3.4	54	1.4	55	5.0	54	5.0	55	1.4
	NRBC/100 WBC	1.8	2.1	4.5	3.1	2.1	1.7	3.1	2.4	2.7	2.3
BLOOD CHEMISTRY AND BODY WEIGHTS	Glucose (mg/dl)	126	26	152	14	122	20	128	23	129	13
	BUN (mg/dl)	18	2.7	20	1.5	21	2.8	21	4.4	19	3.1
	Creatinine (mg/dl)	0.6	0.1	0.7	0.2	0.7	0.1	0.7	0.1	0.7	0.1
	Inorganic Phosphorus (mg/dl)	5.0	0.7	4.9	0.2	4.7	0.6	4.9	0.6	4.5	0.5
	Calcium (meq/L)	4.6	0.2	5.0	0.2	5.4	0.3	5.4	0.4	5.1	0.2
	Total Bilirubin (mg/dl)	0.50	0.07	0.62	0.14	0.59	0.13	0.80	0.55	0.66	0.24
	Cholesterol (mg/dl)	94	31	85	16	100	28	169	121	93	32
	LDH (I.U./L)	543	136	510	118	694	132	639	110	655	169
	SGOT (I.U./L)	90	15	98	21	92	15	111	32	109	42
	Sodium (meq/L)	146	1.6	147	1.7	162	8.5	151	2.7	148	0.9
	Potassium (meq/L)	5.1	0.5	5.2	0.4	5.6	0.5	5.6	0.5	5.3	0.3

TABLE 31. GROUP MEAN VALUES FOR HEMATOLOGIES AND CLINICAL CHEMISTRY PARAMETERS IN FEMALE RATS

	Dose Group	F01		F02		F03		F04		F05	
		Mean	1 S. D.	Mean	1 S. D.	Mean	1 S. D.	Mean	1 S. D.	Mean	1 S. D.
HEMATOLOGY	HCT (%)	42	3.5	43	1.0	43	2.9	43	1.4	43	1.9
	HGB (G%)	14.5	0.9	14.6	0.4	14.6	0.8	14.6	0.6	14.7	0.7
	RBC (10^6 CUMM)	7.76	0.54	7.96	0.19	7.86	0.47	7.97	0.30	7.95	0.25
	RET (% RBC)	1.7	0.5	1.4	0.3	1.2	0.6	1.4	0.5	1.2	0.4
	Platelets (10^3/CUMM)	463	82	429	77	470	87	468	81	455	66
	WBC (10^3/CUMM)	3.9	1.1	4.0	1.2	3.6	1.0	4.5	1.0	4.1	1.3
	DIFF. % Neut. I	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	DIFF. % Neut. M	44	9.3	42	8.4	45	10.8	49	9.1	47	8.2
	DIFF. % Lympho.	54	8.8	56	9.1	53	10.5	48	9.1	51	8.5
	DIFF. % Eosino.	1.2	1.5	1.2	1.2	1.6	1.3	2.1	1.4	1.4	1.4
	DIFF. % Baso.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	DIFF. % Mono.	0.3	0.5	0.2	0.5	0.1	0.3	0.3	0.5	0.3	0.5
	MCV	54	2.3	54	1.0	54	2.0	54	0.9	54	1.5
	NRBC/100 WBCI	4.8	2.8	3.4	1.9	3.7	2.8	4.0	2.2	3.0	1.8
BLOOD CHEMISTRY AND BODY WEIGHTS	Glucose (mg/dl)	144	12	143	24	132	18	138	16	132	16
	BUN (mg/dl)	17	1.4	16	2.6	19	1.8	15	2.0	18	3.5
	Creatinine (mg/dl)	0.7	0.1	0.6	0.1	0.6	0.1	0.6	0.05	0.5	0.1
	Inorganic Phosphorus (mg/dl)	4.9	0.4	4.6	0.8	4.3	1.1	4.1	0.5	4.2	0.5
	Calcium (meq/L)	4.8	0.2	5.2	0.2	5.4	0.3	5.3	0.2	5.2	0.2
	Total Bilirubin (mg/dl)	0.54	0.24	0.54	0.12	0.39	0.29	0.63	0.19	0.65	0.27
	Cholesterol (mg/dl)	122	52	131	28	113	35	150	45	113	35
	LDH (I.U./L)	365	108	334	97	498	89	485	44	427	81
	SGOT (I.U./L)	88	22	103	34	118	36	108	24	126	23
	Sodium (meq/L)	146	1.2	147	3.6	158	7.4	151	3.8	147	2.3
	Potassium (meq/L)	4.9	0.7	5.3	0.4	5.4	0.3	5.4	0.5	5.1	0.6

essentially all within expected limits and comparable to those of control rats, although there were moderate individual variations in most parameters as is normally expected in rats of this age. Such variations in erythrocyte parameters were most prominent in rats with mononuclear cell leukemia, a common finding in aging Fischer 344 rats.

Body Weight and Growth

All rats and monkeys were weighed on a weekly basis for the first month of this chronic study and monthly thereafter. The monkeys were weighed in their cages and the rats were weighed on a digital balance using an automatic capture and recording system. Body weight determinations for dose groups F01 and F03 (April 1980) and F05 (November 1979 and January 1980) were misplaced and are not included.

Three time intervals were selected to statistically compare the body weight data between does groups. There were no significant effects upon body weight from exposure of the rats or monkeys to any of the levles of fiber during the course of the experiment. The following sections are summaries of the statistical observations about each time period and each exposure category.

Monkeys

Table G-1 contains the summary analyses performed on the monkey body weight data. All individual body weight data are tabulated by dose group in Tables G-2 through G-6. The body weight data are presented in Figure 37.

Results of 0-, 9-, and 18-month monkey body weight comparisons. Overall comparisons of the body weight of the monkeys in each dose group showed no significant differences at 0, 9, and 18 months.

Results of 0-18, 0-9, and 9-18 percent weight gain comparisons in monkeys. Overall comparisons of animals dosed in these groups showed no significant differences over the entire 18-month period. Similarly, over the second 9-month period, no statistically significant dose effects were present. The analysis for the first 9 months, however, showed significant differences. Specific inter-group comparisons performed using a two-tailed Dunnett's test revealed that no individual treatment was significantly different from the control. In this case, the mean of F01 group (high dose, wide binder) indicated that group gained weight, while the other four groups had means that indicated animals had lost weight. Thus, F01 group showed a significantly different percent gain, as contrasted with the other four groups, which

control were detected comparing each group individually. This was probably due to the large error term.

Male Rats

Table G-7 contains the summary analyses performed on the male rat body weight data. All individual body weight data are tabulated by dose group in Tables G-8 through G-12. The body weight data are presented in Figure 38.

Results of 0-, 9-, and 21-month male rat body weight comparisons. Overall comparisons of the animals in these dose groups showed no significant differences in body weights at 0, 9, or 21 months.

Results of 0-21, 0-9, and 9-18 percent weight gain comparisons in male rats. Comparisons over all three periods showed no significant dose effects.

Female Rats

Table G-13 contains the summary analyses performed on the female rat body weight data. All individual body weight data are tabulated by dose group in Tables G-14 through G-18. Figure 39 represents the body weight data

Results of 0, 9, and 21 month female rat body weight comparisons. At month 0, differences significant at the .05 level were noticed among average ranks of the dose groups, as computed by the Kruskal-Wallis nonparametric analysis of variance (ANOVA). This significance was not noted by the parametric ANOVA's due to outlying initial weights which decreased the value of the F statistic. Dunn's test was used for inter-group comparisons, revealing that group 2 (15 mg/m^3, yellow binder) ranked significantly higher than the control. At month 9, an analysis of variance revealed overall significance, but the Dunnett's test revealed no significant treatments as compared with control. In this case, the control mean was neither the highest nor the lowest group mean, so the other groups did not show significant departures. No dose effect was statistically significant at 21 months.

Results of 0-21, 0-9, and 9-21 percent weight gain comparisons in female rats. The only interval in which there were significant differences in weight change among the treatment groups was that of the first 9 months. In that interval, the Dunn's inter-group comparisons revealed that the control group ranked significantly higher than F02 group. This indicates that F02 group grew more slowly during the first interval than did the control.

Life Table Analysis

Male Rats

Tables H-1 through H-5 are the life table analyses of mortality and Figure 40 is the corresponding cumulative survival plots. In the analysis none of the inter-group comparisons with the control group were significantly different. However, dose groups F02 and F03 were significantly different and groups F03 and F04 also were significantly different, with group F03 having a lower proportion surviving than either group F02 or F04.

Female Rats

Tables H-6 through H-10 are the life table analyses of mortality and Figure 41 is the corresponding cumulative survival plot. In the analysis none of the between group comparisons with the control group were significant. However, dose groups F02 and F03 were significantly different, and groups F03 and F04 also were significantly different, with group F03 having a higher proportion surviving than either group F02 or F04.

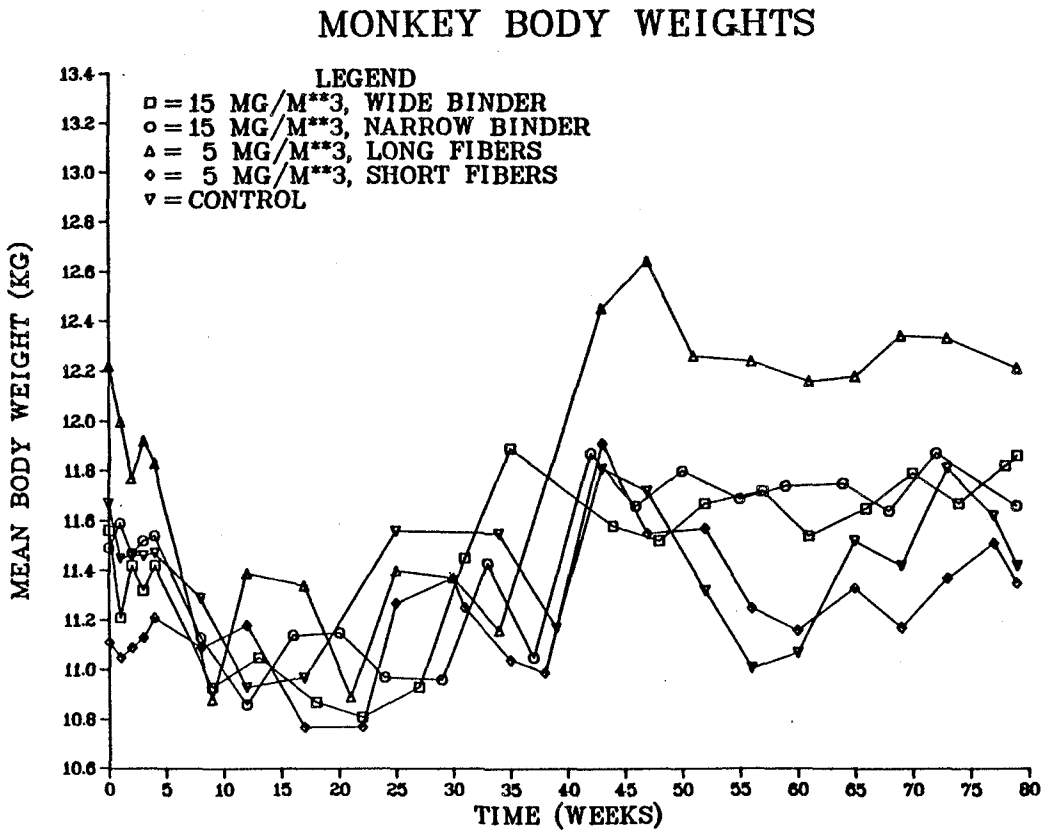


FIGURE 37. BODY WEIGHT GAIN FOR MONKEYS EXPOSED TO FIBER GLASS FOR 18 MONTHS.

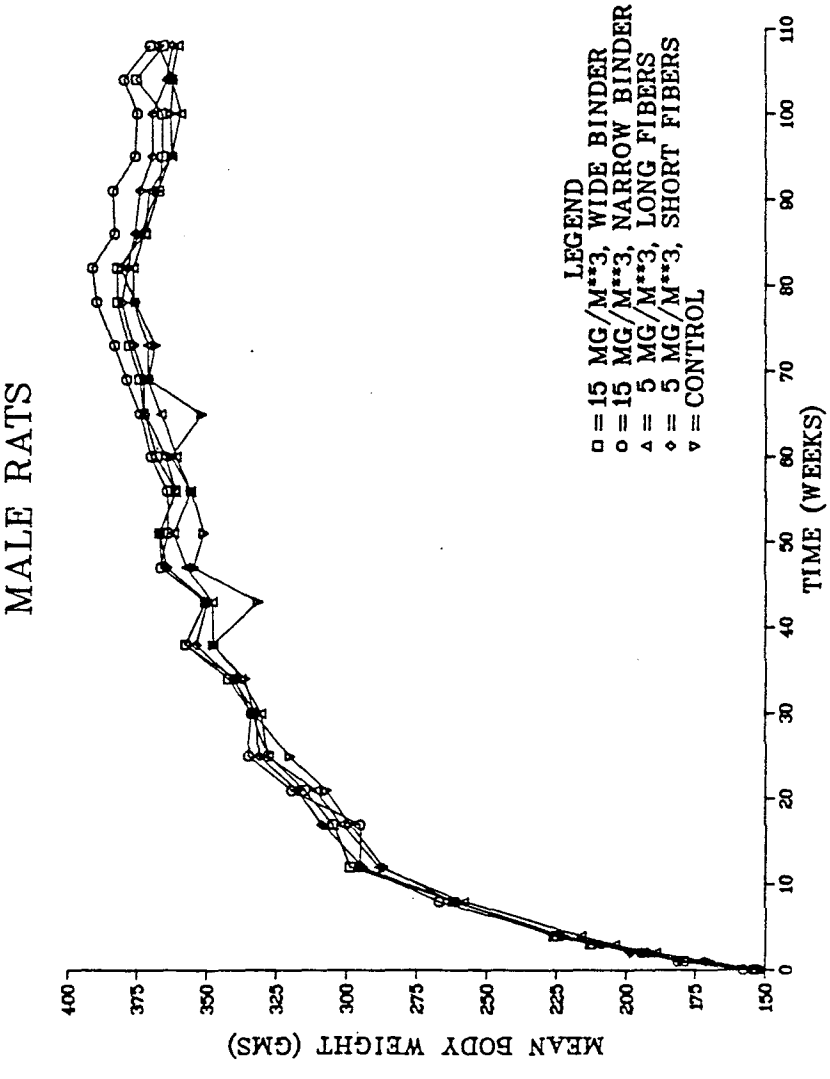


FIGURE 38. BODY WEIGHT GAIN FOR MALE RATS EXPOSED TO FIBER GLASS FOR 21 MONTHS.

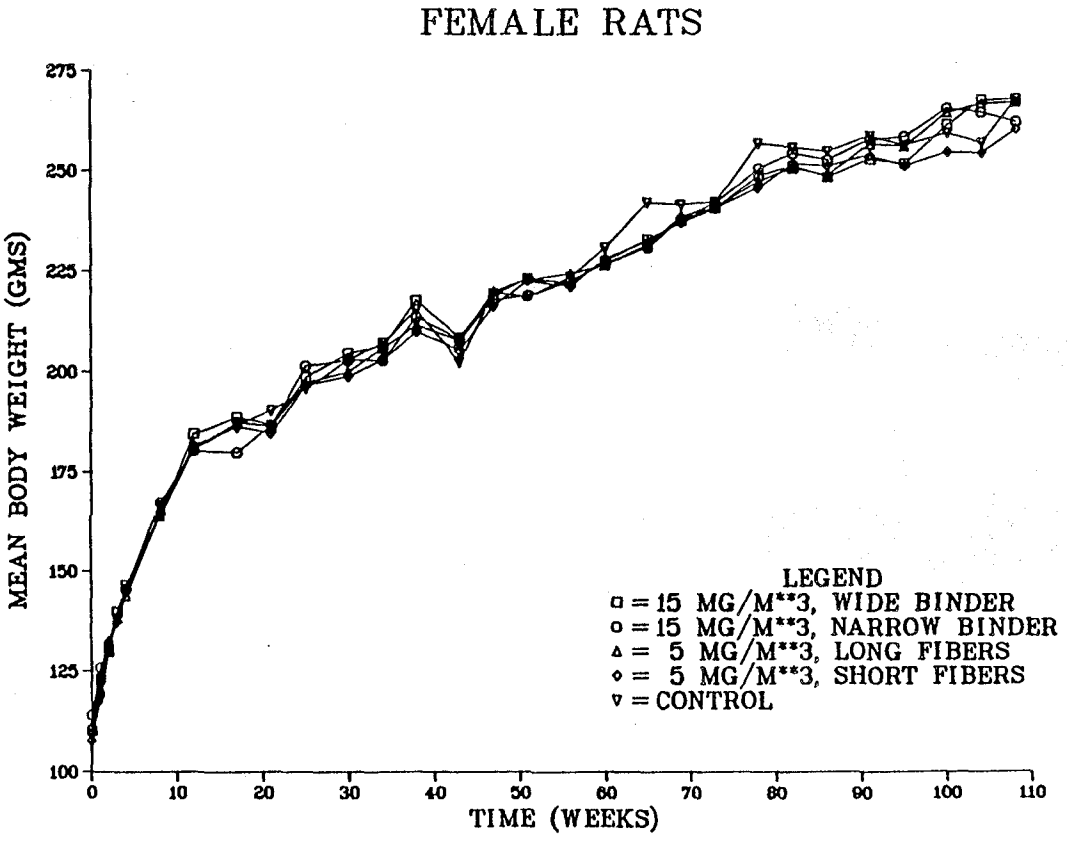


FIGURE 39. BODY WEIGHT GAIN FOR FEMALE RATS EXPOSED TO FIBER GLASS FOR 21 MONTHS.

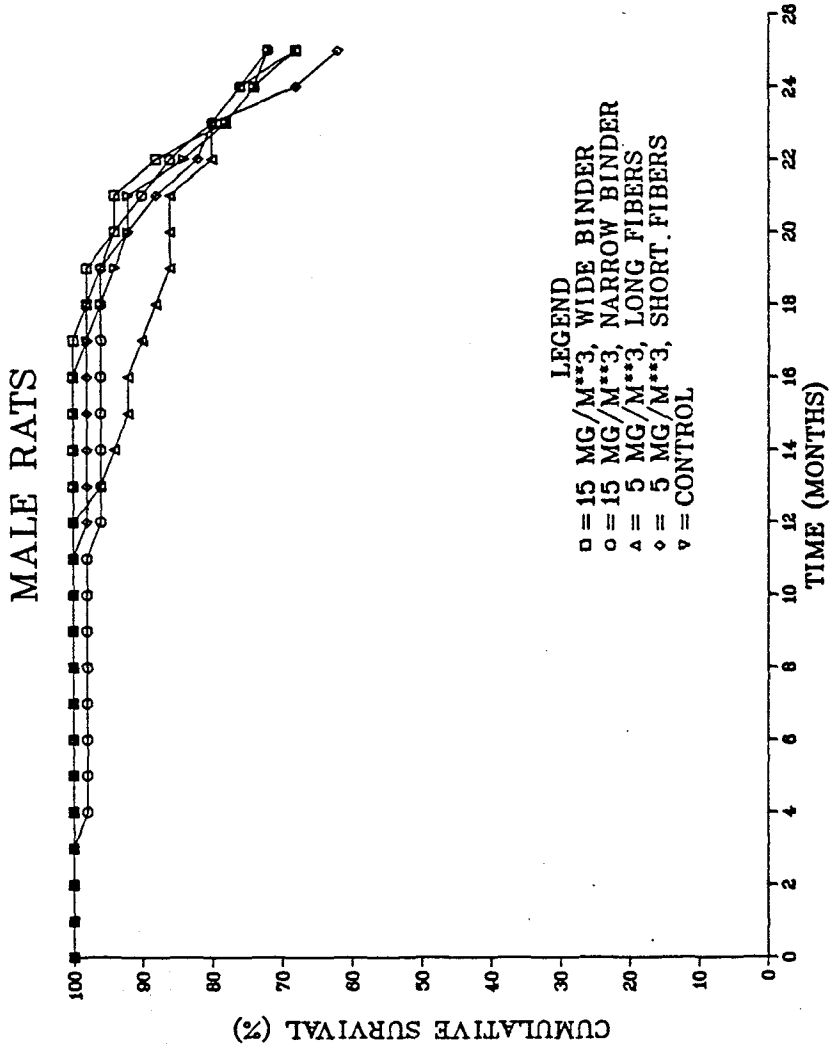


FIGURE 40. CUMULATIVE SURVIVAL OF MALE RATS EXPOSED TO FIBER GLASS.

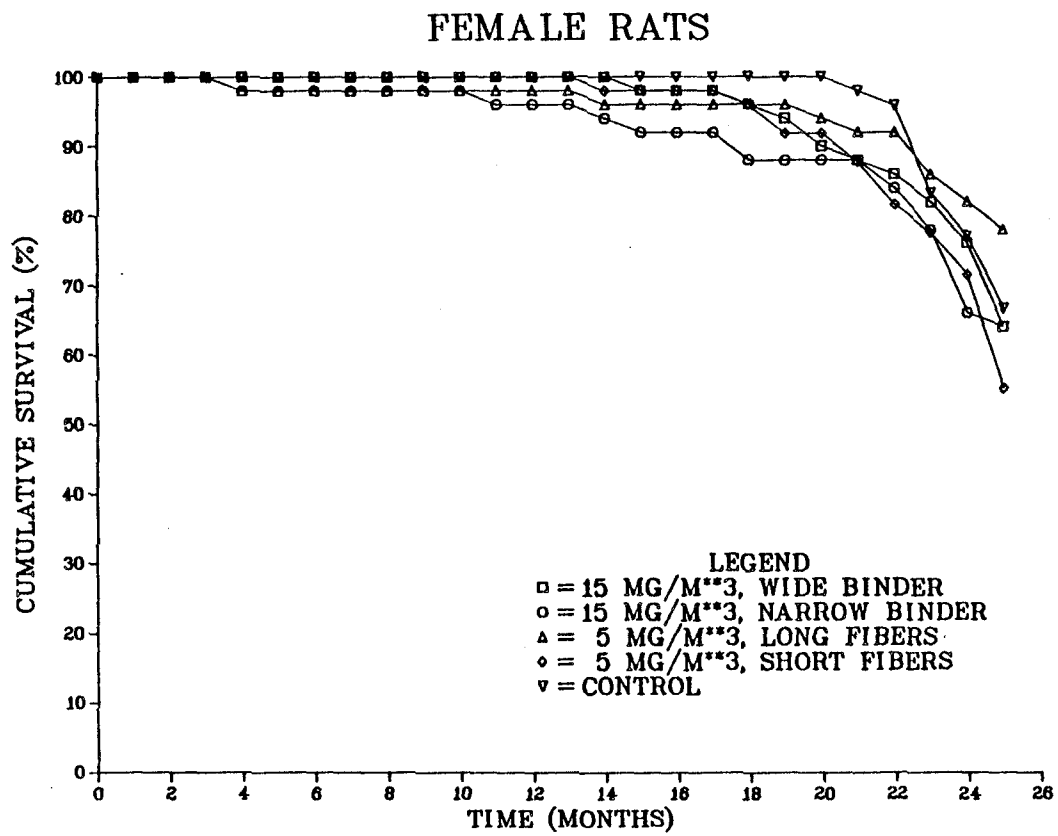


FIGURE 41. CUMULATIVE SURVIVAL OF FEMALE RATS EXPOSED TO FIBER GLASS.

Pulmonary Function Results

The results of the pulmonary function evaluation are summarized in Tables 32 through 36. These tables list the means and standard deviations of all pulmonary function parameters that were calculated for this program at each of the three evaluation periods. Each table represents one exposure group. Those parameters dependent on functional residual capacity are not included because FRC measurements were considered to be unacceptable due to N_2 analyzer malfunction.

The one way analysis of variance (ANOVA) and the Kruskal-Wallis one way rank analysis of variance were used to evaluate the group statistics for the pulmonary data. Bartlett's test was used to validate the ANOVA. Those parameters that demonstrated non-homogeneous variance (Bartlett's $P > 0.05$) were tested by the non-parametric Kruskal-Wallis evaluation. For all procedures, the 95% level of significance was used.

At the 9-month evaluation, several parameters appeared to be different when compared statistically ($P < 0.05$) with controls. Dynamic compliance was higher in the 15 mg/m^3 > 10 μm, 15 mg/m^3 > 20 μm, and the 5 mg/m^3 > 10 μm groups. Volume of anatomical dead space was lower in the 15 mg/m^3 > 20 μm group as well as the 5 mg/m^3 < 20 μm group. Because the nitrogen concentration analyzer did not perform correctly on occasion during the study, little significance is placed upon the measurements of the volume of anatomical dead space.

Of the parameters tested for this study, only expiratory reserve volume (ERV) and forced expiratory volume at 0.5 second normalized to forced vital capacity (FEV.5/FVC) showed significant results ($P < 0.05$) after the 18-month evaluations. ERV was reduced significantly in both the 15 mg/m^3 > 10 μm and 15 mg/m^3 > 20 μm exposure groups but not in either of the 5 mg/m^3 groups. Additionally, the FEV.5/FVC parameter was elevated in the 15 mg/m^3 > 20 μm exposure group when compared to controls. Non-normally distributed parameters did not show significant ($P > 0.05$) difference by Kruskal-Wallis after 18 months of exposure.

TABLE 32. PULMONARY FUNCTION ANALYSIS OF CONTROL GROUP (F05)

Physiology Parameter [1]	Baseline	9 Month	18 Month
Mechanics			
R_L (CMH_2O/l/sec)	5.2 ± 2.2	9.1 ± 7.2	7.9 ± 2.6
C_L (ml/CMH_2O)	28.2 ± 10.6	24.1 ± 10.7	20.2 ± 5.3
Dynamic Lung Volumes			
FVC (ml)	304 ± 46	315 ± 60	403 ± 68
FEV.5/FVC (%)	74.2 ± 15.6	80.8 ± 8.6	71.5 ± 7.8
FEV1/FVC (%)	94.4 ± 4.2	96.1 ± 3.3	94.5 ± 3.3
PEFR (ml/sec)	990 ± 232	1020 ± 160	1101 ± 189
FEF 50% (ml/sec)	877 ± 356	841 ± 244	995 ± 206
FEF 25% (ml/sec)	590 ± 374	431 ± 226	617 ± 327
FEF 10% (ml/sec)	195 ± 209	134 ± 72	145 ± 74
FEF 50%/FVC (FVC/sec)	2.82 ± 1.01	2.71 ± 0.82	2.49 ± 0.50
FEF 25%/FVC (FVC/sec)	1.97 ± 1.16	1.4 ± 0.76	1.48 ± 0.63
FEF 10%/FVC (FVC/sec)	0.65 ± 0.62	0.43 ± 0.26	0.36 ± 0.18
Lung Volumes			
IC (ml)	130 ± 2	132 ± 34	153 ± 44
ERV (ml)	163 ± 33	180 ± 69	252 ± 59
N_2 Washout			
CV (ml)	24.7 ± 22.2	28.8 ± 16.4	34.1 ± 13.8
CV/VC (%)	8.22 ± 6.31	9.13 ± 4.62	8.31 ± 3.82
VADS (ml)	12.2 ± 2.5	28.4 ± 8.7	27.8 ± 4.0
% N_2/100 ml	0.7 ± 0.5	0	0.85 ± 0.7
Viso (ml)	40.6 ± 36.7	40.0 ± 19.0	44.1 ± 16.5
Viso/FVC (%)	12.7 ± 11.8	12.8 ± 5.0	11.1 ± 4.0

1 Physiology Parameter definitions as per Table 1 on page 18 of text.

TABLE 33. RESULTS OF PULMONARY FUNCTION ANALYSIS FOR EXPOSURE LEVEL 15 mg/m^3 AND FIBER LENGTH GREATER THAN 10 MICROMETERS (FO2)

Physiology Parameter [1]	Baseline	9 Month	18 Month
Mechanics			
R_L (CMH_2O/1/sec)	4.99 ± 2.38	6.3 ± 4.4	8.3 ± 2.3
C_L (ml/CMH_2O)	32.85 ± 13.15	33.3 ± 12.1*	24.8 ± 6.3
Dynamic Lung Volumes			
FVC (ml)	308.9 ± 60.5	357 ± 63.8	379.8 ± 83.3
FEV.5/FVC (%)	78.7 ± 10.3	78.7 ± 7.7	75.0 ± 6.42
FEV1/FVC (%)	95.5 ± 4.4	94.2 ± 3.98	97.0 ± 2.58
PEFR (ml/sec)	964 ± 163	980 ± 130	1050 ± 188
FEF 50% (ml/sec)	897 ± 189	830 ± 248	906 ± 233
FEF 25% (ml/sec)	567 ± 258	530 ± 302	577 ± 257
FEF 10% (ml/sec)	209 ± 182	203 ± 177	170 ± 121
FEF 50%/FVC (FVC/sec)	2.97 ± 0.70	2.33 ± 0.58	2.46 ± 0.42
FEF 25%/FVC (FVC/sec)	1.86 ± 0.81	1.45 ± 0.73	1.51 ± 0.48
FEF 10%/FVC (FVC/sec)	0.67 ± 0.51	0.42 ± 0.20	0.43 ± 0.27
Lung Volumes			
IC (ml)	122 ± 23.5	152 ± 42.2	183 ± 38.1
ERV (ml)	175 ± 40.9	204 ± 33.3	196 ± 53.1*
N_2 Washout			
CV (ml)	20.8 ± 12.41	25.5 ± 11.3	40.2 ± 15.5
CV/VC (%)	6.8 ± 3.6	7.0 ± 2.8	10.9 ± 4.9
VADS (ml)	14.1 ± 5.79	31.7 ± 36	29.3 ± 4.5
% N_2/100 ml	0.69 ± 0.34	0	0.52 ± 0.39
Viso (ml)	39 ± 31	31.3 ± 21.7	46.5 ± 13.6
Viso/FVC (%)	11.6 ± 9.1	9.6 ± 6.6	13.1 ± 5.9

1 Physiology Parameter definitions as per Table 1 on page 18 of text.

* Significant difference from control values at the same time period ($P<0.05$).

TABLE 34. RESULTS OF PULMONARY FUNCTION ANALYSIS FOR EXPOSURE LEVEL 5 mg/m^3 AND FIBER LENGTH GREATER THAN 10 MICROMETERS (FO3)

Physiology Parameter[1]	Baseline	9 Month	18 Month
Mechanics			
R_L (CMH_2O/l/sec)	4.9 ± 2.4	6.3 ± 2.9	7.4 ± 1.6
C_L (ml/CMH_2O)	30.5 ± 11.5	33.4 ± 5.6*	23.0 ± 7.6
Dynamic Lung Volumes			
FVC (ml)	3313 ± 53	348 ± 62	390 ± 76
FEV .5/FVC (%)	80.4 ± 9.4	81.2 ± 4.4	77.7 ± 11.9
FEV1/FVC (%)	96.9 ± 2.0	95.5 ± 2.6	96.7 ± 2.0
PEFR (ml/sec)	1069 ± 123	919 ± 184	1021 ± 130
FEF 50% (ml/sec)	1036 ± 125	902 ± 157	924 ± 159
FEF 25% (ml/sec)	738 ± 209	468 ± 109	675 ± 227
FEF 10% (ml/sec)	189 ± 153	148 ± 53	181 ± 83
FEF 50%/FVC (FVC/sec)	3.37 ± 0.63	2.67 ± 0.64	2.46 ± 0.67
FEF 25%/FVC (FVC/sec)	2.42 ± 0.88	1.35 ± 0.22	1.79 ± 0.73
FEF 10%/FVC (FVC/sec)	0.65 ± 0.64	0.42 ± 0.13	0.46 ± 0.18
Lung Volumes			
IC (ml)	136 ± 33	150 ± 42	178 ± 47
ERV (ml)	161 ± 30	196 ± 36	212 ± 49
N_2 Washout			
CV (ml)	16 ± 6.8	25 ± 11.1	39 ± 17.7
CV/VC (%)	5.2 ± 1.8	7.6 ± 2.6	10.2 ± 2.8
VADS (ml)	12.7 ± 2.6	21.6 ± 7.9	30.4 ± 5.7
% N_2/100 ml	0.85 ± 1.0	0	0.51 ± 0.3
Viso (ml)	27.6 ± 11.7	40.1 ± 21.9	49.7 ± 13.5
Viso/FVC (%)	12 ± 13.1	11.0 ± 4.9	12.9 ± 4.2

1 Physiology Parameter definitions as per Table 1 on page 18 of text.

* Significant difference from control values at the same time period ($P<0.05$).

TABLE 35. RESULTS OF PULMONARY FUNCTION ANALYSIS FOR EXPOSURE LEVEL 15 mg/m^3 AND FIBER LENGTH GREATER THAN 20 MICROMETERS (F01)

Physiology Parameter[1]	Baseline	9 Month	18 Month
Mechanics			
R_L (CMH_2O/l/sec)	5.1 ±2.2	5.5 ± 2.0	6.0 ± 3.7
C_L (ml/CMH_2O)	29.0 ±12.1	34.0 ± 11.5*	23.6 ± 5.6
Dynamic Lung Volumes			
FVC (ml)	312 ±74	338 ± 55	377 ± 68
FEV .5/FVC (%)	79.6 ±8.0	78.6 ± 6.4	78.1 ± 6.0*
FEV1/FVC (%)	94.7 ±5.2	95.2 ± 2.0	96.4 ± 1.8
PEFR (ml/sec)	1034 ±163	990 ± 116	1053 ± 165
FEF 50% (ml/sec)	968 ±211	919 ± 143	983 ± 154
FEF 25% (ml/sec)	702 ±210	419 ± 150	701 ± 212
FEF 10% (ml/sec)	186 ±121	119 ± 62	158 ± 69
FEF 50%/FVC (FVC/sec)	3.26 ±1.0	2.76 ± 0.49	2.63 ± 0.31
FEF 25%/FVC (FVC/sec)	2.41 ±1.0	1.22 ± 0.33	1.88 ± 0.54
FEF 10%/FVC (FVC/sec)	0.59 ± 0.35	0.34 ± 0.15	0.41 ± 0.16
Lung Volumes			
IC (ml)	133 ± 33	144 ± 18	178 ± 45
ERV (ml)	167 ± 38	193 ± 45	199 ± 40*
N_2 Washout			
CV (ml)	21 ±11.7	34 ± 18.4	43 ± 12.6
CV/VC (%)	7.2 ±3.6	10.4 ± 6.1	11.7 ± 3.7
VADS (ML)	14.6 ±3.1	19.0 ± 6.0*	29.9 ± 7.1
% N_2/100 ml	0.67 ± 0.36	0	0.55 ± 0.25
Viso (ml)	29.6 ±16.3	37.4 ± 24.9	37.9 ± 13.6
Viso/FVC (%)	8.8 ±4.7	10.5 ± 7.2	9.7 ± 3.0

TABLE 36. RESULTS OF PULMONARY FUNCTION ANALYSIS FOR EXPOSURE LEVEL 5 mg/m^3 AND FIBER LENGTH LESS THAN 10 MICROMETERS (F04)

Physiology Parameter[1]	Baseline	9 Month	18 Month
Mechanics			
R_L ($CMH_2O/_L$/sec)	4.3 ±1.7	9.1 ± 7.0	9.0 ± 2.5
C_L (ml/CMH_2O)	25.7 ±9.5	27.4 ± 11.1	22.2 ± 7.5
Dynamic Lung Volumes			
FVC (ml)	312 ± 49	356 ± 65	379 ± 80
FEV .5/FVC (%)	78.2 ± 15.4	75.8 ± 8.3	70.2 ± 12.6
FEV1/FVC (%)	92.3 ± 11.4	93.8 ± 5.2	95.1 ± 2.1
PEFR (ml/sec)	1025 ± 178	1029 ± 141	1034 ± 149
FEF 50% (ml/sec)	948 ± 231	906 ± 207	896 ± 222
FEF 25% (ml/sec)	695 ± 335	455 ± 215	555 ± 270
FEF 10% (ml/sec)	326 ± 333	133 ± 71	210 ± 179
FEF 50%/FVC (FVC/sec)	3.09 ± 0.90	2.60 ± 0.70	2.41 ± 0.63
FEF 25%/FVC (FVC/sec)	2.28 ± 1.2	1.29 ± 0.65	1.43 ± 0.57
FEF 10%/FVC (FVC/sec)	1.06 ± 1.2	0.37 ± 0.17	0.51 ± 0.34
Lung Volumes			
IC (ml)	129 ±31	161 ± 43	167 ± 47
ERV (ml)	169 ±22	195 ± 26	212 ± 46
N_2 Washout			
CV (ml)	21 ±12.3	33 ± 16.8	44 ± 19.2
CV/VC (%)	7.3 ±4.2	9.5 ± 4.8	12.2 ± 5.8
VADS (ml)	18.2 ±12.3	20.7 ± 6.3*	28.3 ± 7.2
% N_2/100 ml	0.91 ± 0.39	0	0.36 ± 0.19
Viso (ml)	34.7 ±21.0	46.4 ± 18.5	42.7 ± 20.0
Viso/FVC (%)	12.3 ±6.2	13.4 ± 4.9	11.2 ± 6.0

1 Physiology Parameter definitions as per Table 1 on page 18 of text.

* Significant difference from control values at the same time period ($P<0.05$)

The limited number of significant differences demonstrated by pulmonary function analysis does not provide a basis for the diagnosis of any pattern of respiratory compromise. As all calculated parameters in both of the 5 mg/m^3 (FO3 and FO4) exposure groups were not significantly ($P>0.05$) different from the control group, it must be concluded that, within the capabilities of our evaluation, no substantiated changes occurred in those two groups as a result of their exposure to fibrous glass. The reduction of ERV alone, as in the case of the FO2 group exposed to 15 mg/m^3 (> 10 μm) fibers or in conjunction with an increased FEV.5/FVC, as in the FO1 group exposed to 15 mg/m^3 (> 20 μm) fibers, is not representative of either restrictive or obstructive lung impairment patterns. An indication of altered inflation is suggested by a trend to increased inspiratory capacity and a significant decrease in expiratory reserve volume. Such an indication cannot be clarified, however, because of the malfunction of the N_2 analyzer. In conclusion, no significant or meaningful changes could be attributed to exposure to the fibrous glass as determined by our pulmonary function evaluations in monkeys.

Gross and Microscopic Pathology

Monkeys

Observations recorded during necropsy are shown for individual animals in Tables I-1 through I-5 and are summarized in Table 37. Microscopic lesions are shown for individual animals in Tables I-6 through I-10 and are summarized in Table 38. Lesions involving fibrosis or smooth muscle hyperplasia are summarized in Tables 39 and 40 so the distribution and frequency of these changes among the various dosage groups can be more easily seen.

There were extensive numbers of diagnoses made in examining the lungs of monkeys in this study. Although nearly all of these changes were apparently the result of lung mite infestations, it was considered to be necessary to delineate these lesions, and where applicable, to identify involvement in a specific lobe or lobes. Although this allows more definitive evaluation and separation of the changes, it also results in a somewhat confusing array of summarized lesions.

The only unequivocal microscopic changes that resulted from exposure to fiberglass occurred in the lungs and tracheobronchial lymph nodes of monkeys from all exposure groups. Lesions in the tracheobronchial lymph nodes consisted of minimal to moderate amounts of fiberglass in macrophages usually in the medulla of the lymph node (Figures 42 and 43). Changes in the lungs were generally mild and consisted of single macrophages or small aggregates of macrophages that contained fiberglass fibers (Figures 44, 45, and 46). This was the major fiberglass-induced pulmonary change and was diagnosed as macrophage aggregates with fiberglass deposition. A few free fiberglass fibers were visible in alveoli, interstitium, or other areas in the lungs of monkeys

TABLE 37.

NECROPSY SUMMARY BY GROUP AND SEX

PROJECT: G7186-11 STUDY: NIOSH SPECIES: CYNOMOLGUS MONKEY

GROUP	0 MG/M3		05 MG/M3-3		05 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND OBSERVATION										
ABDOMINAL CAVITY										
PERITONEAL ADHESIONS	0	0	0	1	0	0	0	0	0	0
OMENTUM NEMATODIASIS	0	0	0	1	0	0	0	1	0	0
SEROSA CYST	0	0	0	0	0	0	0	1	0	0
BODY CAVITIES										
FAT SEROUS ATROPHY	0	0	0	1	0	0	0	0	0	0
BRAIN										
CEREBRAL CORTEX NECROSIS FOCAL	0	0	0	0	0	0	0	0	0	1
CRANIUM										
SKIN LEAD SHOT	0	0	0	0	0	0	0	0	0	1
TEMPORAL AREA MUSCLE ATROPHY WITH ADHESIONS	0	0	0	0	0	0	0	1	0	0
HEART										
LEFT VENTRICLE EPICARDIUM SCARRED AREA	0	0	0	0	0	1	0	0	0	0
KIDNEY										
CAPSULE NODULE	0	1	0	0	0	0	0	0	0	0
CAPSULE NEMATODIASIS	0	1	0	0	0	0	0	0	0	0
CORTEX CYSTS	0	0	0	0	0	1	0	0	0	0
CORTEX SCARS	0	0	0	0	0	0	0	0	0	1
LEFT ATROPHY	0	0	0	0	0	0	0	1	0	0
RIGHT SMALL	0	0	0	0	0	0	0	0	0	1
LARGE INTESTINE										

TABLE 37. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND OBSERVATION										
MULTIPLE NEMATODE NODULES	0	0	0	1	0	0	0	0	0	0
CECUM 3 MM BLUE NODULE	0	0	0	0	0	0	0	1	0	0
COLON SEROSA RED NODULES	0	0	0	1	0	0	0	0	0	0
LIVER										
CYST	0	1	0	0	0	0	0	0	0	0
NODULE	0	1	0	0	0	0	0	0	0	0
BILIARY CYST	0	0	0	0	0	0	0	1	0	0
WHITE GRANULAR FOCI IN CAPSULE	0	0	0	0	0	0	0	0	0	1
MEDIAN LOBE NODULE NEMATODE	0	0	0	1	0	0	0	0	0	0
MEDIAN LOBE YELLOW FOCUS	0	0	0	0	0	1	0	0	0	0
LUNG										
FOCAL COLLAPSED AREA	0	0	0	0	0	0	0	0	0	1
INCREASED AIR RETENTION	0	0	0	0	0	2	0	0	0	0
ANTHRACOSILICOSIS	0	2	0	2	0	5	0	1	0	2
FIBROUS ADHESIONS MULTIFOCAL	0	0	0	2	0	0	0	1	0	0
LUNG MITE NODULES	0	2	0	0	0	0	0	0	0	0
GRAY-GREEN SUBPLEURAL PLAQUES MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
PARENCHYMAL THICKENING	0	0	0	1	0	0	0	0	0	0
2-3 MM SLIGHTLY RAISED BROWN NODULES	0	0	0	0	0	0	0	0	0	1
PLEURAL ADHESIONS FOCAL OR MULTIFOCAL	0	2	0	0	0	4	0	0	0	0
NODULES FOCAL OR MULTIFOCAL PARASITIC	0	0	0	2	0	0	0	0	0	2

TABLE 37. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND OBSERVATION										
LEFT DIAPHRAGMATIC LOBE NODULE	0	1	0	0	0	1	0	0	0	0
LEFT MIDDLE LOBE 2 X 4 MM WHITE NODULE	0	1	0	0	0	0	0	0	0	0
PLEURA FIBROSIS	0	0	0	0	0	1	0	0	0	0
PLEURA GRAY-GREEN PLAQUES	0	0	0	0	0	0	0	1	0	0
PLEURA MOTTLED AREAS OF BLACK PIGMENT	0	0	0	0	0	0	0	0	0	1
PLEURA WHITE FOCI	0	0	0	0	0	1	0	0	0	0
PLEURA FIBROSIS MULTIFOCAL	0	0	0	0	0	1	0	0	0	1
PLEURA 2 MM MINERALIZED FOCI MULTIPLE	0	0	0	0	0	1	0	0	0	0
PLEURA SMALL BLACK PIGMENTED FOCI	0	0	0	0	0	0	0	1	0	0
RIGHT DIAPHRAGMATIC LOBE BULBOUS RED FOCUS	0	0	0	0	0	0	0	1	0	0
RIGHT DIAPHRAGMATIC LOBE LEAD SHOT	0	1	0	0	0	0	0	0	0	0
SEVERAL LOBES HEMORRHAGE PERIPHERAL	0	0	0	0	0	0	0	1	0	0
LYMPH NODE										
ENLARGED CYSTIC (POSSIBLY THYMUS)	0	0	0	0	0	0	0	1	0	0
BRONCHIAL LYMPHOID HYPERPLASIA	0	0	0	0	0	1	0	0	0	0
MESENTERIC ENLARGED	0	0	0	1	0	1	0	0	0	0
MESENTERY										
5 MM NODULE WITH LIQUID CENTER	0	0	0	0	0	0	0	1	0	0
SEVERAL ENCAPSULATED PENTASTOMIDS	0	0	0	0	0	0	0	1	0	0
MUSCLE										

TABLE 37. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND OBSERVATION										
SKELETAL ATROPHY	0	0	0	0	0	0	0	0	0	1
SMALL INTESTINE										
GAS FILLED AND DEVOID OF INGESTA	0	0	0	0	0	0	0	0	0	1
ILEUM CESTODIASIS (TAPEWORMS)	0	0	0	1	0	0	0	0	0	0
SPLEEN										
ADHESIONS	0	1	0	1	0	0	0	0	0	0
NODULE FOCAL	0	0	0	1	0	0	0	0	0	0
LYMPHOID NODULAR HYPERPLASIA	0	1	0	0	0	2	0	0	0	0
SUBCAPSULAR WHITE FOCI	0	5	0	0	0	0	0	0	0	0
RAISED NODULES MULTIPLE	0	0	0	0	0	0	0	0	0	2
SMOOTH NODULES ON MARGINS	0	0	0	0	0	0	0	1	0	0
PALE CIRCULAR AREAS	0	0	0	1	0	0	0	0	0	0
5-6 MM SMOOTH RED NODULES	0	0	0	0	0	0	0	1	0	0
SUBCAPSULAR OR CAPSULAR WHITE FOCI MULTIPLE	0	0	0	1	0	0	0	2	0	1
STOMACH										
GAS FILLED AND DEVOID OF CONTENT	0	0	0	0	0	0	0	0	0	1
FUNDIC MUCOSA PETECHIA FOCAL	0	0	0	0	0	0	0	1	0	0
FUNDUS MUCOSA NODULES MULTIPLE	0	0	0	0	0	1	0	0	0	0
GREATER CURVATURE WHITE NODULES MULTIPLE	0	0	0	0	0	0	0	0	0	1
GREATER CURVATURE MUCOSA HEMORRHAGE AND EDEMA	0	0	0	0	0	0	0	0	0	1
MUCOSA NEAR CARDIA RAISED WHITE NODULE	0	0	0	0	0	0	0	1	0	0

TABLE 37. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND OBSERVATION										
SEROSA MINERALIZATION	0	0	0	0	0	1	0	0	0	0
TEETH										
TARTAR	0	1	0	0	0	0	0	0	0	1
TESTIS										
LEFT ATROPHY	0	1	0	2	0	1	0	0	0	1
RIGHT ATROPHY	0	0	0	1	0	0	0	0	0	0
RIGHT HYPERTROPHY	0	1	0	0	0	0	0	0	0	0
SUBCAPSULAR AREAS BROWN NODULES	0	0	0	0	0	0	0	0	0	1
THYROID GLAND										
CYST	0	1	0	0	0	0	0	0	0	0
URINARY BLADDER										
SEROSA NEMATODIASIS MULTIPLE	0	0	0	1	0	0	0	0	0	0
TRIGONE AREA LEAD SHOT	0	1	0	0	0	0	0	0	0	1

TABLE 38. HISTOPATHOLOGY SUMMARY BY GROUP AND SEX

PROJECT: G7188-11 STUDY: NIOSH SPECIES: CYNOMOLGUS MONKEY

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
ABDOMINAL CAVITY	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[1]	[0]	[0]
EOSINOPHILIC GRANULOMA	0	0	0	0	0	0	0	1	0	0
GRANULOMA CYSTIC	0	0	0	1	0	0	0	1	0	0
MESENTERY	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[1]	[0]	[0]
EOSINOPHILIC GRANULOMA MULTIPLE	0	0	0	1	0	0	0	0	0	0
GRANULOMA	0	0	0	0	0	0	0	1	0	0
THORACIC CAVITY	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[0]
CYST MULTIPLE	0	0	0	0	0	0	0	1	0	0
HEART	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
INTERVENTRICULAR SEPTUM ENDOCARDIUM AND MYOCARDIUM MYOCARDITIS SUBACUTE	0	0	0	1	0	0	0	0	0	0
INTERVENTRICULAR SEPTUM LYMPHOCYTIC INFILTRATE	0	1	0	0	0	0	0	0	0	0
INTERVENTRICULAR SEPTUM MYOCARDIUM DEGENERATION AND NECROSIS MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
LEFT ATRIOVENTRICULAR JUNCTION FIBROSIS	0	0	0	0	0	1	0	0	0	0
LEFT VENTRICLE MYOCARDIUM LYMPHOCYTIC INFILTRATE	0	0	0	1	0	1	0	0	0	1
LEFT VENTRICLE PAPILLARY MUSCLE INFLAMMATION SUBACUTE FOCAL	0	0	0	0	0	1	0	1	0	0
LIPOCHROME PIGMENT DEPOSITON DIFFUSE	0	0	0	0	0	0	0	1	0	0
MYOCARDIUM LIPOCHROME PIGMENT DEPOSITION	0	0	0	0	0	0	0	0	0	1
MYOCARDIUM LYMPHOCYTIC INFILTRATE MULTIFOCAL	0	0	0	1	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
PAPILLARY MUSCLE MYOCARDITIS WITH DEGENERATION MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
RIGHT VENTRICLE INFLAMMATION SUBACUTE	0	1	0	2	0	0	0	0	0	1
RIGHT VENTRICLE PAPILLARY MUSCLE MYOSITIS DEGENERATIVE FOCAL	0	1	0	0	0	0	0	0	0	0
CECUM	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[1]	[0]	[0]
SUBMUCOSA GRANULOMA MULTIPLE	0	0	0	0	0	0	0	1	0	0
TUNICA MUSCULARIS GRANULOMA PARASITIC	0	0	0	0	0	1	0	0	0	0
COLON	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
ALL LAYERS COLITIS CHRONIC PARASITIC MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
HEMOSIDERIN DEPOSITION MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
MUCOSA AND SUBMUCOSA HEMOSIDERIN DEPOSITION	0	0	0	0	0	0	0	1	0	0
MUCOSA HEMOSIDERIN DEPOSITION	0	0	0	0	0	1	0	0	0	0
PIGMENT DEPOSITION MULTIFOCAL PARASITIC	0	0	0	1	0	0	0	0	0	0
SUBMUCOSA COLITIS EOSINOPHILIC AND HISTIOCYTIC MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
SUBMUCOSA HEMOSIDERIN DEPOSITION	0	1	0	0	0	1	0	0	0	0
SUBMUCOSA VASCULITIS CHRONIC FOCAL	0	0	0	0	0	1	0	0	0	0
TUNICA MUSCULARIS EOSINOPHILIC GRANULOMA MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
TUNICA MUSCULARIS GRANULOMA MULTIPLE PARASITIC	0	0	0	0	0	0	0	0	0	1
TUNICA MUSCULARIS INFLAMMATION EOSINOPHILIC AND GRANULOMATOUS	0	0	0	1	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		3 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
TUNICA MUSCULARIS INFLAMMATION SUBACUTE PARASITIC	0	0	0	0	0	0	0	0	0	1
TUNICA MUSCULARIS PARASITOSIS FOCAL	0	0	0	1	0	0	0	0	0	0
DUODENUM	[0]	[0]	[0]	[1]	[0]	[1]	[0]	[0]	[0]	[0]
ESOPHAGUS	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[11]
CARDIA SQUAMOUS EPITHELIUM HYPERPLASIA	0	1	0	0	0	0	0	0	0	0
PARAESOPHAGEAL TISSUE PARASITOSIS	0	0	0	0	0	1	0	0	0	0
GALLBLADDER	[0]	[12]	[0]	[6]	[0]	[10]	[0]	[11]	[0]	[9]
ILEUM	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
LAMINA PROPRIA EDEMA	0	0	0	0	0	0	0	0	0	1
JEJUNUM	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[0]
LIVER	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
CENTRILOBULAR HEPATOCYTES PIGMENT DEPOSITION	0	0	0	0	0	0	0	0	0	1
CYST PARASITIC	0	0	0	1	0	0	0	0	0	0
FATTY CHANGE FOCAL	0	0	0	0	0	1	0	0	0	0
GRANULOMA FOCAL PARASITIC	0	0	0	0	0	1	0	0	0	0
GRANULOMA NECROTIZING CHRONIC FOCAL	0	1	0	0	0	0	0	0	0	0
HEPATITIS LYMPHOCYTIC MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
HEPATOCYTES AND KUPFFER CELLS PIGMENT DEPOSITION	0	0	0	1	0	0	0	0	0	0
HEPATOCYTES NECROSIS DIFFUSE	0	0	0	1	0	0	0	0	0	0
HEPATOCYTES PIGMENT DEPOSITION	0	0	0	4	0	2	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
HEPATOCYTES VACUOLIZATION MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
KUPFFER CELLS PIGMENT DEPOSITION	0	0	0	1	0	0	0	1	0	0
LYMPHOCYTIC INFILTRATE MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
PIGMENT DEPOSITION	0	0	0	1	0	0	0	0	0	2
PORTAL AREA LYMPHOCYTIC INFILTRATE FOCAL	0	0	0	0	0	1	0	0	0	0
SINUSOIDS MICROFILARIASIS	0	0	0	1	0	0	0	0	0	0
PANCREAS-EXOCRINE	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
ACINAR ATROPHY	0	2	0	1	0	0	0	1	0	0
LYMPHOCYTIC INFILTRATE FOCAL	0	0	0	1	0	0	0	0	0	0
PHARYNX	[0]	[2]	[0]	[1]	[0]	[1]	[0]	[0]	[0]	[0]
MUCOSA VESICLE FOCAL	0	1	0	0	0	0	0	0	0	0
PARASITOSIS	0	0	0	1	0	0	0	0	0	0
PHARYNGITIS SUBACUTE	0	0	0	0	0	1	0	0	0	0
STOMACH	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
CARDIA EPITHELIUM HYPERPLASIA	0	1	0	0	0	0	0	0	0	0
CARDIA LYMPHOID HYPERPLASIA	0	1	0	0	0	0	0	0	0	0
CARDIAC REGION GLANDULAR HYPERPLASIA FOCAL	0	0	0	0	0	0	0	1	0	0
CONGESTION	0	1	0	0	0	0	0	0	0	0
FUNDIC AND PYLORIC AREAS EROSION MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
FUNDIC AREA TUNICA MUSCULARIS ENCAPSULATED PARASITE	0	0	0	0	0	1	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
FUNDIC MUCOSA ADENOSIS FOCAL	0	0	0	0	0	1	0	0	0	0
FUNDIC REGION EROSION WITH HEMORRHAGE MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
MUCOSA AND SUBMUCOSA INFARCTION	0	0	0	0	0	0	0	0	0	1
MUCOSA LYMPHOCYTIC AND EOSINOPHILIC INFILTRATE DIFFUSE	0	0	0	0	0	1	0	0	0	0
PYLORIC AREA MUCOSA LYMPHOCYTIC INFILTRATE FOCAL	0	0	0	1	0	0	0	0	0	0
PYLORIC AREA TUNICA MUSCULARIS PARASITOSIS MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
PYLORUS SUBMUCOSA GRANULOMA FOCAL	0	1	0	0	0	0	0	0	0	0
SUBMUCOSA GRANULOMA CHRONIC FOCAL	0	1	0	0	0	0	0	0	0	0
ADRENAL GLAND	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
CAPSULE CORTICAL HYPERTROPHY	0	0	0	1	0	0	0	0	0	0
CAPSULE NODULAR HYPERPLASIA MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
CORTEX ADENOMA BILATERAL	0	0	0	0	0	0	0	1	0	0
CORTEX FOCI OF CELLULAR HYPERTROPHY BILATERAL	0	0	0	0	0	0	0	1	0	0
CORTEX HYPERPLASIA	0	0	0	1	0	0	0	0	0	0
CORTICAL MEDULLARY JUNCTION FIBRIN DEPOSITION	0	0	0	1	0	1	0	0	0	0
EXTRACAPSULAR PROLIFERATION	0	0	0	0	0	0	0	0	0	1
MEDULLA HYPERPLASIA	0	0	0	1	0	0	0	0	0	0
PERIADRENAL ADIPOSE TISSUE EOSINOPHILIC GRANULOMAS PARASITIC	0	1	0	0	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
PERICAPSULAR AREA GRANULOMA MULTIPLE	0	0	0	1	0	0	0	0	0	0
PERICAPSULAR AREAS INFLAMMATION EOSINOPHILIC	0	0	0	1	0	0	0	0	0	0
ZONA FASCICULATA CELLULAR HYPERTROPHY MULTIFOCAL	0	1	0	1	0	0	0	0	0	1
ZONA RETICULARIS PIGMENT DEPOSITION FOCAL	0	1	0	1	0	0	0	0	0	0
PANCREATIC ISLET	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
AMYLOIDOSIS	0	0	0	1	0	0	0	0	0	0
PARATHYROID GLAND	[0]	[1]	[0]	[4]	[0]	[4]	[0]	[4]	[0]	[3]
PITUITARY GLAND	[0]	[12]	[0]	[12]	[0]	[11]	[0]	[12]	[0]	[12]
CYST MULTIPLE	0	0	0	0	0	0	0	0	0	1
PARS DISTALIS CHROMOPHOBE HYPERPLASIA	0	1	0	0	0	0	0	0	0	0
PARS DISTALIS FIBROSIS MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
THYROID GLAND	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
CYST FOCAL	0	1	0	0	0	0	0	0	0	0
CYST MULTIPLE	0	1	0	0	0	0	0	0	0	0
FOLLICULAR ATROPHY MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
FOLLICULAR CYST	0	0	0	0	0	1	0	0	0	0
FOLLICULAR LINING EPITHELIUM AND PARAFOLLICULAR CELLS PIGMENT DEPOSITION	0	0	0	1	0	0	0	0	0	0
INTERSTITIUM FIBROSIS MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
THYROIDITIS SUBACUTE FOCAL	0	0	0	0	0	0	0	1	0	0
BONE MARROW-STERNUM	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[0]

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
LYMPH NODE-MESENTERIC	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
CORTEX LYMPHADENITIS EOSINOPHILIC CHRONIC FOCAL	0	1	0	0	0	0	0	0	0	0
CYST GRANULOMATOUS MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
EOSINOPHIL INFILTRATE DIFFUSE	0	1	0	0	0	0	0	0	0	0
HEMOSIDERIN DEPOSITION	0	2	0	1	0	0	0	0	0	2
HISTIOCYTOSIS	0	0	0	0	0	0	0	1	0	0
LYMPHADENITIS EOSINOPHILIC	0	0	0	0	0	1	0	0	0	0
LYMPHOID DEPLETION	0	0	0	1	0	0	0	0	0	0
PIGMENT DEPOSITION PARASITIC	0	0	0	1	0	0	0	0	0	0
VASCULATURE EOSINOPHILIC INFILTRATE	0	0	0	0	0	0	0	1	0	0
LYMPH NODE-PANCREATIC	[0]	[1]	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[0]
EOSINOPHIL INFILTRATE FOCAL	0	1	0	0	0	0	0	0	0	0
HISTIOCYTOSIS AND HEMOSIDERIN DEPOSITION	0	0	0	1	0	0	0	0	0	0
LYMPH NODE-TRACHEOBRONCHIAL	[0]	[11]	[0]	[12]	[0]	[12]	[0]	[11]	[0]	[12]
CAPSULE HISTIOCYTE AND EOSINOPHIL INFILTRATE	0	1	0	0	0	0	0	0	0	0
EOSINOPHIL AND HISTIOCYTE INFILTRATE FOCAL	0	1	0	0	0	0	0	0	0	0
EOSINOPHIL INFILTRATION	0	1	0	0	0	0	0	0	0	0
FIBERGLASS DEPOSITION	0	0	0	12	0	10	0	4	0	10
HEMOSIDERIN DEPOSITION	0	0	0	0	0	0	0	0	0	1
LUNG MITE PIGMENT DEPOSITION	0	11	0	12	0	11	0	11	0	11

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
LYMPHADENITIS ACUTE	0	0	0	0	0	1	0	0	0	0
LYMPHADENITIS EOSINOPHILIC	0	2	0	0	0	2	0	1	0	0
LYMPHOID DEPLETION	0	0	0	1	0	0	0	0	0	0
PERINODAL ADIPOSE TISSUE SUBACUTE INFLAMMATION	0	0	0	0	0	0	0	1	0	0
SPLEEN	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
EOSINOPHILIC GRANULOMA MULTIPLE PARASITIC	0	0	0	0	0	0	0	2	0	1
GRANULOMA MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
INCREASED HEMOSIDERIN DEPOSITION	0	0	0	1	0	0	0	0	0	0
INFLAMMATION HISTIOCYTIC AND EOSINOPHILIC FOCAL	0	0	0	1	0	0	0	0	0	0
LYMPHOID DEPLETION	0	0	0	0	0	0	0	0	0	1
SPLENITIS HISTIOCYTIC AND EOSINOPHILIC	0	0	0	1	0	0	0	0	0	0
SPLENITIS NEUTROPHILIC WITH RETICULUM CELL HYPERPLASIA FOCAL	0	0	0	0	0	1	0	0	0	0
SUBCAPSULAR AREAS EOSINOPHILIC GRANULOMA MULTIFOCAL	0	1	0	1	0	1	0	0	0	0
SUBCAPSULAR AREAS RETICULUM CELL HYPERPLASIA FOCAL OR MULTIFOCAL	0	3	0	0	0	0	0	0	0	1
THYMUS	[0]	[1]	[0]	[0]	[0]	[2]	[0]	[0]	[0]	[0]
CYST	0	0	0	0	0	1	0	0	0	0
BRAIN	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
BASAL GANGLIA AXONAL SWELLING MULTIFOCAL	0	3	0	0	0	0	0	2	0	2

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
BASAL GANGLIA MINERALIZATION MULTIFOCAL	0	0	0	0	0	1	0	0	0	1
CHOROID PLEXUS LYMPHOCYTIC INFILTRATE	0	0	0	0	0	0	0	1	0	0
LATERAL VENTRICLE CHOROID PLEXUS CYSTS	0	0	0	0	0	1	0	0	0	0
NUCLEUS GRACILIS GIANT AXONAL SWELLING	0	1	0	0	0	0	0	0	0	0
THALAMUS ENCEPHALITIS SUBACUTE WITH DEMYELINATION FOCAL	0	0	0	0	0	1	0	0	0	0
NERVE-SCIATIC	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[0]
EYE	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[11]
CILARY BODY LYMPHOCYTIC INFILTRATE FOCAL	0	0	0	0	0	1	0	0	0	0
CILIARY MUSCLE LYMPHOID INFILTRATE FOCAL	0	1	0	0	0	0	0	0	0	0
CONJUNCTIVA LYPHOCYTIC INFILTRATE FOCAL	0	1	0	0	0	0	0	0	0	0
RETINA HYPOPLASIA FOCAL	0	1	0	0	0	0	0	0	0	0
EPIDIDYMIS	[0]	[10]	[0]	[9]	[0]	[10]	[0]	[9]	[0]	[8]
DUCTULI EFFERENTES PIGMENT DEPOSITION	0	0	0	1	0	0	0	0	0	0
PROSTATE GLAND	[0]	[10]	[0]	[12]	[0]	[11]	[0]	[12]	[0]	[12]
GLANDULAR HYPERPLASIA FOCAL	0	0	0	1	0	0	0	0	0	0
INTERSTITIAL TISSUE INFLAMMATION SUBACUTE FOCAL OR MULTIFOCAL	0	3	0	2	0	4	0	4	0	3
PROSTATITIS EOSINOPHILIC AND LYMPHOCYTIC MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
SUBURETHRAL TISSUE LYMPHOCYTIC INFILTRATE	0	0	0	0	0	0	0	1	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
TESTIS	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
LEFT SEMINIFEROUS TUBULES DEGENERATION AND ATROPHY	0	0	0	0	0	1	0	0	0	0
LEFT SEMINIFEROUS TUBULES DEGENERATION MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
LYMPHOCYTIC INFILTRATE MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
RIGHT SEMINIFEROUS TUBULES DEGENERATION	0	0	0	1	0	0	0	0	0	0
SEMINIFEROUS TUBULES DEGENERATION	0	0	0	1	0	0	0	0	0	0
SEMINIFEROUS TUBULES DEGENERATION AND ATROPHY MULTIFOCAL OR DIFFUSE	0	1	0	2	0	0	0	0	0	0
SEMINIFEROUS TUBULES HYPOPLASIA MULTIFOCAL OR DIFFUSE	0	0	0	0	0	0	0	1	0	1

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)
HISTOPATHOLOGY SUMMARY BY GROUP AND SEX

PROJECT: G7188-11 STUDY: NIOSH SPECIES: CYNOMOLGUS MONKEY

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
LARYNX	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
EPITHELIUM EROSION	0	0	0	0	0	0	0	0	0	1
INFLAMMATION SUBACUTE	0	0	0	0	0	0	0	1	0	0
LARYNGEAL MUSCLE SARCOSPORIDIOSIS	0	0	0	0	0	0	0	0	0	1
LARYNGITIS SUBACUTE DIFFUSE	0	0	0	0	0	0	0	1	0	0
SUBMUCOSA LARYNGITIS SUBACUTE	0	0	0	0	0	1	0	0	0	0
LUNG	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
BRONCHI AND BRONCHIOLES INFLAMMATION SUBACUTE EOSINOPHILIC	0	0	0	0	0	1	0	0	0	0
BRONCHIAL BRONCHIOLAR AND PERIVASCULAR AREAS INFLAMMATION SUBACUTE	0	0	0	0	0	0	0	1	0	0
BRONCHIOLAR PERIBRONCHIOLAR AND PERIVASCULAR AREAS EOSINOPHIL INFILTRATE	0	0	0	1	0	1	0	0	0	0
BRONCHIOLAR PERIBRONCHIOLAR AND PERIVASCULAR AREAS INFLAMMATION SUBACUTE MULTIFOCAL	0	3	0	0	0	0	0	1	0	0
BRONCHIOLECTASIS	0	0	0	2	0	0	0	0	0	0
BRONCHIOLES SMOOTH MUSCLE HYPERPLASIA MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
BRONCHIOLITIS SUBACUTE EOSINOPHILIC MULTIFOCAL	0	0	0	1	0	0	0	0	0	1
BRONCHIOLITIS SUBACUTE EOSINOPHILIC WITH BRONCHIOLAR ALVEOLAR CELL HYPERPLASIA PARASTIC	0	0	0	0	0	0	0	0	0	1
EMPHYSEMA DIFFUSE	0	0	0	1	0	0	0	1	0	0
EOSINOPHIL INFILTRATES	0	1	0	0	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
FIBROSIS	0	0	0	0	0	0	0	1	0	0
FIBROSIS MULTIFOCAL	0	3	0	3	0	0	0	1	0	0
INFLAMMATION EOSINOPHILIC MULTIFOCAL OR DIFFUSE	0	1	0	0	0	0	0	1	0	0
INTERSTITIAL AND INTRA-ALVEOLAR AREAS HISTIOCYTE INFILTRATION	0	0	0	0	0	0	0	1	0	0
INTERSTITIAL AREAS HISTIOCYTE INFILTRATE	0	0	0	0	0	1	0	0	0	1
INTERSTITIUM FIBROSIS FOCAL OR MULTIFOCAL	0	0	0	1	0	0	0	1	0	0
INTERSTITIUM HISTIOCYTE INFILTRATE MULTIFOCAL TO DIFFUSE	0	7	0	3	0	3	0	6	0	1
LEFT AND RIGHT UPPER LOBE AND RIGHT CARDIAC LOBE INTERSTITIUM HISTIOCYTE INFILTRATE	0	0	0	0	0	0	0	1	0	0
LEFT LOWER AND LEFT MIDDLE LOBE BRONCHI BRONCHIOLES AND PERIVASULAR AREAS INFLAMMATION SUBACUTE EOSINOPHILIC	0	0	0	0	0	1	0	0	0	0
LEFT LOWER LOBE ARTERY FIBRINOID NECROSIS FOCAL	0	0	0	0	0	0	0	1	0	0
LEFT LOWER LOBE ARTERY ORGANIZING THROMBUS	0	0	0	0	0	0	0	1	0	0
LEFT LOWER LOBE BRONCHIOLAR PERIBRONCHIOLAR AND PERIVASCULAR AREAS EOSINOPHIL INFILTRATE	0	0	0	1	0	0	0	0	0	0
LEFT LOWER LOBE BRONCHIOLITIS SUBACUTE EOSINOPHILIC	0	0	0	0	0	0	0	1	0	0
LEFT LOWER LOBE EOSINOPHILIC BRONCHIOLITIS	0	1	0	0	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
LEFT LOWER LOBE EOSINOPHILIC GRANULOMAS	0	0	0	0	0	0	0	1	0	0
LEFT LOWER LOBE FIBROSIS FOCAL	0	1	0	0	0	1	0	0	0	0
LEFT LOWER LOBE GRANULOMA FOCAL	0	0	0	0	0	0	0	1	0	1
LEFT LOWER LOBE INTERSTITIUM HISTIOCYTE INFILTRATE FOCAL OR MULTIFOCAL	0	0	0	1	0	1	0	0	0	0
LEFT LOWER LOBE PERIVASCULAR AREA PNEUMONIA SUBACUTE EOSINOPHILIC FOCAL	0	0	0	0	0	0	0	0	0	1
LEFT LOWER LOBE PLEURA FIBROSIS FOCAL	0	0	0	0	0	0	0	1	0	0
LEFT LOWER LOBE SMOOTH MUSCLE HYPERPLASIA FOCAL	0	1	0	1	0	0	0	0	0	0
LEFT MIDDLE LOBE BRONCHIOLITIS SUBACUTE AND EOSINOPHILIC FOCAL	0	0	0	0	0	0	0	0	0	1
LEFT MIDDLE LOBE FIBROSIS FOCAL OR MULTIFOCAL	0	1	0	0	0	0	0	2	0	0
LEFT MIDDLE LOBE HEMORRHAGE FOCAL	0	0	0	0	0	0	0	1	0	0
LEFT MIDDLE LOBE INFLAMMATION EOSINOPHILIC FOCAL OR MULTIFOCAL	0	0	0	0	0	0	0	2	0	0
LEFT MIDDLE LOBE INTERSTITIUM HISTIOCYTE INFILTRATE	0	0	0	0	0	0	0	1	0	0
LEFT MIDDLE LOBE INTERSTITIUM MACROPHAGE INFILTRATE	0	0	0	0	0	1	0	0	0	0
LEFT MIDDLE LOBE INTRA-ALVEOLAR AREAS GRANULOMA MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
LEFT MIDDLE LOBE PNEUMONIA SUBACUTE	0	1	0	0	0	0	0	0	0	0
LEFT MIDDLE LOBE SUBPLEURAL AREA ORGANIZED GRANULOMAS	0	0	0	0	0	1	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
LEFT UPPER AND LEFT LOWER LOBES SMOOTH MUSCLE HYPERPLASIA	0	0	0	0	0	1	0	0	0	0
LEFT UPPER LOBE BRONCHIOLAR ALVEOLAR CELL HYPERPLASIA	0	0	0	1	0	1	0	0	0	0
LEFT UPPER LOBE BRONCHIOLITIS EOSINOPHILIC SUBACUTE	0	0	0	0	0	1	0	0	0	0
LEFT UPPER LOBE FIBROSIS FOCAL	0	0	0	0	0	0	0	0	0	1
LEFT UPPER LOBE INFLAMMATION NEUTROPHILIC FOCAL	0	0	0	0	0	0	0	1	0	0
LEFT UPPER LOBE INTERSTITIAL FIBROSIS WITH BRONCHIOLAR ALVEOLAR CELL HYPERPLASIA FOCAL	0	0	0	0	0	1	0	0	0	0
LEFT UPPER LOBE INTERSTITIUM HISTIOCYTE INFILTRATE DIFFUSE	0	0	0	0	0	0	0	0	0	1
LEFT UPPER LOBE INTERSTITIUM HISTIOCYTE INFILTRATE FOCAL	0	0	0	0	0	0	0	0	0	2
LUNG MITE PIGMENT DEPOSITION	0	11	0	11	0	12	0	12	0	12
LYMPHOID AGGREGATES DIFFUSE	0	0	0	0	0	0	0	1	0	0
LYMPHOID HYPERPLASIA	0	0	0	0	0	0	0	9	0	0
MACROPHAGE AGGREGATES WITH FIBERGLASS DEPOSITION	0	0	0	12	0	12	0	6	0	12
MACROPHAGE AGGREGATES WITH LUNG MITE PIGMENT DEPOSITION	0	1	0	0	0	0	0	0	0	0
PERIBRONCHIAL OR PERIVASCULAR AREAS EOSINOPHIL INFILTRATE	0	0	0	0	0	0	0	1	0	0
PERIBRONCHIOLAR AREA BRONCHIOLAR ALVEOLAR CELL HYPERPLASIA	0	0	0	0	0	0	0	0	0	1
PERIVASCULAR AREAS MACROPHAGE ACCUMULATIONS	0	1	0	0	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
PLEURA HISTIOCYTOSIS WITH FIBERGLASS DEPOSITION	0	0	0	1	0	0	0	0	0	0
PLEURAL AND SUBPLEURAL AREAS FIBROSIS AND SMOOTH MUSCLE HYPERPLASIA MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
PLEURAL AND/OR SUBPLEURAL AREAS FIBROSIS MULTIFOCAL	0	0	0	1	0	0	0	1	0	0
PLEURITIS SUBACUTE MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
PNEUMONIA SUBACUTE MULTIFOCAL	0	1	0	0	0	1	0	0	0	0
RIGHT CARDIAC AND LEF MIDDLE LOBES HEMOSIDERIN DEPOSITION	0	0	0	1	0	0	0	0	0	0
RIGHT CARDIAC AND LEFT MIDDLE LOBES INTERSTITIUM HISTIOCYTE INFILTRATE	0	0	0	0	0	0	0	2	0	0
RIGHT CARDIAC AND LEFT UPPER LOBE INFLAMMATION EOSINOPHILIC MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
RIGHT CARDIAC LOBE FIBROSIS	0	0	0	0	0	2	0	0	0	1
RIGHT CARDIAC LOBE INTERSTITIUM HISTIOCYTE INFILTRATE	0	0	0	0	0	1	0	0	0	0
RIGHT CARDIAC LOBE INTERSTITIUM PNEUMONIA SUBACUTE FOCAL	0	1	0	0	0	0	0	0	0	0
RIGHT CARDIAC LOBE PLEURA PLEURITIS CHRONIC EOSINOPHILIC FOCAL	0	0	0	0	0	1	0	0	0	0
RIGHT CARDIAC LOBE SMOOTH MUSCLE HYPERPLASIA	0	0	0	1	0	0	0	0	0	0
RIGHT LOWER LOBE EOSINOPHILIC GRANULOMA FOCAL	0	1	0	0	0	0	0	0	0	0
RIGHT LOWER LOBE INFLAMMATION NEUTROPHILIC FOCAL	0	0	0	0	0	0	0	1	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
RIGHT LOWER LOBE INTERSTITIAL AND INTRA-ALVEOLAR AREAS HISTIOCYTE AND MACROPHAGE ACCUMULATIONS	0	0	0	0	0	1	0	0	0	0
RIGHT LOWER LOBE PERIBRONCHIAL AREA INFLAMMATION SUBACUTE FOCAL	0	0	0	0	0	0	0	0	0	1
RIGHT LUNG PNEUMONIA PURULENT	0	0	0	0	0	1	0	0	0	0
RIGHT MIDDLE LOBE ARTERY ARTERITIS EOSINOPHILIC	0	0	0	0	0	0	0	1	0	0
RIGHT MIDDLE LOBE BRONCHIOLECTASIS	0	0	0	0	0	0	0	0	0	1
RIGHT MIDDLE LOBE FIBROSIS FOCAL	0	0	0	0	0	0	0	1	0	1
RIGHT MIDDLE LOBE INTERSTITIUM HISTIOCYTE INFILTRATE FOCAL	0	0	0	0	0	1	0	0	0	0
RIGHT MIDDLE LOBE NEUTROPHIL INFILTRATE FOCAL	0	1	0	0	0	0	0	0	0	0
RIGHT UPPER LOBE INTERSTITIAL AREAS FIBROSIS FOCAL	0	1	0	0	0	0	0	0	0	0
RIGHT UPPER LOBE INTRA-ALVEOLAR AREAS GRANULOMA MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
RIGHT UPPER LOBE PERIVASCULAR AREAS INFLAMMATION EOSINOPHILIC	0	0	0	0	0	0	0	1	0	0
RIGHT UPPER LOBE PLEURA FIBROSIS FOCAL	0	1	0	0	0	0	0	0	0	0
RIGHT UPPER LOBE PNEUMONIA NEUTROPHILIC FOCAL	0	0	0	0	0	0	0	0	0	1
SMOOTH MUSCLE HYPERPLASIA MULTIFOCAL	0	6	0	3	0	1	0	3	0	3
SUBPLEURAL AREAS HISTIOCYTE INFILTRATE MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
NASAL PASSAGE	[0]	[12]	[0]	[11]	[0]	[12]	[0]	[12]	[0]	[12]

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	3	12
ORGAN AND DIAGNOSIS										
MUCOSA RHINITIS SUBACUTE DIFFUSE	0	0	0	0	0	1	0	0	3	0
MUCOSA SUBEPITHELIAL AREAS LYMPHOCYTIC AND EOSINOPHILIC INFILTRATE	0	0	0	0	0	0	0	0	0	1
MUCOSAL EPITHELIUM METAPLASIA MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
NASAL SEPTUM SUBMUCOSA CONGESTION AND HEMORRHAGE	0	0	0	0	0	1	0	0	0	0
NASAL TURBINATE EPITHELIUM DEGENERATION MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
RESPIRATORY EPITHELIUM METAPLASIA FOCAL	0	0	0	0	0	1	0	0	0	0
RHINITIS EOSINOPHILIC DIFFUSE PARASITIC	0	0	0	1	0	0	0	0	0	0
RHINITIS SUBACUTE	0	0	0	1	0	1	0	0	0	0
TURBINATE RHINITIS DIFFUSE LYMPHOCYTIC	0	0	0	0	0	0	0	1	0	0
VOMERONASAL ORGAN INFLAMMATION SUBACUTE	0	0	0	0	0	1	0	0	0	0
PARANASAL SINUS	[0]	[12]	[0]	[11]	[0]	[12]	[0]	[12]	[0]	[12]
INFLAMMATION SUBACUTE	0	0	0	0	0	2	0	0	0	0
SQUAMOUS METAPLASIA FOCAL	0	0	0	0	0	1	0	0	0	0
TRACHEA	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[11]
EPITHELIUM DEGENERATION	0	0	0	0	0	0	0	0	0	1
EROSION	0	0	0	0	0	0	0	1	0	2
SQUAMOUS METAPLASIA	0	0	0	1	0	0	0	0	0	0
SUBMUCOSA TRACHEITIS SUBACUTE	0	0	0	0	0	1	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
TRACHEITIS EOSINOPHILIC AND NEUTROPHILIC	0	0	0	0	0	0	0	2	0	0
TRACHEITIS NEUTROPHILIC	0	0	0	0	0	0	0	0	0	1
TRACHEITIS SUBACUTE	0	2	0	0	0	4	0	2	0	2
TRACHEITIS ULCERATIVE FOCAL OR MULTIFOCAL	0	0	0	0	0	0	0	2	0	0
TRACHEITIS ULCERATIVE WITH SUPPURATION FOCAL OR MULTIFOCAL	0	1	0	0	0	0	0	1	0	0
SKIN	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[0]
KIDNEY	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]	[0]	[12]
ARTERIES MEDIAL THICKENING	0	0	0	0	0	1	0	0	0	0
ARTERITIS LYMPHOCYTIC MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
CORTEX CARCINOMA	0	0	0	1	0	0	0	0	0	0
CORTEX CYST MULTIPLE	0	0	0	0	0	1	0	0	0	0
CORTEX INTERSTITIUM NEPHRITIS LYMPHOCYTIC FOCAL OR MULTIFOCAL	0	2	0	0	0	1	0	1	0	1
CORTEX TUBULAR HYPERPLASIA MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
CORTICOMEDULLARY JUNCTION LYMPHOCYTIC INFILTRATE FOCAL	0	1	0	0	0	0	0	0	0	0
GLOMERULITIS CHRONIC	0	0	0	0	0	0	0	0	0	1
GLOMERULONEPHRITIS	0	0	0	1	0	0	0	1	0	0
HILUS INFLAMMATION CHRONIC FOCAL	0	0	0	1	0	0	0	0	0	0
INFLAMMATION ACUTE AND CHRONIC FOCAL	0	0	0	0	0	1	0	0	0	0
INTERSTITIUM NEPHRITIS MULTIFOCAL	0	1	0	0	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 38. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	0	12	0	12	0	12	0	12	0	12
ORGAN AND DIAGNOSIS										
LEFT CLEFT FORMATION WITH DEPOSITION OF ADIPOSE TISSUE	0	0	0	0	0	0	0	0	0	1
LEFT GLOMERULAR NEPHROSCLEROSIS FOCAL	0	0	0	0	0	0	0	0	0	1
LEFT GLOMERULONEPHRITIS CHRONIC MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
LEFT MEDULLA TUBULAR EPITHELIUM HYPERPLASIA MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
MEDULLA INTERSTITIUM FIBROSIS MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
MEDULLA MINERALIZATION MULTIFOCAL	0	1	0	0	0	0	0	2	0	0
MEDULLA TUBULAR ADENOMA	0	1	0	0	0	0	0	0	0	0
MEDULLA TUBULAR DEGENERATION	0	1	0	0	0	0	0	0	0	0
MEDULLA TUBULAR EPITHELIUM HYPERPLASIA	0	1	0	0	0	0	0	0	0	0
NEPHRITIS CHRONIC FOCAL	0	1	0	0	0	1	0	0	0	0
NEPHROPATHY CHRONIC MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
PELVIC EPITHELIUM HYPERPLASIA BILATERAL	0	1	0	0	0	0	0	0	0	0
PELVIS SUBEPITHELIAL AREA HEMOSIDERIN DEPOSITION	0	1	0	0	0	0	0	0	0	0
TUBULAR EPITHELIUM HEMOSIDERIN DEPOSITION	0	1	0	0	0	0	0	0	0	0
URETER	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[1]
DILATATION WITH CALCULUS FORMATION BILATERAL	0	0	0	0	0	0	0	0	0	1
URINARY BLADDER	[0]	[11]	[0]	[11]	[0]	[11]	[0]	[4]	[0]	[12]
SUBEPITHELIAL AREAS INFLAMMATION SUBACUTE	0	0	0	0	0	1	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 39. SUMMARY TOTAL OF SMOOTH MUSCLE HYPERPLASIA AND FIBROSIS FOR INDIVIDUAL ANIMALS AMONG ALL DOSAGE GROUPS BY LEVEL OF INTENSITY

	0 mg/m^3	5 mg/m^3 (FO3)	5 mg/m^3 (FO4)	15 mg/m^3 (FO1)	15 mg/m^3 (FO2)
Smooth Muscle Hyperplasia					
Minimum	3	1	1		
Mild	1	2		3	1
Moderate	3	2	1		2
Marked					1
Severe					
Total	7	5	2	3	4
Fibrosis					
Minimum		1	1	1	2
Mild	5	1	1	3	1
Moderate	1		1	1	
Marked	1			1	
Severe					
Total	7	2	3	6	3

TABLE 40. SUMMARY OF SMOOTH MUSCLE HYPERPLASIA AND FIBROSIS AMONG ALL DOSAGE GROUPS

Diagnosis and Severity	Dose Group	F05	F03	F04	F01	F02
	Sex	M	M	M	M	M
	Number in Group	12	12	12	12	12
Bronchioles, smooth muscle hyperplasia, multifocal						
Marked						1
Fibrosis						
Minimal					1	
Fibrosis, multifocal						
Mild		3			1	
Interstitium, fibrosis, focal or multifocal						
Minimal			1			
Mild				1		
Left lower lobe, fibrosis, focal						
Minimal					1	
Mild		1				
Left lower lobe, smooth muscle hyperplasia						
Minimal		1				
Mild			1			
Left lower lobe, pleura, fibrosis, focal						
Present					1	
Left middle lobe, fibrosis, focal or multifocal						
Moderate					1	
Marked		1			1	

TABLE 40. (Continued)

Diagnosis and Severity	Dose Group	F05	F03	F04	F01	15 F02 -2
	Sex	M	M	M	M	M
	Number in Group	12	12	12	12	12
Left upper lobe, fibrosis, focal						
Minimal						1
Left upper lobe, interstitial fibrosis with bronchiolar alveolar cell hyperplasia, focal						
Minimal				1		
Left upper and left lower lobes, smooth muscle hyperplasia						
Minimal				1		
Pleural and subpleural areas, fibrosis and smooth muscle hyperplasia, multifocal						
Moderate				1		
Pleural and/or subpleural areas, fibrosis, multifocal						
Mild			1		1	
Right apical lobe, interstitial areas, fibrosis, focal						
Mild		1				
Right apical lobe, pleura, fibrosis, focal						
Moderate		1				
Right cardiac lobe, fibrosis						
Minimal				1		1
Mild					1	

TABLE 40. (Continued)

Diagnosis and Severity	Dose Group	F05	F03	F04	F01	F02
	Sex	M	M	M	M	M
	Number in Group	12	12	12	12	12
Right cardiac lobe, smooth muscle hyperplasia						
Moderate			1			
Right middle lobe, fibrosis, focal						
Mild						1
Marked					1	
Smooth muscle hyperplasia, multifocal						
Minimal		2	1			
Mild		1	1		4	1
Moderate		3	1			2

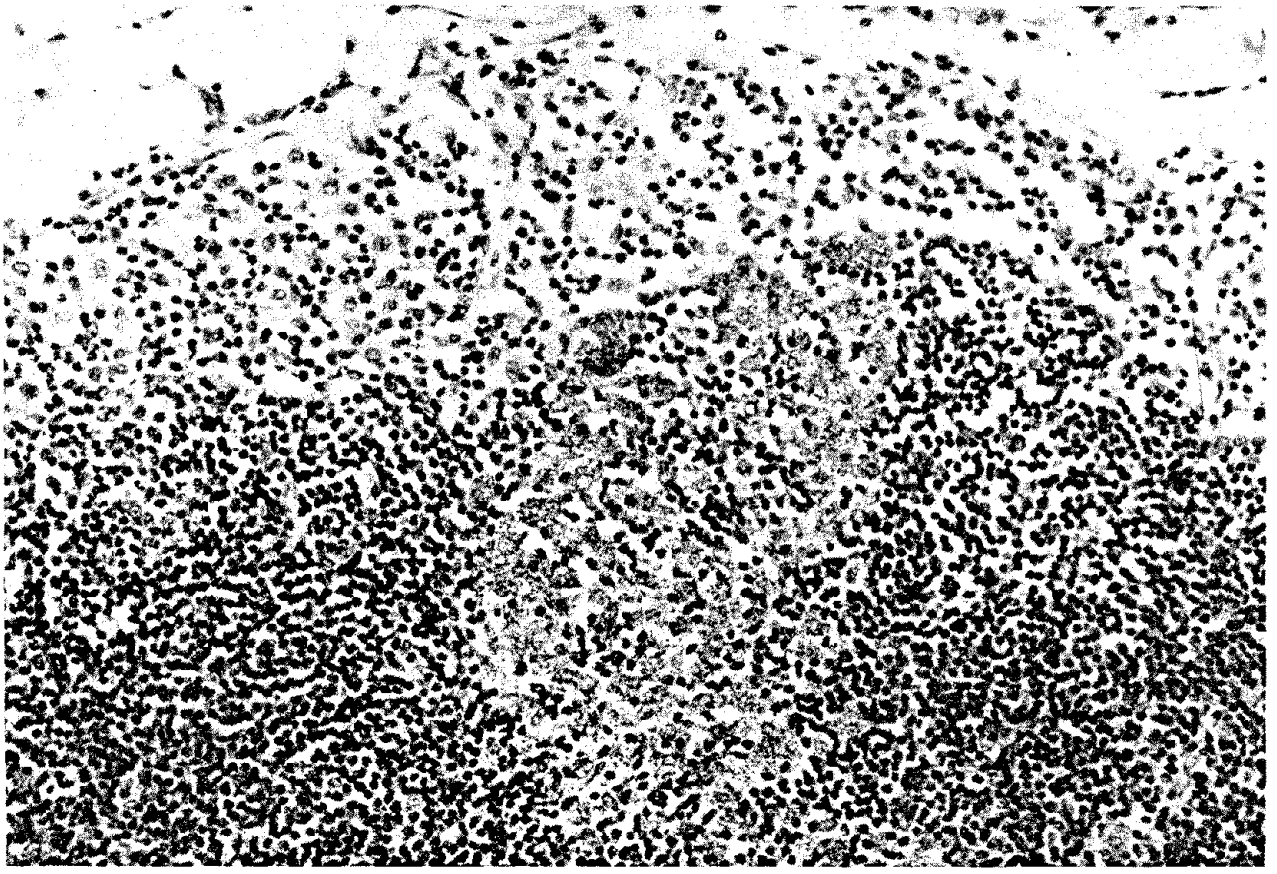


Figure 42. Tracheobronchial lymph node (50X), male monkey, F04 group. A large macrophage aggregate is present in the medulla and contains moderate amounts of fibrous glass and lung mite pigment.

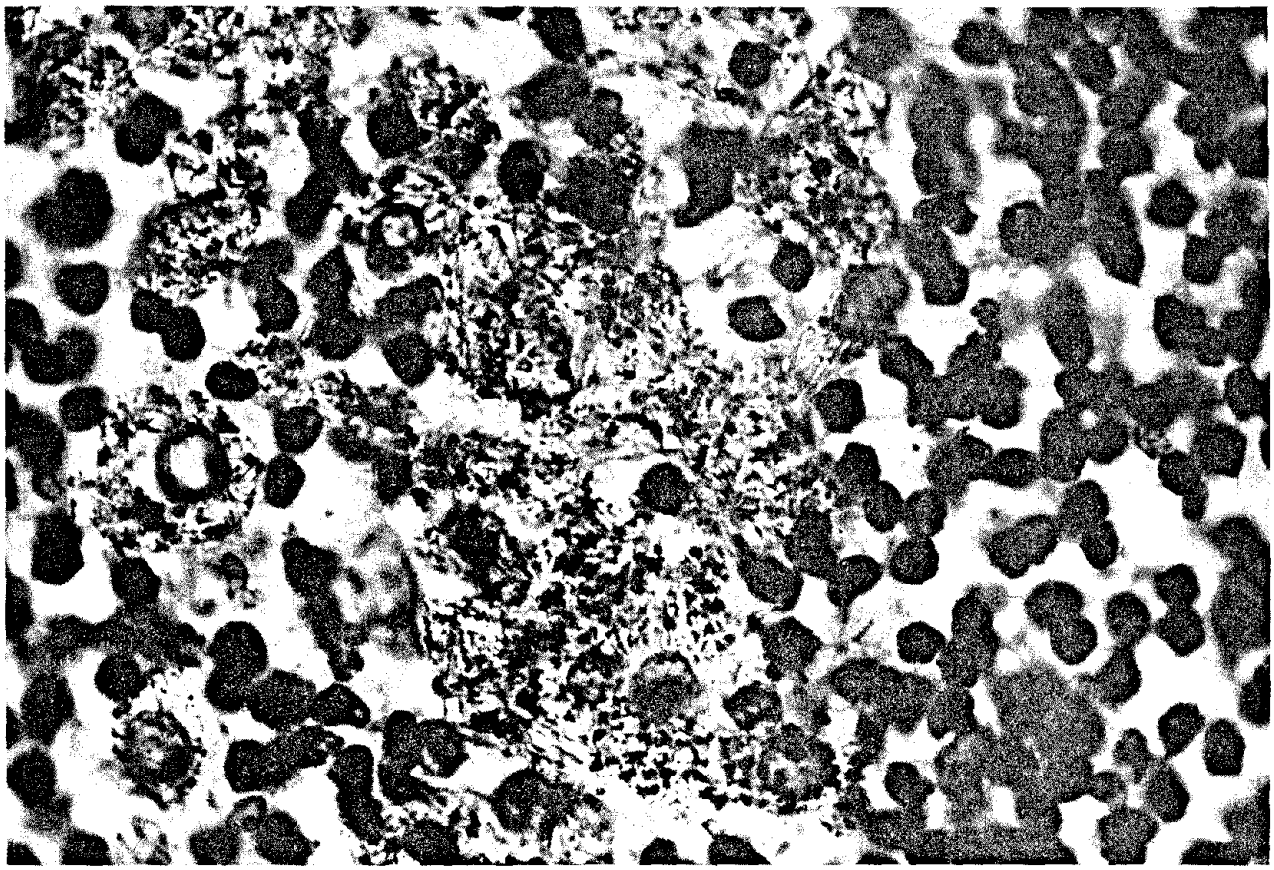


Figure 43. Tracheobronchial lymph node (250X - reduced light), male monkey, F04 group. Fibrous glass particles are clearly depicted in the macrophage aggregate.

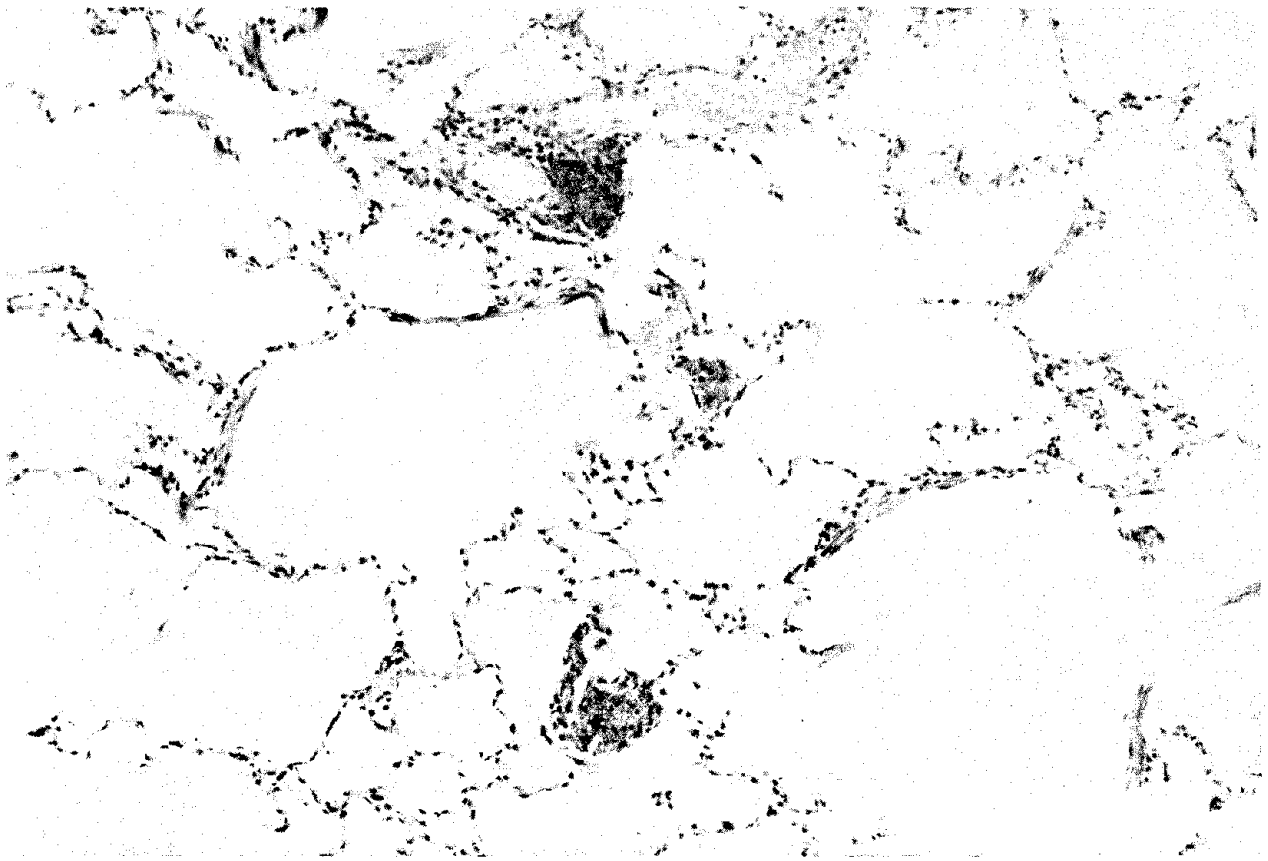


Figure 44. Lung (25X), male monkey, F04 group. Macrophage aggregates are present in the alveoli and about blood vessels which contain fibrous glass and lung mite pigment.

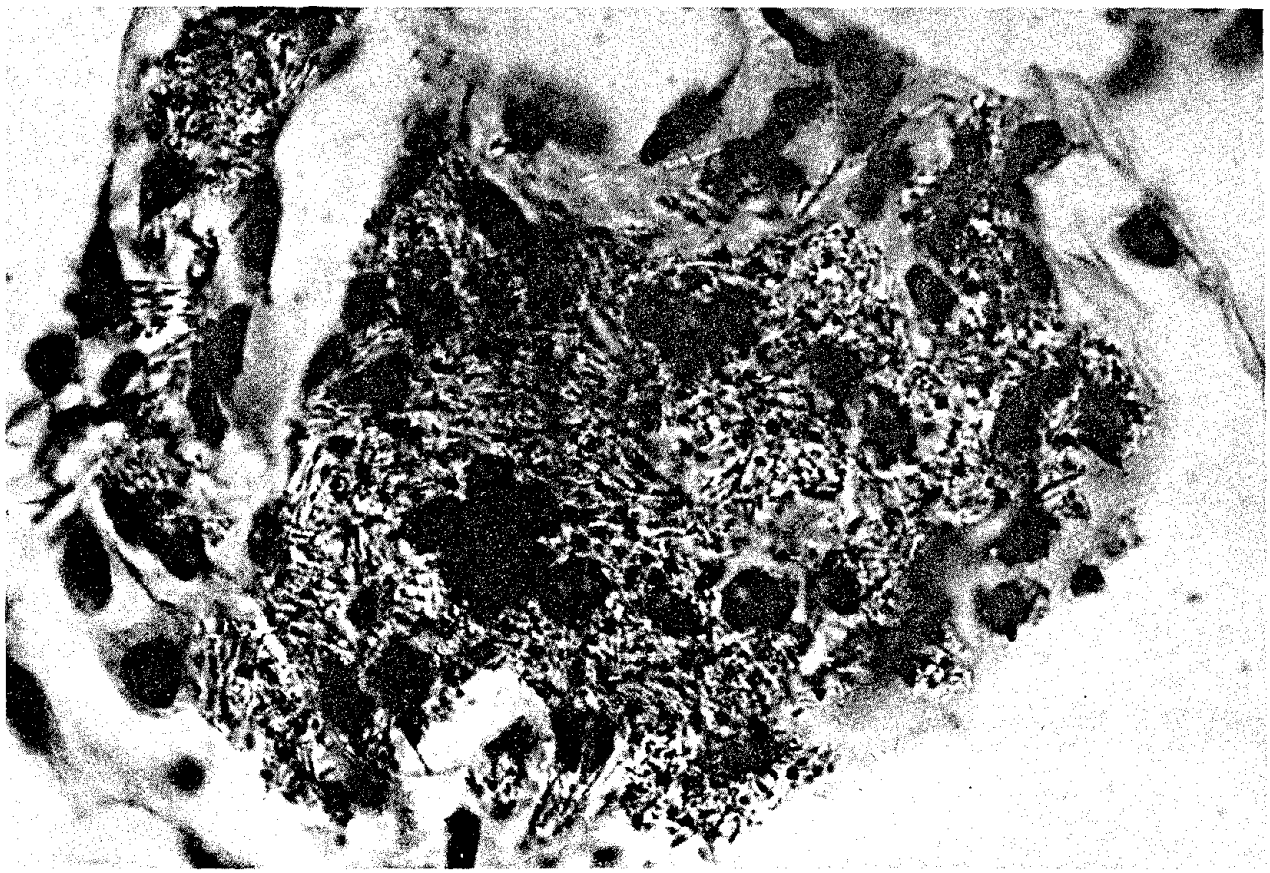


Figure 45. Lung (250X - reduced light), male monkey, F04 group. Fibrous glass particles and lung mite pigment are clearly depicted in this alveolar macrophage aggregate.

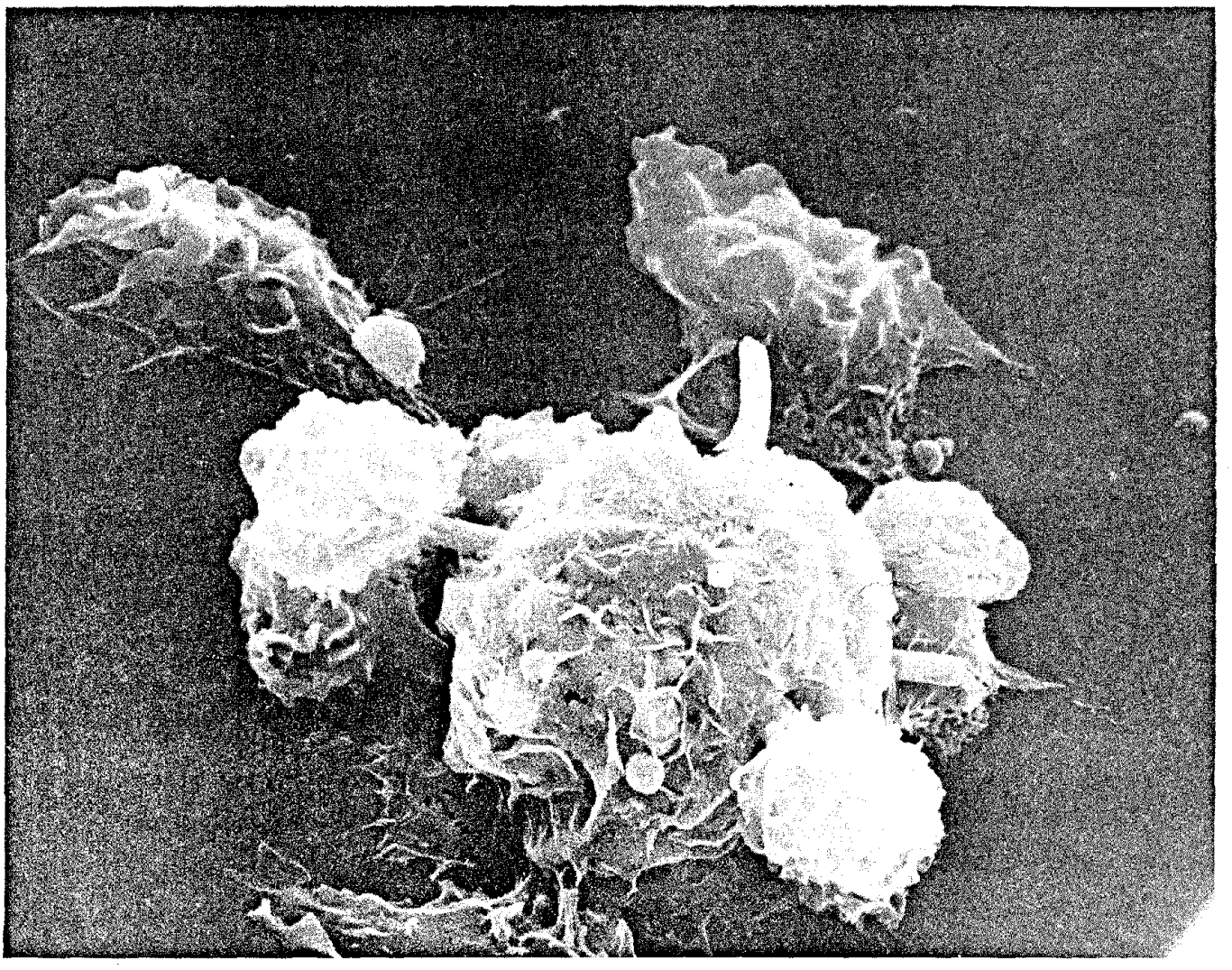


Figure 46. This SEM photograph (2500X) depicts several fibrous glass-laden alveolar macrophages that were obtained by pulmonary gavage from a male monkey (Group F02, Animal #811A) that died spontaneously.

exposed to fiberglass fibers and was included in the above diagnosis rather than being listed as a separate change. Macrophages containing fiberglass were usually located in peribronchiolar, peribronchial, or perivascular areas as well as within alveoli and in pleural and subpleural locations. There were no obvious differences in the lobar distribution of these fiberglass-containing macrophages or free fiberglass fibers. In many instances, the macrophages that contained fiberglass also contained pigment and debris typical of that resulting from infestation with lung mites (Pneumonyssus simicola). Although fiberglass-containing macrophages and free fibers occurred in pleural and subpleural locations and fiberglass-containing macrophages were prominent in tracheobronchial lymph nodes, there was no further evidence of translocation of fiberglass fibers. There was no evidence of fiberglass in organs other than lungs and tracheobronchial lymph nodes.

The only other change that was apparent in fiberglass-exposed monkeys occurred solely in Group F01. This change consisted of mildly increased numbers of lymphoid nodules or aggregates in peribronchiolar and perivascular areas. There were no other associated changes nor did this change occur in other fiberglass-exposed groups or in controls.

There were differences in the extent of involvement among the various exposure groups. This was observed as a substantially less extensive involvement of animals from the F01 group (15 mg/m^3 > 20 micrometer with binder) as compared to the other exposed groups. There were minimal variations in qualitative or quantitative fiberglass-related changes in lungs or tracheobronchial lymph nodes among animals from the other three exposure groups. Numbers and qualitative severities of the fiberglass-induced pulmonary lesion and tracheobronchial lymph node lesion (i.e., macrophage aggregates with fiberglass deposition [lung] and fiberglass deposition [tracheobronchial lymph node]) are as follows:

		Number Involved			
		Group	Group	Group	Group
Lesion	Severity	F01	F02	F03	F04
Pulmonary	Minimal	5	1	-	-
	Mild		10	11	12
	Moderate	1	1	1	-
	No lesion	6	-	-	-

Tracheobronchial lymph node	Minimal	2	5	1	1
	Mild	2	3	6	4
	Moderate	-	2	5	5
	No lesion	7	2	-	2

The only difference was a slightly greater general severity for groups F03 and F04 as compared to Group F02 for the tracheobronchial lymph node lesion. The fiberglass-containing macrophages, in the lungs of virtually all monkeys, occupied less than 5 percent of the total area of the lung sections.

Fifty-nine of the 60 monkeys used in this study had lesions consistent with lung mite infestation. These lesions ranged from the presence of lung mite pigment and debris in macrophages to extensive lesions, including bronchiolitis that was usually eosinophilic and/or granulomatous. Bronchiectasis was present in a few animals and parasites or remnants of parasites were observed in the lungs of some monkeys. Fibrosis and/or smooth muscle hyperplasia was common in the lungs of animals from all groups. These changes were nearly always focal or multifocal and were qualitatively and quantitatively similar among all dosage groups. The smooth muscle hyperplasia, fibrosis, pleural adhesions, and most inflammatory changes in the lungs of these monkeys were apparently related to the lung mite infestations. The distribution of the smooth muscle hyperplasia suggested that it occurred primarily as a result of local changes in ventilatory mechanics. Lung mite pigments and debris usually coexisted with fiberglass in the pulmonary macrophages of monkeys from groups exposed to fiberglass. The numbers of single macrophages and macrophage aggregates were, however, mildly to moderately increased in some animals from each of the exposure groups.

Inflammatory lesions of the nasal passages, trachea, and paranasal sinuses were slightly more prominent in monkeys from Group F04 as compared to controls. However, the diversity of these changes and their mild intensity does not make a definitive interpretation possible.

Other microscopic lesions in these monkeys were apparently unrelated to the fiberglass exposures because they occurred in both control and exposed groups with similar frequency, because they commonly occur in monkeys of this species, or because of the presence of an identifiable etiology such as

There was no evidence that any of the changes observed at necropsy were associated with exposure to fiberglass. Many of the lesions observed grossly were consistent with parasite infestations. The anthracosilicosis that was described grossly in monkeys from all groups resulted from the black or green-black depositions of lung mite pigments which are common in cynomologous monkeys. Most pulmonary changes that were described grossly were apparently the result of lung mite infestations.

Grossly observed subcapsular splenic nodules are noteworthy although not related to fiberglass exposure. Although the basic changes were similar, the specific characteristics varied so that several different diagnoses were made in different animals. These changes included eosinophilic or neutrophilic infiltrates, reticulum cell hyperplasia, or granulomatous inflammation, all of which were focal or multifocal and occurred in various combinations. Microfilarial parasites were observed in these lesions in several animals and appeared to be the inciting agent.

Two monkeys died spontaneously during the course of the study. One of these monkeys was from Group F02 (811A) and the other was from Group F03 (863A). There was no indication that the deaths of either of these monkeys were related to fiberglass exposure. The cause of death in monkey 811A could not be determined from changes observed grossly, microscopically, or by serum chemistry or hematologic anlaysis. The apparent cause of death in monkey 863A was amyloidosis of pancreatic islets resulting in diabetes mellitus as reflected in the profoundly elevated serum glucose. Other histological changes were observed in this monkey, the most notable being tubular hyperplasia and tubular carcinoma that occurred in the left kidney. There was no evidence that any of these changes resulted from fiberglass exposure.

Early Death Rats

Observations recorded during necropsy are shown for individual animals in Tables I-11 through I-15 and are summarized in Table 41. Microscopic lesions are shown for individual animals in Tables I-16 through I-20 and are summarized in Table 42.

TABLE 41.

NECROPSY SUMMARY BY GROUP AND SEX

PROJECT: G7188-13 STUDY: NIOSH SPECIES: RAT

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND OBSERVATION										
ABDOMINAL CAVITY										
ASCITES	2	0	0	1	1	3	1	0	0	0
MASS PERIRENAL	0	0	0	0	1	0	0	0	0	0
TUMOR	0	1	0	0	0	0	0	0	0	0
TUMOR DIFFUSE	0	0	1	0	0	0	0	0	0	0
RIGHT DORSAL MASS	0	1	0	0	0	0	0	0	0	0
SEROSA GRANULAR DIFFUSE	0	0	0	0	0	1	0	0	0	0
SEROSA MASS DIFFUSE	0	0	0	0	0	0	0	0	1	0
ADRENAL GLAND										
ENLARGED	0	0	0	0	0	0	0	0	1	0
ENLARGED BILATERAL	0	1	0	0	2	0	1	1	0	0
LEFT ENLARGED	0	1	0	0	0	0	1	0	0	0
RIGHT ENLARGED	0	1	0	1	0	0	0	0	0	0
RIGHT FOCI WHITE MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
BRAIN										
CEREBELLUM BLACK FOCI	0	0	0	0	0	0	0	0	0	1
CEREBELLUM DARK FOCUS	0	0	0	0	0	0	2	0	0	0
CEREBRUM BLACK FOCI	0	0	0	0	0	0	1	0	0	0
CEREBRUM DARK FOCUS	0	0	0	0	0	0	1	0	0	0
CEREBRUM RED FOCUS MULTIFOCAL	0	0	0	0	1	0	0	0	0	0
MENINGES THICKENED	0	1	0	0	0	0	0	0	0	0
CECUM										

TABLE 41. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND OBSERVATION										
ENLARGED	0	0	0	0	0	0	0	1	0	0
CERVICAL AREA										
MASS	0	0	0	0	0	1	0	0	0	0
DUODENUM										
FOCUS CREAM/YELLOW	0	0	0	0	1	0	0	0	0	0
MUCOSA WHITE FOCI	0	0	0	0	0	0	0	1	0	0
EPIDIDYMIS										
RIGHT ENLARGED	0	0	0	1	0	0	0	0	0	0
EYE										
LEFT LENS ENLARGED OPAQUE	0	1	0	0	0	0	0	0	0	0
LEFT LENS RED AND THICK	0	0	0	1	0	0	0	0	0	0
RIGHT LENS OPAQUE	0	0	1	0	0	0	0	0	0	0
HEAD										
MASS	0	1	0	0	0	0	0	0	0	0
HEART										
APEX FOCUS YELLOW	0	0	0	0	0	1	0	0	0	0
KIDNEY										
FOCUS WHITE MULTIFOCAL	1	0	0	0	0	0	0	0	0	0
GRANULAR SURFACE BILATERAL	1	1	0	1	0	0	1	0	0	1
CORTEX SMALL BILATERAL	0	0	0	1	0	0	0	0	0	0
CORTEX CYST MULTIFOCAL BILATERAL	0	0	0	0	1	0	0	0	0	0
LEFT CYSTIC	0	0	0	0	0	0	0	0	1	0

TABLE 41. (Continued

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND OBSERVATION										
LEFT ENLARGED	0	0	0	0	1	0	0	0	0	0
LEFT PELVIS ECTASIA	1	0	0	0	0	0	0	0	0	0
RIGHT COLLAPSED	0	0	0	0	1	0	0	0	0	0
RIGHT NODULES MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
RIGHT GRANULAR SURFACE	0	0	1	0	0	0	0	0	0	0
LIVER										
ENLARGED	0	0	0	1	1	0	0	1	0	2
MOTTLED SURFACE	7	1	3	2	3	5	2	6	6	5
RED FOCUS MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
SLIGHTLY MOTTLED	1	0	0	0	0	0	0	0	0	0
CAUDATE LOBE CYST FOCAL	0	0	0	0	0	0	1	0	0	0
LEFT LATERAL LOBE NODULE YELLOW	0	1	0	0	0	0	0	0	0	0
MEDIAN LOBE NODULE	0	0	0	0	1	2	1	0	0	0
MEDIAN LOBE NODULE WHITE	0	0	0	1	0	0	0	0	0	0
MEDIAN LOBE RIGHT SIDE NODULE	0	1	0	0	0	0	0	0	0	0
LUNG										
MOTTLED	0	0	0	0	1	0	0	0	0	0
MOTTLED RED	0	0	0	0	1	0	0	0	0	0
WHITE FOCUS MULTIFOCAL	1	0	0	0	0	0	0	0	0	0
RED AREAS MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
ALL LOBES PLEURA MARGINS WHITISH FOCI	0	0	0	0	0	0	0	0	0	1
LEFT LOBE FOCUS	0	0	0	0	1	0	0	0	0	0

TABLE 41. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND OBSERVATION										
LEFT LOBE NODULE	0	0	1	0	0	0	0	0	0	0
LEFT LOBE NODULE WHITE FOCAL	0	0	0	0	0	1	0	1	0	0
LEFT LOBE PLEURA PLAQUE GRAY MULTIFOCAL SMALL	0	0	0	0	0	0	0	0	1	0
LEFT LOBE PLEURA WHITE MARGIN	0	0	0	0	1	0	0	0	0	0
PLEURA ADHESIONS MULTIFOCAL	0	0	0	0	1	0	0	0	0	0
PLEURA PLAQUE FOCAL	1	0	0	0	0	0	0	0	0	0
PLEURA PLAQUE MULTIFOCAL	0	0	0	0	1	0	0	0	0	0
PLEURA PLAQUE GRAY MULTIFOCAL	0	0	2	4	4	0	1	0	5	0
RIGHT AND LEFT DIAPHRAGMATIC PLEURA MARGINS WHITE FOCI	0	0	0	1	0	0	0	0	0	0
LYMPH NODE										
LUMBAR ENLARGED	0	0	0	0	0	0	0	0	0	1
MANDIBULAR ENLARGED	0	0	0	0	0	0	0	0	1	0
MEDIASTINAL ENLARGED	0	0	0	0	0	0	0	0	1	0
MESENTERIC ENLARGED	1	0	1	2	3	2	1	4	1	2
PANCREATIC ENLARGED	0	0	0	2	1	0	0	1	1	0
RENAL ENLARGED	0	0	0	0	1	0	0	0	0	0
SUBMANDIBULAR ENLARGED	0	1	0	0	0	0	0	0	0	0
THYMIC ENLARGED	0	0	0	0	1	0	0	0	0	0
MESENTERY										
MASS	1	1	0	0	0	0	0	0	0	0
MASS WHITE FOCAL	1	0	0	0	0	0	0	0	0	0

TABLE 41. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND OBSERVATION										
ADHESIONS MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
NODULAR AND WHITE FAT NECROSIS	0	0	0	0	0	0	0	0	0	1
OVARY										
LEFT CYSTIC	0	0	0	0	1	0	0	0	1	0
LEFT ENLARGED	0	0	0	0	0	0	0	0	1	0
RIGHT CYSTIC	1	0	1	0	0	0	0	0	0	0
RIGHT ENLARGED	0	0	0	0	1	0	0	0	0	0
PANCREAS										
MASS RED	0	0	0	0	1	0	0	0	0	0
CYSTIC MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
NODULE WHITE FIRM	0	0	0	0	0	0	0	1	0	0
PENIS										
MASS	0	0	0	0	0	0	0	0	0	1
PERIURINARY BLADDER										
MASS	0	0	0	1	0	0	0	0	0	0
PITUITARY GLAND										
BLACK DOT	0	0	0	1	0	0	0	0	0	0
BLACK FOCI	1	0	0	0	0	0	0	0	0	0
CYST FOCAL	0	0	0	0	0	1	0	0	0	0
DARK FOCUS	0	0	1	1	0	0	0	0	0	0
ENLARGED	3	3	2	3	9	2	2	6	2	2
ENLARGED RED	3	0	0	0	1	0	2	2	1	2

TABLE 41. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND OBSERVATION										
ENLARGED TAN	0	0	0	0	1	0	0	0	0	0
ENLARGED DARK RED FOCUS	0	0	0	0	1	0	0	0	0	0
DARK RED FOCUS	0	0	0	0	1	0	0	0	0	0
RED FOCUS	0	0	0	0	0	1	1	0	0	0
BLACK FOCUS	2	1	0	0	1	0	0	1	3	0
BROWN FOCUS	0	0	0	0	1	0	0	0	0	0
ENLARGED BROWN	1	0	0	0	0	0	0	0	0	0
ENLARGED CYSTIC RED	0	0	0	0	1	0	0	0	0	0
RIB										
LEFT FIFTH MASS TO LEFT OF SPINAL COR D	0	1	0	0	0	0	0	0	0	0
RIB CAGE										
RIGHT LOWER SUBCUTICULAR MASS	0	1	0	0	0	0	0	0	0	0
SALIVARY GLAND										
RIGHT ENLARGED	0	0	0	0	0	1	0	0	0	0
SEROSA										
MASS MULTIFOCAL	1	0	0	0	0	0	0	0	0	0
YELLOWISH	0	2	0	0	0	0	0	0	0	0
SKIN										
ALOPECIA FOCAL	0	0	0	0	0	0	0	1	0	0
ABDOMEN MASS	0	0	0	0	0	0	0	0	1	0
DORSAL-LUMBAR AREA MASS	0	0	0	0	0	1	0	0	0	0
FACIAL AREA SCABS	0	0	0	0	0	0	1	0	0	0

TABLE 41. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		15 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND OBSERVATION										
GENITAL AREA MASS	1	0	0	0	0	0	0	0	0	0
HEAD MASS	0	0	0	0	0	0	0	0	1	0
HEAD DORSAL AREA MASS	0	0	0	0	0	0	0	0	0	1
LEFT ABDOMINAL AREA MASS	0	0	0	0	0	0	0	0	1	0
LEFT AXILLARY AREA MASS	0	0	0	1	0	0	0	0	0	0
LEFT AXILLARY AREA MASS WHITE	0	0	0	0	0	0	1	0	0	0
LEFT BRACHIAL AREA MASS	0	0	0	0	1	0	0	0	1	0
LEFT FORELEG MASS WHITE	0	0	0	0	0	0	0	1	0	0
LEFT HIND LEG MASS	0	0	0	0	1	0	1	0	0	0
LEFT INGUINAL AREA MASS	0	0	0	0	2	0	0	0	0	0
LEFT LATERAL CERVICAL AREA MASS	1	0	0	0	0	0	0	0	0	0
LEFT SIDE OF HEAD MASS	0	0	0	0	0	0	0	0	1	0
LEFT THORACIC/ABDOMINAL AREA MASS	0	0	0	0	0	1	0	0	0	0
MANDIBLE MASS	1	0	0	0	0	0	0	0	0	0
PERIANAL AREA MASS	0	1	0	1	0	0	0	0	0	1
PERIANAL AREA MASS FOCAL	1	0	0	0	0	0	0	0	0	0
RIGHT ABDOMEN MASS	1	0	0	0	0	0	0	0	0	0
RIGHT AXILLARY AND THORACIC AREA MASS	1	0	0	0	0	0	0	0	0	0
RIGHT AXILLARY AREA MASS	0	0	0	0	0	0	0	0	1	1
RIGHT BRACHIAL AREA MASS	0	0	0	0	1	0	0	0	0	0
RIGHT FOREARM MASS	0	0	0	0	0	0	0	0	0	1
RIGHT INGUINAL AREA MASS	0	0	0	0	0	0	0	0	1	0

TABLE 41. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND OBSERVATION										
RIGHT LUMBAR AREA MASS	0	0	0	1	0	0	0	0	0	0
RIGHT MANDIBLE MASS	0	0	0	0	1	0	0	0	0	0
RIGHT SHOULDER MASS	1	0	0	0	0	0	0	0	0	0
RIGHT THORACIC AREA MASS	0	0	0	0	0	0	0	0	2	0
SUBCUTIS LEFT CERVICAL AREA MASS CYSTIC	0	0	0	0	0	0	0	0	0	1
SPLEEN										
ENLARGED	9	3	5	8	11	12	11	10	9	10
STOMACH										
BLACK FOCUS MULTIFOCAL	0	0	0	0	1	0	0	0	0	0
ULCER FOCAL	0	1	0	0	0	0	0	0	0	0
CARDIAC REGION MUCOSA ULCERATED	0	0	0	1	0	0	0	0	0	0
FUNDIC PORTION MUCOSA EROSIONS	0	0	1	0	0	0	0	0	0	0
MUCOSA WHITE FOCI	0	0	0	0	0	0	0	1	0	0
PYLORUS ULCERATION RED	1	0	0	0	0	0	0	0	0	0
SUBCUTIS										
RIGHT INGUINAL AREA MASS WHITE	0	0	0	0	1	0	0	0	0	0
THORACIC AREA MASS SOFT	0	0	0	0	1	0	0	0	0	0
TESTIS										
ENLARGED BILATERAL	0	1	0	0	0	0	0	0	0	0
SMALL BILATERAL	0	1	0	3	0	2	0	2	0	1
SMALL AND SOFT BILATERAL	0	0	0	1	0	0	0	0	0	0
NODULES WHITE BILATERAL	0	5	0	5	0	6	0	2	0	6

TABLE 41. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND OBSERVATION										
SMALL WITH NODULES WHITE BILATERAL	0	0	0	0	0	0	0	0	0	1
LEFT NODULES WHITE	0	0	0	0	0	1	0	1	0	1
LEFT SMALL	0	0	0	1	0	0	0	0	0	1
RIGHT CYSTIC	0	0	0	1	0	0	0	0	0	0
RIGHT NODULES WHITE	0	0	0	2	0	1	0	0	0	0
RIGHT SMALL	0	1	0	0	0	0	0	1	0	0
TUNICA VAGINALIS GRANULAR SURFACE BIL ATERAL	0	0	0	0	0	1	0	0	0	0
THORACIC CAVITY										
ASCITES	1	0	0	1	0	0	0	0	2	0
MASS BROWN	0	0	0	0	0	0	0	1	0	0
NODULES WHITE MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
RIGHT SIDE MASS	0	0	0	0	0	0	0	0	1	0
THYMUS										
ENLARGED	1	0	0	0	1	0	0	0	2	0
THYROID GLAND										
LEFT ENLARGED	0	0	0	0	0	0	0	0	0	1
RIGHT ENLARGED	0	0	0	0	0	0	1	0	0	0
RIGHT ENLARGED RED	0	0	0	1	0	0	0	0	0	0
URINARY BLADDER										
DILATED	0	0	0	0	0	0	0	0	0	1
MASS	0	0	1	0	0	0	0	0	0	0
UTERINE HORN										
DILATED BILATERAL	1	0	0	0	0	0	0	0	1	0

TABLE 41. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND OBSERVATION										
LEFT DILATED	0	0	1	0	0	0	0	0	1	0
LEFT MASS	0	0	0	0	2	0	1	0	0	0
RIGHT DILATED	1	0	0	0	1	0	0	0	1	0
RIGHT ENLARGED	0	0	1	0	0	0	1	0	0	0
UTERUS										
DILATED	1	0	0	0	0	0	0	0	0	0
ANIMAL MISSING-NO NECROPSY PERFORMED	1	0	0	0	1	0	0	0	0	0

TABLE 42. HISTOPATHOLOGY SUMMARY BY GROUP AND SEX

PROJECT: G7188-13 STUDY: NIOSH SPECIES: RAT

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
ADIPOSE TISSUE	[0]	[0]	[0]	[1]	[0]	[2]	[0]	[1]	[0]	[0]
MONONUCLEAR CELL LEUKEMIA	0	0	0	1	0	1	0	0	0	0
STEATITIS ACUTE MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
MESENTERY	[1]	[2]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]
FAT NECROSIS DIFFUSE	0	1	0	0	0	0	0	0	0	0
STEATITIS CHRONIC FOCAL	1	1	0	0	0	0	0	0	0	0
PLEURAL MEMBRANE	[0]	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[0]	[0]
MONONUCLEAR CELL LEUKEMIA	0	0	0	0	1	0	0	0	0	0
ARTERY	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[0]
EYE SCLERA LIPOMATOUS TUMOR METASTATIC UNILATERAL	0	0	0	1	0	0	0	0	0	0
ARTERY-PULMONARY	[0]	[0]	[0]	[2]	[1]	[0]	[0]	[1]	[0]	[1]
LYMPHOMA FOCAL	0	0	0	0	0	0	0	0	0	1
MINERALIZATION DYSTROPHIC FOCAL	0	0	0	1	1	0	0	0	0	0
MINERALIZATION DYSTROPHIC MULTIFOCAL	0	0	0	1	0	0	0	1	0	0
BLOOD VESSEL	[1]	[0]	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[0]
CEREBRUM INFARCT FOCAL	0	0	0	0	0	1	0	0	0	0
MUSCLE SKELETAL PERIVASCULITIS SUBACUTE DIFFUSE	1	0	0	0	0	0	0	0	0	0
BLOOD VESSEL-PULMONARY	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[0]
TUMOR ENDOCRINOID PATTERN FOCAL	0	1	0	0	0	0	0	0	0	0
VASCULITIS SUBACUTE DIFFUSE	0	0	0	0	0	0	0	1	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		.5 MG/M3-3		.5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
HEART	[18]	[14]	[12]	[18]	[25]	[20]	[19]	[17]	[23]	[19]
ADENOCARCINOMA TUBULAR METASTATIC ORIGIN INTESTINE	0	0	0	0	0	0	0	0	1	0
ATRIUM ATRIAL THROMBOSIS	0	0	0	0	0	1	0	0	0	0
ATRIUM MYOCARDIUM MYOCARDITIS ACUTE DIFFUSE	0	0	0	1	0	0	0	0	0	0
ATRIUM MYOCARDIUM MYOCARDITIS SUPPURATIVE DIFFUSE	0	0	0	0	0	1	0	0	0	1
EPICARDIUM EPICARDITIS SUBACUTE MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
HEART VALVE LEAFLET ENDOCARDIOSIS DIFFUSE	0	0	0	0	1	0	0	0	0	0
HEART VALVE LEAFLET ENDOCARDIOSIS FOCAL	0	0	0	0	0	0	0	0	1	0
LEFT ATRIUM THROMBUS SUBACUTE	0	0	0	0	0	0	0	0	1	0
LIPOMATOUS TUMOR METASTATIC SITE	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	9	3	5	6	11	13	11	9	10	9
MYOCARDIUM CARDIOMYOPATHY FOCAL	0	0	0	0	1	0	0	0	0	0
MYOCARDIUM DEGENERATION MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
MYOCARDIUM MINERALIZATION DYSTROPHIC MULTIFOCAL	0	0	1	1	0	0	0	0	0	0
MYOCARDIUM MYOCARDITIS ACUTE MULTIFOCAL	1	0	0	1	0	0	0	0	0	0
MYOCARDIUM MYOCARDITIS CHRONIC ACTIVE FOCAL	0	0	0	0	0	0	1	0	0	0
MYOCARDIUM MYOCARDITIS LYMPHOCYTIC MULTIFOCAL	0	0	0	0	0	0	1	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		.5 MG/M3-3		.5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
MYOCARDIUM MYOCARDITIS SUBACUTE FOCAL	0	0	0	0	0	0	1	0	1	0
MYOCARDIUM MYOCARDITIS SUBACUTE MULTI FOCAL	6	6	3	4	9	6	2	6	5	7
CECUM	[0]	[0]	[1]	[1]	[0]	[0]	[2]	[2]	[1]	[1]
MONONUCLEAR CELL LEUKEMIA	0	0	1	0	0	0	0	2	0	0
COLON	[17]	[13]	[11]	[14]	[21]	[18]	[18]	[14]	[21]	[18]
ADENOCARCINOMA TUBULAR PRIMARY SITE	0	0	0	0	0	0	0	0	1	0
COLITIS GRANULOMATOUS FOCAL FOREIGN BODY HAIR SHAFT	0	0	0	0	0	0	0	0	0	1
COLITIS SUBACUTE FOCAL	0	0	0	1	0	0	0	0	0	0
COLITIS SUBACUTE MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
MESOTHELIOMA	0	0	0	0	0	2	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	1	0	0	2	3	0	1	0	2	3
MUCOSA DEGENERATION MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
NEMATODIASIS	1	1	2	1	2	1	1	0	0	0
SEROSA MONONUCLEAR CELL LEUKEMIA	0	0	1	0	0	0	0	0	0	0
SEROSA SEROSITIS SUBACUTE DIFFUSE	0	0	0	0	0	0	0	1	0	0
DUODENUM	[0]	[0]	[0]	[0]	[1]	[0]	[0]	[2]	[1]	[0]
DUODENITIS ACUTE FOCAL	0	0	0	0	1	0	0	0	0	0
DUODENITIS ACUTE NECROTIZING MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
ESOPHAGUS	[18]	[14]	[12]	[18]	[24]	[20]	[19]	[17]	[23]	[19]
MONONUCLEAR CELL LEUKEMIA	2	1	0	1	3	2	5	1	3	1

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		.5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
SEROSA SEROSITIS SUBACUTE DIFFUSE	0	0	0	0	0	0	0	1	0	0
ILEUM	[15]	[9]	[7]	[13]	[18]	[12]	[13]	[11]	[15]	[10]
MONONUCLEAR CELL LEUKEMIA	1	0	0	2	3	1	1	1	2	1
MUCOSA MUCOSAL GLANDS DEGENERATION FOCAL	1	0	0	0	0	0	0	0	0	0
SEROSA SEROSITIS PURULENT FOCAL	0	0	0	0	0	0	0	0	0	1
SEROSA SEROSITIS SUBACUTE DIFFUSE	0	0	0	0	0	0	0	1	0	0
JEJUNUM	[2]	[1]	[0]	[0]	[0]	[3]	[3]	[1]	[1]	[1]
MESOTHELIOMA	0	0	0	0	0	1	0	0	0	0
LIVER	[18]	[14]	[12]	[17]	[25]	[20]	[19]	[17]	[23]	[19]
ACIDOPHILIC CELL FOCUS FOCAL	0	0	0	0	1	0	0	0	0	0
ADENOCARCINOMA TUBULAR METASTATIC ORIGIN INTESTINE	0	0	0	0	0	0	0	0	1	0
ANGIECTASIS FOCAL	0	1	0	0	0	0	0	0	0	0
BASOPHILIC FOCUS FOCAL	0	0	0	0	0	0	0	1	0	0
BILE DUCT BILE DUCT HYPERPLASIA MULTIFOCAL	0	5	0	2	0	3	0	2	1	1
BILE DUCT BILE DUCT HYPERPLASIA WITH FIBROSIS MULTIFOCAL	0	0	0	1	0	1	0	2	0	1
CONGESTION ACUTE CENTRILOBULAR	0	0	0	0	0	0	0	0	1	0
CONGESTION ACUTE DIFFUSE	1	0	0	0	1	0	0	1	1	0
CYST MULTILOCULATED	0	0	0	0	0	0	1	0	0	0
EXTRAMEDULLARY HEMATOPOIESIS MULTIFOCAL	1	0	0	0	1	0	1	0	1	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
FOCUS OF CELLULAR ALTERATION	0	1	0	0	0	0	0	0	0	0
GLISSONS CAPSULE CARCINOSARCOMA FOCAL	1	0	0	0	0	0	0	0	0	0
HEPATITIS ACUTE MULTIFOCAL	3	0	1	1	1	0	0	0	0	0
HEPATITIS GRANULOMATOUS FOCAL	0	0	0	0	0	0	1	0	0	0
HEPATITIS MULTIFOCAL	0	0	0	0	0	0	1	0	0	1
HEPATITIS SUBACUTE FOCAL	0	0	0	0	0	0	0	0	0	1
HEPATITIS SUBACUTE MULTIFOCAL	2	2	2	2	4	0	1	2	5	0
HEPATOCELLULAR REGENERATION FOCAL	0	1	0	0	0	0	0	0	0	0
HEPATOCYTES VACUOLAR CHANGE DIFFUSE	1	0	0	1	0	0	0	0	0	0
HEPATOCYTES VACUOLAR CHANGE MULTIFOCAL	1	1	0	0	0	0	0	0	0	0
LYMPHOMA UNDIFFERENTIATED	0	0	0	0	0	0	0	0	0	1
MESOTHELIOMA	0	0	0	0	0	1	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	10	3	5	8	12	13	14	9	11	10
NECROSIS ACUTE MULTIFOCAL	1	0	0	0	1	0	0	0	1	0
NECROSIS CENTRILOBULAR ACUTE MULTIFOCAL	1	0	0	0	0	1	0	0	0	0
PANCREAS-EXOCRINE	[18]	[14]	[12]	[16]	[24]	[19]	[18]	[16]	[23]	[18]
ATROPHY LOBULAR FOCAL	1	0	0	0	0	0	0	0	1	0
ATROPHY LOBULAR MULTIFOCAL	1	0	0	0	0	0	0	0	0	1
CARCINOSARCOMA	1	0	0	0	0	0	0	0	0	0
CARINCOMA	0	0	0	1	0	0	0	0	0	0
CYST MULTILOCULATED FOCAL	0	0	0	0	0	0	0	0	0	1

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
DEGENERATION LOBULAR FOCAL	0	0	0	0	0	0	0	0	0	1
DEGENERATION LOBULAR MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
LYMPHOMA MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
LYMPHOMA UNDIFFERENTIATED MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
MESOTHELIOMA	0	0	0	0	0	2	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	3	2	3	4	5	6	8	6	4	3
PANCREATIC DUCT HYPERPLASIA FOCAL	0	0	0	0	0	0	0	0	1	0
PANCREATIC DUCT HYPERPLASIA MULTIFOCAL	0	0	0	0	0	0	1	0	0	0
PANCREATITIS ACUTE MULTIFOCAL	1	0	0	0	0	0	0	0	0	1
PANCREATITIS GRANULOMATOUS MULTIFOCAL	0	0	0	0	0	0	1	0	0	0
PANCREATITIS LYMPHOCYTIC FOCAL	0	1	1	0	0	0	0	0	1	0
PANCREATITIS LYMPHOCYTIC MULTIFOCAL	0	0	1	0	0	0	1	0	0	0
PANCREATITIS SUBACUTE DIFFUSE	0	0	0	0	0	0	0	0	1	0
PANCREATITIS SUBACUTE FOCAL	1	1	0	0	1	1	1	0	1	0
PANCREATITIS SUBACUTE MULTIFOCAL	1	0	1	3	2	1	2	1	0	1
RECTUM	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[0]
SALIVARY GLAND	[0]	[0]	[2]	[0]	[0]	[0]	[1]	[1]	[0]	[0]
STOMACH	[18]	[14]	[12]	[17]	[24]	[20]	[19]	[17]	[23]	[19]
GLANDULAR PORTION GASTRIC MUCOSA NECROSIS ACUTE FOCAL	0	0	0	0	0	0	0	1	0	0
GLANDULAR PORTION GASTRIC MUCOSA NECROSIS ACUTE MULTIFOCAL	0	0	0	0	0	0	1	0	0	0
GLANDULAR PORTION GASTRITIS ACUTE FOCAL	0	1	1	1	1	1	2	1	1	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		.5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
GLANDULAR PORTION GASTRITIS ACUTE MULTIFOCAL	0	0	0	0	1	0	0	0	0	1
GLANDULAR PORTION GASTRITIS NECROTIZING FOCAL	0	0	1	0	0	0	0	0	0	0
GLANDULAR PORTION GLANDULAR ECTASIA MULTIFOCAL	2	0	1	0	5	1	0	0	5	4
GLANDULAR PORTION GLANDULAR ECTASIA MULTIFOCAL BILATERAL	1	0	0	0	0	0	0	0	0	0
GLANDULAR PORTION MINERALIZATION DYSTROPHIC MULTIFOCAL	0	0	2	1	0	0	0	0	0	0
GLANDULAR PORTION MONONUCLEAR CELL LEUKEMIA	0	0	0	0	2	0	0	0	0	0
GLANDULAR PORTION MONONUCLEAR CELL LEUKEMIA FOCAL	0	0	0	0	0	0	1	0	0	0
GLANDULAR PORTION MUCOSA GASTRITIS SUPPURATIVE FOCAL	0	0	0	0	0	0	0	0	0	1
GLANDULAR PORTION NECROSIS ACUTE FOCAL	0	1	0	0	0	0	0	0	0	0
GLANDULAR PORTION NECROSIS MULTIFOCAL ACUTE	0	0	0	0	0	1	0	0	0	0
MESOTHELIOMA	0	0	0	0	0	1	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	2	2	2	2	1	2	1	1	2	3
MUCOSA ULCERATION CHRONIC ACTIVE MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
NONGLANDULAR PORTION GASTRITIS ACUTE FOCAL	0	0	0	0	0	0	0	1	0	1
NONGLANDULAR PORTION GASTRITIS ACUTE MULTIFOCAL	0	0	0	0	0	1	0	0	1	0
NONGLANDULAR PORTION GASTRITIS NECROTIZING FOCAL	0	0	0	0	0	0	0	0	1	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		.5 MG/M3-3		.5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
NONGLANDULAR PORTION GASTRITIS SUBACUTE DIFFUSE	0	0	0	0	0	0	0	0	0	1
NONGLANDULAR PORTION GASTRITIS SUBACUTE MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
NONGLANDULAR PORTION GASTRITIS SUPPURATIVE FOCAL	0	1	0	0	1	0	0	0	0	2
NONGLANDULAR PORTION GASTRITIS SUPPURATIVE WITH ULCERATION MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
NONGLANDULAR PORTION MONONUCLEAR CELL LEUKEMIA	0	0	0	0	2	0	0	0	0	0
SEROSA SEROSITIS SUBACUTE DIFFUSE	0	0	0	0	0	0	0	1	0	0
TOOTH	[5]	[3]	[4]	[4]	[0]	[5]	[0]	[7]	[2]	[4]
INCISOR PERIODONTITIS ACUTE DIFFUSE	0	0	0	0	0	0	0	1	0	0
INCISOR PERIODONTITIS ACUTE FOCAL UNILATERAL	0	1	0	0	0	1	0	2	1	0
INCISOR PERIODONTITIS ACUTE MULTIFOCAL BILATERAL	0	1	0	0	0	0	0	1	0	0
INCISOR PERIODONTITIS ACUTE MULTIFOCAL UNILATERAL	0	0	0	1	0	1	0	0	0	1
INCISOR PERIODONTITIS CHRONIC ACTIVE DIFFUSE UNILATERAL	0	0	0	0	0	0	0	0	1	0
INCISOR PERIODONTITIS SUBACUTE DIFFUSE UNILATERAL	0	0	0	1	0	0	0	2	0	0
INCISOR PERIODONTITIS SUBACUTE FOCAL UNILATERAL	1	0	0	0	0	0	0	0	0	0
INCISOR PERIODONTITIS SUBACUTE MULTIFOCAL BILATERAL	0	0	0	0	0	0	0	0	0	1
INCISOR PERIODONTITIS SUBACUTE MULTIFOCAL UNILATERAL	3	1	2	1	0	0	0	1	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		.5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
INCISOR PERIODONTITIS SUPPURATIVE FOCAL UNILATERAL	0	0	0	0	0	0	0	0	0	1
INCISOR PULPITIS CHRONIC ACTIVE FOCAL UNILATERAL	1	1	1	1	0	1	0	0	0	1
INCISOR PULPITIS CHRONIC ACTIVE MULTIFOCAL UNILATERAL	0	0	0	1	0	0	0	0	0	0
INCISOR PULPITIS CHRONIC FOCAL BILATERAL	0	0	0	0	0	1	0	0	0	0
INCISOR PULPITIS CHRONIC FOCAL UNILATERAL	0	0	1	1	0	1	0	1	0	0
INCISOR PULPITIS SUBACUTE FOCAL UNILATERAL	0	0	1	0	0	0	0	0	0	0
ADRENAL GLAND	[18]	[14]	[12]	[18]	[25]	[20]	[19]	[17]	[23]	[19]
ADRENAL CORTEX LIPIDOSIS MULTIFOCAL BILATERAL	0	0	1	0	0	0	0	0	0	0
ADRENALITIS LYMPHOCYTIC MULTIFOCAL BILATERAL	0	0	0	1	0	0	0	0	0	0
ANGIECTASIS MULTIFOCAL BILATERAL	1	0	1	1	2	0	0	0	0	0
ANGIECTASIS MULTIFOCAL UNILATERAL	0	0	0	0	1	0	0	0	0	0
ANGIECTASIS UNILATERAL	0	0	0	0	0	0	0	0	0	1
CAPSULE CARCINOSARCOMA FOCAL UNILATERAL	1	0	0	0	0	0	0	0	0	0
CARCINOMA ADRENAL CORTICAL UNILATERAL	0	1	0	0	0	0	0	0	0	0
CONGESTION ACUTE DIFFUSE BILATERAL	0	0	1	0	0	0	1	0	1	0
CONGESTION ACUTE MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
CORTEX ANGIECTASIS MULTIFOCAL BILATERAL	0	0	0	1	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		.5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
CORTEX ANGIECTASIS MULTIFOCAL UNILATERAL	1	0	0	0	0	0	0	1	0	0
CORTEX DEGENERATION MULTIFOCAL BILATERAL	0	0	0	0	0	0	1	0	0	0
CORTEX LIPIDOSIS FOCAL	0	0	1	0	0	0	0	0	0	0
CORTEX LIPIDOSIS FOCAL UNILATERAL	0	0	0	0	0	0	0	1	0	1
CORTEX LIPIDOSIS MULTIFOCAL BILATERAL	0	0	0	0	0	0	0	1	0	0
CORTEX LIPIDOSIS MULTIFOCAL UNILATERAL	1	0	0	0	1	0	0	0	0	0
CORTEX MEDULLA DEGENERATION DIFFUSE UNILATERAL	1	0	0	0	0	0	0	0	0	0
CORTEX OSTEOMETAPLASIA DIFFUSE UNILATERAL	1	0	0	0	0	0	0	0	0	0
CORTICAL MEDULLARY AREA NECROSIS ACUTE MULTIFOCAL BILATERAL	0	0	0	0	0	1	0	0	0	0
CORTICAL MEDULLARY JUNCTION ANGIECTASIS MULTIFOCAL BILATERAL	0	0	0	0	0	0	0	0	1	0
MEDULLA MINERALIZATION MULTIFOCAL UNILATERAL	0	0	1	0	0	0	0	0	0	0
MESOTHELIOMA BILATERAL	0	0	0	0	0	1	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	1	2	3	3	3	3	1	1
MONONUCLEAR CELL LEUKEMIA BILATERAL	4	3	1	3	7	8	8	4	7	4
MONONUCLEAR CELL LEUKEMIA UNILATERAL	1	0	0	0	0	0	0	0	0	0
PERIADRENAL CONNECTIVE TISSUE STEATITIS SUBACUTE MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
PHEOCHROMOCYTOMA BILATERAL	0	0	0	0	0	0	1	0	0	0
PHEOCHROMOCYTOMA UNILATERAL	0	0	0	1	1	2	0	1	0	0

( ) = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
PANCREATIC ISLET	[18]	[14]	[12]	[16]	[24]	[19]	[18]	[16]	[23]	[18]
ISLET CELL ADENOMA FOCAL	0	2	0	0	0	1	0	3	0	0
ISLET CELL CARCINOMA	0	0	0	0	1	0	0	0	0	2
PARATHYROID GLAND	[13]	[10]	[11]	[15]	[20]	[15]	[17]	[13]	[19]	[16]
ADENOMA FOCAL UNILATERAL	0	0	1	0	0	0	0	0	0	0
HEMATOCYST FOCAL	0	0	0	0	0	0	1	0	0	0
HYPERPLASIA MULTIFOCAL	0	0	1	0	0	0	0	0	0	0
PITUITARY GLAND	[16]	[14]	[12]	[16]	[23]	[18]	[18]	[17]	[23]	[19]
ADENOMA	9	5	3	4	14	6	6	9	5	6
CYST FOCAL	0	0	0	0	0	1	0	0	0	0
CYST MULTIFOCAL	0	0	0	0	0	0	1	0	0	0
HEMORRHAGE ACUTE FOCAL	0	0	0	0	0	0	1	0	0	0
HYPERPLASTIC FOCUS	0	0	0	0	0	0	0	0	1	0
MINERALIZATION FOCAL	0	0	1	0	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	2	2	0	2	3	4	6	3	3	3
THYROID GLAND	[18]	[14]	[11]	[18]	[24]	[20]	[19]	[17]	[23]	[19]
ADENOMA FOLLICULAR FOCAL UNILATERAL	1	1	1	0	0	0	0	0	0	0
C CELL CARCINOMA UNILATERAL	0	1	1	2	2	1	2	0	0	2
C CELL HYPERPLASIA FOCAL UNILATERAL	1	0	0	1	0	2	1	0	2	1
C CELL HYPERPLASIA MULTIFOCAL	0	1	0	0	0	0	0	0	2	0
C CELL HYPERPLASIA MULTIFOCAL BILATERAL	2	0	0	1	0	0	0	0	1	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
C CELL HYPERPLASIA MULTIFOCAL UNILATERAL	1	0	1	0	0	0	0	0	1	0
FOLLICLE CYST FOCAL UNILATERAL	0	0	0	0	0	0	0	0	1	0
FOLLICLE CYST MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
FOLLICLE CYST MULTIFOCAL UNILATERAL	0	0	0	0	1	0	0	0	0	0
FOLLICLE SQUAMOUS METAPLASIA FOCAL UNILATERAL	0	0	0	0	0	1	0	0	0	0
FOLLICLE SQUAMOUS METAPLASIA MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
FOLLICLE SQUAMOUS METAPLASIA MULTIFOCAL UNILATERAL	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	0	2	0	0	1	1	0	0
MONONUCLEAR CELL LEUKEMIA BILATERAL	1	1	0	1	1	2	1	0	0	1

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. HISTOPATHOLOGY SUMMARY BY GROUP AND SEX (CONTINUED)

PROJECT: G7108-13 STUDY: NIOSH SPECIES: RAT

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
LYMPH NODE	[0]	[0]	[0]	[1]	[2]	[0]	[0]	[0]	[3]	[0]
ADENOCARCINOMA TUBULAR DIFFUSE METASTATIC ORIGIN INTESTINE	0	0	0	0	0	0	0	0	1	0
HEMORRHAGE ACUTE MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
LYMPHOID HYPERPLASIA DIFFUSE	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	0	0	1	0	0	0	2	0
LYMPH NODE-BRONCHIAL	[1]	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[0]	[0]
MACROPHAGE AGGREGATES MULTIFOCAL FIBROUS GLASS	0	0	0	0	1	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	1	0	0	0	0	0	0	0	0	0
LYMPH NODE-MANDIBULAR	[0]	[0]	[1]	[0]	[0]	[0]	[1]	[0]	[0]	[0]
LYMPHOID HYPERPLASIA DIFFUSE	0	0	1	0	0	0	1	0	0	0
LYMPH NODE-MESENTERIC	[15]	[13]	[9]	[11]	[22]	[17]	[15]	[13]	[19]	[16]
HEMORRHAGE ACUTE DIFFUSE	0	0	0	0	0	0	0	1	0	0
LYMPHADENITIS ACUTE DIFFUSE	0	0	0	1	0	0	0	0	0	0
LYMPHADENITIS ACUTE MULTIFOCAL	0	0	0	0	0	0	1	1	0	0
LYMPHADENITIS SUBACUTE DIFFUSE	0	0	1	0	0	0	0	0	1	0
LYMPHOID HYPERPLASIA DIFFUSE	9	9	7	4	10	10	8	6	10	7
MESOTHELIOMA	0	0	0	0	0	1	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	2	1	1	3	7	5	4	6	3	2
NECROSIS ACUTE MULTIFOCAL DIFFUSE	0	0	0	0	0	0	1	0	0	0
RETICULOENDOTHELIAL HYPERPLASIA MULTIFOCAL	0	1	0	0	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
LYMPH NODE-PANCREATIC	[1]	[2]	[0]	[1]	[0]	[1]	[2]	[4]	[1]	[3]
LYMPHOID HYPERPLASIA DIFFUSE	1	1	0	1	0	0	2	0	0	0
LYMPHOID HYPERPLASIA MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	1	0	0	0	0	0	3	1	2
LYMPH NODE-SUBMANDIBULAR	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]
LYMPHOID HYPERPLASIA DIFFUSE	0	1	0	0	0	0	0	0	0	0
LYMPH NODE-THORACIC	[0]	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[1]	[0]
MONONUCLEAR CELL LEUKEMIA	0	0	0	0	0	0	1	0	1	0
LYMPH NODE-THYMIC	[12]	[10]	[10]	[11]	[18]	[15]	[13]	[13]	[13]	[10]
HEMOSIDEROSIS DIFFUSE	1	7	1	0	0	0	0	0	3	1
HEMOSIDEROSIS MULTIFOCAL	4	0	1	2	1	1	6	4	1	3
LYMPHADENITIS SUPPURATIVE DIFFUSE	1	0	0	0	0	0	0	0	0	0
LYMPHOID HYPERPLASIA DIFFUSE	2	5	6	2	9	6	5	1	4	3
MACROPHAGE AGGREGATES MULTIFOCAL FIBROUS GLASS	0	0	9	9	15	14	5	2	7	6
MONONUCLEAR CELL LEUKEMIA	8	3	3	6	6	7	2	7	3	4
LYMPH NODE-TRACHEOBRONCHIAL	[17]	[11]	[11]	[16]	[24]	[20]	[17]	[12]	[21]	[17]
HEMOSIDEROSIS DIFFUSE	0	0	1	1	1	0	1	1	1	1
HEMOSIDEROSIS FOCAL	0	0	1	0	0	0	0	0	0	0
HEMOSIDEROSIS MULTIFOCAL	3	8	3	2	2	2	3	1	3	1
LYMPHADENITIS GRANULOMATOUS MULTIFOCAL	0	0	0	0	1	0	0	0	0	0
LYMPHOID HYPERPLASIA DIFFUSE	2	2	1	4	0	0	1	2	2	1

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		.5 MG/M3-3		.5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
MACROPHAGE AGGREGATES DIFFUSE FIBROUS GLASS	0	0	0	0	0	0	1	0	0	0
MACROPHAGE AGGREGATES FOCAL FIBROUS GLASS	0	0	0	1	1	0	0	0	0	0
MACROPHAGE AGGREGATES MULTIFOCAL FIBROUS GLASS	0	0	3	6	11	15	0	1	2	1
MONONUCLEAR CELL LEUKEMIA	7	2	4	6	9	10	10	8	11	8
SPLEEN	[18]	[14]	[12]	[18]	[25]	[20]	[19]	[17]	[23]	[19]
CAPSULE SPINDLE CELL TUMOR UNDIFFERENTIATED FOCAL	1	0	0	0	0	0	0	0	0	0
EXTRAMEDULLARY HEMATOPOIESIS DIFFUSE	3	1	0	0	2	0	1	0	3	1
EXTRAMEDULLARY HEMATOPOIESIS MULTIFOCAL	0	0	1	1	0	0	1	1	1	0
HEMANGIOSARCOMA	0	0	0	0	0	0	0	1	0	0
HEMOSIDEROSIS DIFFUSE	4	4	3	3	6	3	2	6	5	4
INFARCT FOCAL	0	0	0	1	0	0	2	0	1	1
INFARCT MULTIFOCAL	0	0	0	0	0	1	0	0	0	1
LYMPHOID DEPLETION DIFFUSE	0	0	0	0	0	1	0	0	0	0
LYMPHOID DEPLETION MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
LYMPHOID HYPERPLASIA DIFFUSE	0	0	0	0	1	0	0	0	0	0
LYMPHOID HYPERPLASIA MULTIFOCAL	0	0	0	0	0	0	0	0	2	1
LYMPHOID NECROSIS ACUTE MULTIFOCAL	0	0	0	0	1	0	0	0	0	0
LYMPHOMA UNDIFFERENTIATED	0	0	0	0	0	0	0	0	0	1
MESOTHELIOMA	0	0	0	0	0	1	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
MONONUCLEAR CELL LEUKEMIA	10	3	5	9	12	13	14	9	11	10
SPLENIC CAPSULE CAPSULITIS SUBACUTE D IFFUSE	0	0	0	0	0	0	0	1	0	0
SPLENITIS PYOGRANULOMATOUS MULTIFOCAL	1	0	0	0	0	0	0	0	0	0
THYMUS	[0]	[0]	[0]	[1]	[1]	[1]	[2]	[0]	[0]	[0]
LYMPHOID DEPLETION DIFFUSE	0	0	0	1	0	1	1	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	0	0	1	0	1	0	0	0
MUSCLE-SKELETAL	[2]	[0]	[0]	[1]	[1]	[0]	[0]	[0]	[1]	[1]
FIBROSARCOMA	0	0	0	0	0	0	0	0	1	0
MONONUCLEAR CELL LEUKEMIA	0	0	0	0	1	0	0	0	0	0
SARCOMA UNDIFFERENTIATED	0	0	0	0	0	0	0	0	0	1
SPINDLE CELL TUMOR UNDIFFERENTIATED F OCAL	1	0	0	0	0	0	0	0	0	0
VERTEBRAE	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]
LATERAL PROCESS OSTEOSARCOMA	0	1	0	0	0	0	0	0	0	0
BRAIN	[18]	[14]	[12]	[18]	[25]	[20]	[19]	[17]	[23]	[19]
CEREBELLUM HEMORRHAGE ACUTE FOCAL	0	0	0	1	1	0	0	0	0	0
CEREBELLUM HEMORRHAGE ACUTE MULTIFOCAL	1	0	0	2	0	2	0	0	0	2
CEREBELLUM HEMORRHAGE SUBACUTE FOCAL	0	0	0	0	0	0	1	0	0	0
CEREBELLUM MALIGNANT EPENDYNOMA	0	0	0	0	0	0	0	0	0	1
CEREBELLUM MENINGOENCEPHALITIS NONSUP PURATIVE MULTIFOCAL	0	0	1	0	0	0	0	0	0	0
CEREBELLUM MONONUCLEAR CELL LEUKEMIA	1	1	0	0	3	2	4	3	5	2

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
CEREBRUM AND MEDULLA MENINGOENCEPHALITIS SUPPURATIVE MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
CEREBRUM AND MIDBRAIN MENINGOENCEPHALITIS SUPPURATIVE MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
CEREBRUM ENCEPHALITIS SUPPURATIVE MULTIFOCAL	0	0	1	0	0	0	0	0	0	1
CEREBRUM HEMORRHAGE ACUTE FOCAL	0	0	0	1	0	1	0	0	0	0
CEREBRUM HEMORRHAGE ACUTE MULTIFOCAL	1	0	0	0	2	1	2	0	0	0
CEREBRUM LATERAL VENTRICLES HYDROCEPHALUS	5	1	2	2	8	3	2	5	2	2
CEREBRUM MENINGOENCEPHALITIS NONSUPPURATIVE MULTIFOCAL	0	0	1	0	0	0	0	0	0	0
CEREBRUM MINERALIZATION DYSTROPHIC FOCAL	0	0	0	0	0	0	0	0	0	1
CEREBRUM MONONUCLEAR CELL LEUKEMIA	2	2	1	0	4	3	4	2	4	3
CEREBRUM PITUITARY ADENOMA	0	1	0	0	1	0	0	0	1	0
ENCEPHALITIS ACUTE DIFFUSE	0	0	0	0	1	0	0	0	0	0
ENCEPHALITIS SUPPURATIVE MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
HEMORRHAGE ACUTE FOCAL	0	0	0	0	0	0	1	0	0	0
HEMORRHAGE ACUTE MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
MEDULLA HEMORRHAGE ACUTE FOCAL	0	0	0	0	1	0	1	1	1	0
MEDULLA HEMORRHAGE ACUTE MULTIFOCAL	0	0	0	0	1	1	0	0	0	0
MEDULLA HYDROCEPHALUS	0	0	0	0	1	0	0	0	0	0
MEDULLA MENINGES MENINGIOSARCOMA	0	1	0	0	0	0	0	0	0	0
MEDULLA MENINGOENCEPHALITIS NONSUPPURATIVE DIFFUSE	0	0	1	0	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
MEDULLA MONONUCLEAR CELL LEUKEMIA	1	1	0	0	3	2	4	4	4	1
MEDULLA PITUITARY ADENOMA	0	0	0	0	1	0	0	0	0	0
MENINGES MENINGITIS SUPPURATIVE MULTI FOCAL	0	0	1	0	0	0	0	0	0	1
MIDBRAIN HEMORRHAGE ACUTE FOCAL	0	1	1	0	0	0	0	0	0	0
MIDBRAIN HEMORRHAGE ACUTE MULTIFOCAL	0	0	0	1	1	0	0	0	0	0
MIDBRAIN MENINGOENCEPHALITIS NONSUPPU RATIVE DIFFUSE	0	0	1	0	0	0	0	0	0	0
MIDBRAIN MINERALIZATION DYSTROPHIC MU LTIFOCAL	0	1	0	0	0	0	0	0	0	0
MIDBRAIN MONONUCLEAR CELL LEUKEMIA	2	2	1	0	3	2	4	2	4	2
MIDBRAIN PITUITARY ADENOMA	1	1	1	0	2	0	0	0	1	0
MIDBRIAN HEMORRHAGE ACUTE FOCAL	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	0	2	2	2	2	4	1	1
NERVE-OPTIC	[0]	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[0]	[1]
PERINEURAL SHEATH PERINEURITIS ACUTE MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
PERINEURAL SHEATH PERINEURITIS SUBACU TE MULTIFOCAL	0	0	1	0	0	0	0	0	0	0
OLFACTORY BULB	[0]	[0]	[1]	[0]	[0]	[0]	[1]	[0]	[1]	[1]
HEMORRHAGE ACUTE FOCAL	0	0	1	0	0	0	0	0	0	0
MENINGES MENINGITIS ACUTE MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
MENINGES MENINGITIS SUPPURATIVE MULTI FOCAL	0	0	0	0	0	0	1	0	0	0
MENINGOENCEPHALITIS SUPPURATIVE MULTI FOCAL	0	0	0	0	0	0	0	0	1	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
NEUROPIL ENCEPHALITIS ACUTE MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
EYE	[17]	[14]	[12]	[18]	[24]	[20]	[18]	[17]	[23]	[19]
ANTERIOR AND POSTERIOR CHAMBERS HEMORRHAGE ACUTE DIFFUSE	0	0	0	0	0	0	0	0	0	1
CORNEA KERATITIS ACUTE DIFFUSE UNILATERAL	0	0	1	0	0	0	0	0	0	0
CORNEA KERATITIS ACUTE MULTIFOCAL UNILATERAL	0	0	0	0	0	0	0	0	0	1
CORNEA KERATITIS CHRONIC ACTIVE DIFFUSE UNILATERAL	1	0	0	0	0	0	0	0	0	0
CORNEA KERATITIS NECROTIZING DIFFUSE UNILATERAL	0	1	0	0	0	0	0	0	0	0
CORNEA KERATITIS PURULENT DIFFUSE UNILATERAL	0	1	0	0	0	0	0	0	0	0
CORNEA KERATITIS SUBACUTE MULTIFOCAL UNILATERAL	0	1	0	0	0	0	0	0	0	0
CORNEA KERATITIS SUPPURATIVE MULTIFOCAL BILATERAL	0	0	1	0	0	0	0	0	0	0
CORNEA KERATITIS SUPPURATIVE MULTIFOCAL UNILATERAL	0	0	0	1	0	0	0	0	0	0
CORNEA MINERALIZATION FOCAL UNILATERAL	0	0	0	0	1	0	0	0	1	0
LENS CATARACT UNILATERAL	0	0	1	0	2	0	0	0	0	0
LENS CATARACTOUS CHANGE MULTIFOCAL BILATERAL	0	0	1	0	0	0	0	0	0	0
LENS CATARACTOUS CHANGE MULTIFOCAL UNILATERAL	0	1	0	0	0	2	0	1	0	0
LENS CATARACTOUS CHANGE SUBACUTE MULTIFOCAL UNILATERAL	1	0	0	0	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
LENS MINERALIZATION MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
MINERALIZATION MULTIFOCAL UNILATERAL	0	0	1	0	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	0	2	1	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA BILATERAL	0	1	0	0	1	2	2	1	1	0
RETINA DEGENERATION DIFFUSE UNILATERAL	0	0	0	0	0	1	0	1	0	0
RETINA DEGENERATION DIFFUSE UNILATERAL POSSIBLY GLAUCOMA	1	0	0	0	0	0	0	0	0	0
RETINA DEGENERATION MULTIFOCAL BILATERAL	0	0	0	0	1	0	0	0	0	0
RETINA DEGNERATION DIFFUSE UNILATERAL	0	0	1	0	0	0	0	0	0	0
SYNECHIA POSTERIOR BILATERAL	0	0	0	0	0	0	0	0	0	1
SYNECHIA POSTERIOR SUBACUTE UNILATERAL	1	0	0	0	0	0	0	0	0	0
HARDERIAN GLAND	[6]	[4]	[5]	[6]	[8]	[2]	[8]	[4]	[6]	[8]
ADENITIS ACUTE DIFFUSE UNILATERAL	0	0	0	0	0	0	0	0	0	1
ADENITIS LYMPHOCYTIC DIFFUSE BILATERAL	0	0	0	0	0	0	1	0	0	0
ADENITIS LYMPHOCYTIC FOCAL	0	0	0	0	1	0	0	0	0	0
ADENITIS LYMPHOCYTIC FOCAL BILATERAL	1	0	0	0	1	0	0	0	0	0
ADENITIS LYMPHOCYTIC FOCAL UNILATERAL	0	1	0	2	1	0	1	1	0	2
ADENITIS LYMPHOCYTIC MULTIFOCAL BILATERAL	3	0	1	3	1	0	3	1	3	1
ADENITIS LYMPHOCYTIC MULTIFOCAL UNILATERAL	2	3	4	1	3	2	2	1	4	3
ADENITIS LYMPHOCYTIC UNILATERAL	0	0	0	0	0	0	1	0	0	0
ADENITIS SUBACUTE FOCAL UNILATERAL	0	0	0	0	0	1	0	0	0	1

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
MONONUCLEAR CELL LEUKEMIA	0	0	0	0	1	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA BILATERAL	0	0	0	0	1	0	0	0	0	0
SQUAMOUS METAPLASIA MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
LACRIMAL GLAND	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[1]
INFRAORBITAL ADENITIS ACUTE DIFFUSE	0	0	0	0	0	0	0	0	0	1
CERVIX	[0]	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[1]	[0]
EPITHELIUM HYPERKERATOSIS MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
EPIDIDYMIS	[0]	[14]	[0]	[16]	[0]	[20]	[0]	[16]	[0]	[18]
EPIDIDYMITIS ACUTE MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
EPIDIDYMITIS LYMPHOCYTIC FOCAL	0	1	0	0	0	0	0	0	0	0
EPIDIDYMITIS SUBACUTE DIFFUSE	0	0	0	0	0	0	0	1	0	0
MESOTHELIOMA	0	0	0	0	0	3	0	1	0	0
MONONUCLEAR CELL LEUKEMIA	0	1	0	1	0	3	0	1	0	1
TUBULAR EPITHELIUM MINERALIZATION DYS TROPHIC MULTIFOCAL	0	0	0	1	0	0	0	0	0	1
FALLOPIAN TUBE	[1]	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[1]	[0]
MONONUCLEAR CELL LEUKEMIA BILATERAL	0	0	0	0	1	0	0	0	1	0
SPINDLE CELL TUMOR UNDIFFERENTIATED M ULTIFOCAL	1	0	0	0	0	0	0	0	0	0
OVARY	[18]	[0]	[12]	[0]	[24]	[0]	[19]	[0]	[23]	[0]
CYST FOCAL UNILATERAL	1	0	1	0	2	0	1	0	1	0
GRANULOSA CELL TUMOR UNILATERAL	0	0	0	0	1	0	0	0	0	0
LUTEAL CYST FOCAL UNILATERAL	0	0	0	0	1	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
MESOVARIUM CARCINOSARCOMA FOCAL	1	0	0	0	0	0	0	0	0	0
MESOVARIUM SALPINGITIS ACUTE DIFFUSE	0	0	0	0	1	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	1	0	0	0	0	0	4	0	2	0
MONONUCLEAR CELL LEUKEMIA BILATERAL	4	0	3	0	6	0	5	0	5	0
OOPHORITIS ACUTE DIFFUSE UNILATERAL	1	0	0	0	0	0	0	0	0	0
OOPHORITIS ACUTE MULTIFOCAL BILATERAL	0	0	0	0	0	0	0	0	1	0
OOPHORITIS SUPPURATIVE MULTIFOCAL UNI LATERAL	0	0	0	0	0	0	0	0	1	0
SPINDLE CELL TUMOR UNDIFFERENTIATED M ULTIFOCAL BILATERAL	1	0	0	0	0	0	0	0	0	0
PROSTATE GLAND	[0]	[14]	[0]	[16]	[0]	[20]	[0]	[16]	[0]	[19]
ACINI ECTASIA MULTIFOCAL	0	0	0	0	0	0	0	1	0	1
CYSTIC HYPERPLASIA MULTIFOCAL	0	0	0	1	0	1	0	0	0	0
MESOTHELIOMA	0	0	0	1	0	3	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	1	0	2	0	1	0	3	0	3
PROSTATITIS ACUTE MULTIFOCAL	0	3	0	2	0	3	0	1	0	2
PROSTATITIS CHRONIC ACTIVE MULTIFOCAL	0	1	0	0	0	0	0	1	0	0
PROSTATITIS SUBACUTE MULTIFOCAL	0	0	0	1	0	0	0	0	0	1
PROSTATITIS SUPPURATIVE DIFFUSE	0	0	0	0	0	0	0	0	0	1
PROSTATITIS SUPPURATIVE FOCAL	0	0	0	0	0	1	0	0	0	1
PROSTATITIS SUPPURATIVE MULTIFOCAL	0	7	0	5	0	11	0	8	0	6
TESTIS*	[0]	[14]	[0]	[16]	[0]	[20]	[0]	[16]	[0]	[19]
INTERSTITIAL CELL HYPERPLASIA FOCAL	0	1	0	1	0	1	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

* Total number of interstitial cell tumors may exceed the number of animals examined because the tumor in both the right and left testis may have had different distribution patterns (focal, multifocal, and diffuse).

TABLE 42. CONTINUED

GROUP	0 MG/M3		.5 MG/M3-3		.5 MG/M3-4		1.5 MG/M3-1		1.5 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
INTERSTITIAL CELL HYPERPLASIA MULTIFOCAL	0	9	0	3	0	12	0	8	0	12
INTERSTITIAL CELL TUMOR	0	1	0	0	0	0	0	0	0	0
INTERSTITIAL CELL TUMOR DIFFUSE	0	1	0	3	0	7	0	0	0	0
INTERSTITIAL CELL TUMOR FOCAL	0	3	0	2	0	5	0	1	0	3
INTERSTITIAL CELL TUMOR MULTIFOCAL	0	6	0	5	0	12	0	8	0	11
INTERSTITIAL CELL TUMOR UNILATERAL	0	0	0	1	0	0	0	0	0	0
MESOTHELIOMA	0	0	0	0	0	4	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	1	0	1	0	3	0	2	0	2
SEMINIFEROUS TUBULES DEGENERATION DIFFUSE	0	5	0	5	0	7	0	6	0	12
SEMINIFEROUS TUBULES DEGENERATION MULTIFOCAL	0	9	0	4	0	8	0	5	0	7
SEMINIFEROUS TUBULES DEGENERATION MULTIFOCAL BILATERAL	0	0	0	0	0	0	0	1	0	0
TUNICA VAGINALIS MESOTHELIOMA	0	0	0	0	0	1	0	1	0	0
UTERUS	[18]	[0]	[12]	[0]	[24]	[0]	[19]	[0]	[23]	[0]
ADENOCARCINOMA UNILATERAL	0	0	0	0	1	0	0	0	0	0
ENDOMETRAL STROMAL SARCOMA	0	0	1	0	0	0	0	0	0	0
ENDOMETRIAL GLANDS CYSTIC HYPERPLASIA FOCAL	1	0	0	0	1	0	0	0	1	0
ENDOMETRIAL GLANDS CYSTIC HYPERPLASIA MULTIFOCAL	2	0	1	0	3	0	1	0	1	0
ENDOMETRIAL STROMAL POLYP FOCAL	5	0	2	0	4	0	4	0	3	0
ENDOMETRIUM ENDOMETRITIS ACUTE MULTIFOCAL	1	0	0	0	0	0	2	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
ENDOMETRIUM ENDOMETRITIS PURULENT MULTIFOCAL	2	0	1	0	1	0	0	0	0	0
EPITHELIUM METRITIS ACUTE MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
FIBROSARCOMA	0	0	1	0	0	0	0	0	0	0
LEIOMYOSARCOMA	0	0	1	0	0	0	0	0	0	0
LUMEN ECTASIA	0	0	0	0	0	0	0	0	1	0
METRITIS SUPPURATIVE DIFFUSE	0	0	0	0	0	0	1	0	0	0
MONONUCLEAR CELL LEUKEMIA	4	0	2	0	3	0	7	0	4	0
MYOMETRIUM LYMPHECTASIA MULTIFOCAL	0	0	1	0	0	0	0	0	0	0
SPINDLE CELL TUMOR UNDIFFERENTIATED FOCAL	1	0	0	0	0	0	0	0	0	0
VAGINA	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[1]	[0]
VAGINITIS ACUTE MULTIFOCAL	0	0	0	0	0	0	0	0	1	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. HISTOPATHOLOGY SUMMARY BY GROUP AND SEX (CONTINUED)

PROJECT: G7188-13 STUDY: NIOSH SPECIES: RAT

GROUP	0 MG/M3		>5 MG/M3-3		>5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
BRONCHUS	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[0]
BRONCHITIS GRANULOMATOUS FOCAL	0	0	0	0	0	0	0	1	0	0
LARYNX	[18]	[12]	[11]	[17]	[23]	[19]	[16]	[15]	[22]	[18]
LARYNGITIS ACUTE MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
LARYNGITIS SUBACUTE MULTIFOCAL	1	0	0	0	0	0	1	0	0	0
MONONUCLEAR CELL LEUKEMIA	1	0	0	1	1	1	3	1	1	1
SUBMUCOSAL GLAND ADENITIS ACUTE FOCAL	0	1	0	1	0	2	0	2	1	0
SUBMUCOSAL GLAND ADENITIS ACUTE MULTI FOCAL	2	1	1	0	1	1	1	0	2	3
SUBMUCOSAL GLAND ADENITIS DIFFUSE MUL TIFOCAL	0	0	0	0	0	1	0	0	0	0
SUBMUCOSAL GLAND ECTASIA	0	0	0	0	0	1	0	0	0	0
SUBMUCOSAL GLAND ECTASIA MULTIFOCAL	3	2	2	2	3	5	1	1	3	4
LUNG	[18]	[14]	[12]	[18]	[25]	[20]	[19]	[17]	[23]	[19]
ADENOCARCINOMA TUBULAR MULTIFOCAL MET ASTATIC ORIGIN INTESTINE	0	0	0	0	0	0	0	0	1	0
ADENOMATOUS CHANGE FOCAL	0	0	1	0	0	0	0	0	0	0
ADRENAL CORTICAL CARCINOMA METASTATIC	0	1	0	0	0	0	0	0	0	0
ALVEOLAR BRONCHIOLAR ADENOCARCINOMA F OCAL	0	0	1	0	0	0	0	0	0	0
CARCINOMA PROBABLY TRANSITIONAL CELL MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
CARCINOSARCOMA METASTATIC	0	0	0	0	0	0	0	0	1	0
CONGESTION ACUTE DIFFUSE	2	3	0	1	0	0	2	0	2	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
EPIDERMOID CARCINOMA FOCAL	0	0	0	0	0	1	0	0	0	0
FIBROSIS FOCAL	0	0	0	0	0	0	0	0	0	1
FIBROSIS MULTIFOCAL	0	0	0	0	0	0	1	0	0	0
INTERSTITIAL CELL TUMOR METASTATIC	1	0	0	0	0	0	0	0	0	0*
LIPOMATOUS TUMOR MULTIFOCAL METASTATIC	0	0	0	1	0	0	0	0	0	0
LYMPHOMA MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
MACROPHAGE AGGREGATES FOCAL FIBROUS GLASS	0	0	0	0	0	0	1	0	0	0
MACROPHAGE AGGREGATES MULTIFOCAL FIBROUS GLASS	0	0	12	17	25	20	17	15	19	18
MALIGNANT INTERSTITIAL CELL TUMOR MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	10	3	5	8	12	13	14	9	14	10
PLEURA FIBROSIS FOCAL	0	0	0	0	1	0	1	0	0	0
PLEURA PLEURITIS GRANULOMATOUS FOCAL	0	1	0	0	0	0	0	0	0	0
PLEURA PLEURITIS GRANULOMATOUS FOCAL FIBROUS GLASS	0	0	2	1	1	1	2	2	0	2
PLEURA PLEURITIS GRANULOMATOUS MULTIFOCAL FIBROUS GLASS	0	0	6	8	19	17	0	0	2	0
PNEUMONIA GRANULOMATOUS FOCAL	0	1	0	0	0	0	1	0	0	0
PNEUMONIA GRANULOMATOUS MULTIFOCAL FIBROUS GLASS	0	0	7	12	22	19	0	0	1	1
PNEUMONIA HISTIOCYTIC DIFFUSE	0	0	0	0	0	0	1	0	0	0
PNEUMONIA HISTIOCYTIC FOCAL	0	0	0	0	0	0	0	2	0	0
PNEUMONIA HISTIOCYTIC MULTIFOCAL	0	0	3	1	3	4	1	0	0	2
PNEUMONIA INTERSTITIAL SUBACUTE FOCAL	1	0	0	0	0	0	0	0	0	0

[1 = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
PNEUMONIA INTERSTITIAL SUBACUTE MULTI FOCAL	0	0	1	0	1	0	0	0	0	0
PNEUMONIA PYOGRANULOMATOUS FOCAL	1	0	0	0	0	0	0	0	0	0
PNEUMONIA SUBACUTE FOCAL	1	2	0	0	0	0	0	1	0	0
PNEUMONIA SUBACUTE FOCAL FIBROUS GLASS	0	0	0	0	1	0	0	0	0	0
PNEUMONIA SUBACUTE MULTIFOCAL	0	0	2	3	4	4	0	0	1	0
SPINDLE CELL TUMOR UNDIFFERENTIATED M ULTIFOCAL	1	0	0	0	0	0	0	0	0	0
NASAL PASSAGE	[17]	[12]	[12]	[18]	[25]	[19]	[19]	[17]	[23]	[19]
ADENITIS ACUTE MULTIFOCAL BILATERAL	0	0	0	0	0	0	0	0	0	1
EPITHELIUM ADENOMA FOCAL	0	0	1	0	0	0	0	0	0	0
EPITHELIUM DYSPLASIA FOCAL	0	0	0	0	1	0	0	1	0	0
EPITHELIUM DYSPLASIA MULTIFOCAL	2	0	3	2	1	1	5	2	3	1
EPITHELIUM RHINITIS ACUTE FOCAL	0	0	0	0	0	0	0	1	0	0
EPITHELIUM RHINITIS ACUTE MULTIFOCAL	0	0	2	2	1	1	4	2	0	2
EPITHELIUM SQUAMOUS METAPLASIA MULTIF OCAL	0	0	2	1	0	0	0	1	0	0
GINGIVA SQUAMOUS CELL CARCINOMA FOCAL	0	0	0	1	0	0	0	0	0	0
HEMORRHAGE ACUTE MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
LAMINA PROPRIA MINERALIZATION DYSTROP HIC FOCAL	0	0	0	0	0	0	1	1	0	1

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
LAMINA PROPRIA MINERALIZATION DYSTROPHIC MULTIFOCAL	2	2	3	3	0	3	2	3	1	4
LAMINA PROPRIA RHINITIS ACUTE FOCAL	0	0	0	0	1	0	1	0	0	0
MEDIAN SEPTUM LAMINA PROPRIA RHINITIS SUBACUTE FOCAL	1	0	0	0	0	0	0	0	0	0
MEDIAN SEPTUM LAMINA PROPRIA RHINITIS SUBACUTE MULTIFOCAL	1	0	0	0	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	3	2	1	4	4	5	6	6	4	5
NASOLACRIMAL DUCT DACRYOSOLENITIS ACUTE MULTIFOCAL BILATERAL	0	0	0	1	0	0	2	0	0	0
NASOLACRIMAL DUCT DACRYOSOLENITIS ACUTE MULTIFOCAL UNILATERAL	3	4	3	0	6	5	3	1	2	0
NASOLACRIMAL DUCT DACRYOSOLENITIS SUBACUTE MULTIFOCAL UNILATERAL	0	0	0	0	1	0	0	0	0	0
NASOLACRIMAL DUCT EPITHELIUM HYPERPLASIA DIFFUSE UNILATERAL	0	0	0	0	1	0	0	0	0	0
NASOLACRIMAL DUCT EPITHELIUM SQUAMOUS METAPLASIA MULTIFOCAL UNILATERAL	0	0	1	0	1	0	0	0	0	0
NASOLACRIMAL DUCT LYMPHOID POLYP UNILATERAL	1	0	0	0	0	0	0	0	0	0
RHINITIS PURULENT FOCAL	0	0	1	0	0	1	1	1	0	0
RHINITIS PURULENT FOCAL FOREIGN BODY	0	0	1	0	0	0	0	0	0	0
RHINITIS PURULENT MULTIFOCAL	0	0	2	1	0	2	2	3	1	1
RHINITIS SEROPURULENT FOCAL	0	0	0	0	0	0	0	0	1	0
RHINITIS SEROPURULENT MULTIFOCAL	3	0	1	2	3	1	0	2	0	1
RHINITIS SEROUS FOCAL	0	0	0	0	0	0	0	0	1	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
RHINITIS SEROUS MULTIFOCAL	0	0	0	0	1	0	0	2	0	0
RHINITIS SUPPURATIVE FOCAL	0	0	0	0	0	0	0	1	0	0
RHINITIS SUPPURATIVE MULTIFOCAL	2	0	0	0	0	0	2	3	0	0
SQUAMOUS CELL CARCINOMA HEAD AREA	0	0	0	0	0	0	0	1	0	0
SUBMUCOSAL GLAND ADENITIS ACUTE MULTI FOCAL	2	2	3	6	6	7	7	9	3	9
SUBMUCOSAL GLAND ADENITIS MULTIFOCAL	0	1	0	0	0	0	0	0	0	3
SUBMUCOSAL GLAND ADENITIS SUBACUTE DI FFUSE	0	0	0	0	0	0	0	0	1	0
SUBMUCOSAL GLAND ECTASIA MULTIFOCAL	1	1	0	0	0	0	0	0	0	1
SUBMUCOSAL GLAND SQUAMOUS METAPLASIA MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
VOMERONASAL ORGAN ADENITIS ACUTE DIFF USE BILATERAL	0	0	1	0	1	0	0	0	1	1
VOMERONASAL ORGAN ADENITIS ACUTE FOCA L UNILATERAL	0	0	0	0	0	0	1	0	0	0
VOMERONASAL ORGAN ADENITIS ACUTE MULT IFOCAL BILATERAL	9	11	10	11	16	14	13	12	13	15
VOMERONASAL ORGAN ADENITIS ACUTE MULT IFOCAL UNILATERAL	1	0	0	1	2	0	1	1	1	2
PARANASAL SINUS	[17]	[12]	[12]	[18]	[25]	[19]	[19]	[17]	[23]	[19]
TRACHEA	[18]	[14]	[12]	[18]	[25]	[19]	[19]	[17]	[23]	[19]
MONONUCLEAR CELL LEUKEMIA	1	1	0	0	2	0	2	1	1	0
SUBMUCOSAL GLAND ECTASIA MULTIFOCAL	0	0	1	1	0	1	0	0	0	0
TRACHEITIS ACUTE MULTIFOCAL	0	0	1	0	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
DERMIS	[0]	[3]	[0]	[1]	[1]	[1]	[0]	[2]	[0]	[0]
NASAL PASSAGE DERMATITIS ACUTE DIFFUSE	0	0	0	0	0	0	0	1	0	0
NASAL PASSAGE DERMATITIS SUBACUTE DIFFUSE	0	0	0	0	0	0	0	1	0	0
NASAL PASSAGE DERMATITIS SUPPURATIVE DIFFUSE	0	0	0	0	0	1	0	1	0	0
NOSE DERMATITIS ACUTE MULTIFOCAL	0	2	0	0	0	0	0	0	0	0
NOSE DERMATITIS GRANULOMATOUS FOCAL	0	0	0	1	0	0	0	0	0	0
NOSE DERMATITIS SUPPURATIVE DIFFUSE	0	1	0	0	0	0	0	0	0	0
TAIL DERMATITIS ACUTE MULTIFOCAL	0	0	0	0	1	0	0	1	0	0
MAMMARY GLAND	[2]	[0]	[0]	[1]	[6]	[0]	[1]	[0]	[6]	[1]
ADENOCARCINOMA	0	0	0	0	0	0	0	0	3	0
ADENOCARCINOMA WITH SQUAMOUS DIFFERENTIATION	0	0	0	0	1	0	0	0	0	0
CYSTIC HYPERPLASIA	0	0	0	0	1	0	0	0	0	1
CYSTIC HYPERPLASIA FOCAL	0	0	0	1	0	0	0	0	0	0
CYSTIC HYPERPLASIA MULTIFOCAL	0	0	0	0	1	0	0	0	0	0
FIBROADENOMA	2	0	0	0	3	0	1	0	3	0
MONONUCLEAR CELL LEUKEMIA	0	0	0	0	0	0	0	0	1	0
PAPILLARY CYST ADENOMA	0	0	0	0	1	0	0	0	0	0
SUBCUTIS FIBROMA	0	0	0	0	1	0	0	0	0	0
PREPUTIAL GLAND	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[1]
CARCINOMA	0	0	0	0	0	0	0	0	0	1

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
SKIN	[1]	[4]	[0]	[2]	[0]	[3]	[1]	[1]	[4]	[2]
BASAL CELL CARCINOMA	0	0	0	0	0	1	0	0	0	0
DERMIS DERMATITIS CHRONIC	0	0	0	0	0	0	1	0	0	0
DERMIS DERMATITIS SUBACUTE DIFFUSE	0	1	0	0	0	0	0	0	0	0
DERMIS DERMATITIS SUBACUTE MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
DERMIS FIBROSARCOMA UNDIFFERENTIATED	0	0	0	0	0	0	0	0	1	0
DERMIS KERATIN CYST FOCAL	0	0	0	0	0	0	0	0	1	0
EPIDERMAL INCLUSION CYST FOCAL	0	0	0	0	0	0	0	0	1	1
FACIAL AREA SQUAMOUS CELL CARCINOMA	0	1	0	0	0	0	0	0	0	0
FIBROSARCOMA	1	0	0	0	0	0	0	0	0	0
LEFT FACIAL AREA SQUAMOUS CELL CARCINOMA	0	1	0	0	0	0	0	0	0	0
LEFT SIDE OF HEAD SQUAMOUS CELL CARCINOMA	0	0	0	0	0	0	0	0	1	0
LIPOMA	0	0	0	0	0	0	0	0	0	1
MUZZLE AREA MONONUCLEAR CELL LEUKEMIA	0	0	0	0	0	0	0	0	0	1
SQUAMOUS CELL CARCINOMA	0	0	0	1	0	0	0	0	0	0
SUBCUTIS ABSCESS MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
SUBCUTIS FIBROSARCOMA	0	1	0	0	0	0	0	0	0	0
SUBCUTIS LIPOMA	0	0	0	0	0	1	0	0	0	0
SUBCUTICULAR TISSUE	[1]	[1]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]
LIPOSARCOMA	1	0	0	0	0	0	0	0	0	0
NASAL PASSAGE CELLULITIS SUPPURATIVE DIFFUSE	0	1	0	0	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
KIDNEY	[18]	[14]	[12]	[17]	[25]	[20]	[19]	[17]	[23]	[19]
ADENOCARCINOMA TUBULAR METASTATIC ORIGIN INTESTINE	0	0	0	0	0	0	0	0	1	0
CHRONIC RENAL DISEASE DIFFUSE BILATERAL	3	7	4	7	9	8	4	6	4	11
CHRONIC RENAL DISEASE DIFFUSE UNILATERAL	0	0	0	0	0	1	0	0	0	0
CHRONIC RENAL DISEASE MULTIFOCAL BILATERAL	1	0	1	0	1	0	1	0	2	1
CHRONIC RENAL DISEASE MULTIFOCAL UNILATERAL	0	0	0	0	1	0	0	0	0	0
COLLECTING TUBULES MINERALIZATION MULTIFOCAL	0	0	0	0	0	0	1	0	0	0
CONGESTION ACUTE DIFFUSE	1	0	0	0	0	0	0	0	0	0
CORTEX CYST FOCAL UNILATERAL	0	0	0	0	0	1	0	0	0	0
HYDRONEPHROSIS BILATERAL	1	0	0	0	0	0	0	2	0	0
HYDRONEPHROSIS UNILATERAL	1	0	1	0	1	0	0	0	1	0
INTERSTITIAL FIBROSIS FOCAL UNILATERAL	0	0	0	0	0	0	0	1	0	0
LIPOMATOUS TUMOR UNILATERAL	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	1	2	4	8	6	3	5	4
MONONUCLEAR CELL LEUKEMIA BILATERAL	8	3	4	3	5	5	6	5	4	4
NEPHRITIS ACUTE MULTIFOCAL BILATERAL	0	0	0	1	0	0	0	0	0	0
NEPHRITIS INTERSTITIAL SUBACUTE MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
NEPHRITIS LYMPHOCYTIC MULTIFOCAL BILATERAL	0	0	0	1	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. 62 CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
NEPHRITIS PYOGRANULOMATOUS MULTIFOCAL	1	0	0	0	0	0	0	0	0	0
NEPHRITIS SUBACUTE FOCAL UNILATERAL	0	0	0	0	0	0	0	0	1	0
NEPHRITIS SUPPURATIVE MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
PYELONEPHRITIS SUPPURATIVE MULTIFOCAL BILATERAL	0	0	0	0	0	0	0	0	0	1
PYELONEPHRITIS SUPPURATIVE MULTIFOCAL UNILATERAL	0	0	0	0	0	0	1	0	0	0
RENAL CAPSULE CAPSULITIS SUBACUTE MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
RENAL CAPSULE MESOTHELIOMA UNILATERAL	0	0	0	0	0	1	0	0	0	0
RENAL CORTEX CYST FOCAL	0	0	0	0	0	1	0	0	0	0
RENAL CORTICAL TUBULES MINERALIZATION MULTIFOCAL BILATERAL	0	0	1	0	0	0	2	0	1	0
RENAL CORTICAL TUBULES NECROSIS ACUTE MULTIFOCAL BILATERAL	1	0	0	0	0	0	0	0	0	0
RENAL PELVIS ADIPOSE TISSUE STEATITIS SUBACUTE MULTIFOCAL UNILATERAL	0	0	0	0	0	0	0	1	0	0
RENAL TUBULES CORTEX ECTASIA MULTIFOCAL	1	0	0	0	0	0	0	0	0	0
RENAL TUBULES CORTICOMEDULLARY JUNCTION ECTASIA FOCAL UNILATERAL	0	0	0	1	0	0	0	0	0	0
RENAL TUBULES CORTICOMEDULLARY JUNCTION ECTASIA MULTIFOCAL	0	0	0	1	0	1	0	1	0	1
RENAL TUBULES CORTICOMEDULLARY JUNCTION ECTASIA MULTIFOCAL BILATERAL	4	5	3	3	3	5	2	6	4	2
RENAL TUBULES CORTICOMEDULLARY JUNCTION ECTASIA MULTIFOCAL UNILATERAL	2	0	0	0	2	1	0	0	1	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
RENAL TUBULES ECTASIA MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
URETER	[0]	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[0]	[0]
MONONUCLEAR CELL LEUKEMIA	0	0	0	0	1	0	0	0	0	0
URINARY BLADDER	[17]	[14]	[10]	[17]	[24]	[20]	[18]	[15]	[23]	[19]
ADENOCARCINOMA TUBULAR METASTATIC ORIGIN INTESTINE	0	0	0	0	0	0	0	0	1	0
CARCINOSARCOMA DIFFUSE	1	0	0	0	0	0	0	0	0	0
CYSTITIS ACUTE MULTIFOCAL	0	0	1	0	0	0	0	0	1	0
CYSTITIS SUPPURATIVE MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
LAMINA PROPRIA HEMORRHAGE ACUTE MULTIFOCAL	0	0	0	0	0	0	1	0	1	0
MESOTHELIOMA	0	0	0	0	0	1	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	3	0	1	0	4	3	6	3	3	2
TRANSITIONAL CELL CARCINOMA WITH GLANDULAR METAPLASIA DIFFUSE	1	0	0	0	0	0	0	0	0	0
TRANSITIONAL EPITHELIUM CYSTITIS ACUTE MULTIFOCAL	0	0	0	0	0	0	1	0	0	0
ORGAN UNKNOWN	[2]	[2]	[0]	[0]	[0]	[1]	[1]	[2]	[0]	[2]
ADENOCARCINOMA	0	0	0	0	0	0	1	0	0	0
ADRENAL CORTICAL CARCINOMA	0	1	0	0	0	0	0	0	0	0
CARCINOMA UNDIFFERENTIATED	0	1	0	0	0	0	0	0	0	0
LEFT FORELEG FIBROMA	0	0	0	0	0	0	0	1	0	0
LYMPHOMA	0	0	0	0	0	0	0	0	0	1
MAMMARY GLAND ADENOCARCINOMA	0	0	0	0	0	0	0	0	0	1

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 42. CONTINUED

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	19	14	12	18	26	20	19	17	23	19
ORGAN AND DIAGNOSIS										
MONONUCLEAR CELL LEUKEMIA	1	0	0	0	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA DIFFUSE	0	0	0	0	0	0	0	1	0	0
SPINDLE CELL TUMOR PROBABLY FIBROSARCOMA	0	0	0	0	0	1	0	0	0	0
SPINDLE CELL TUMOR UNDIFFERENTIATED	1	0	0	0	0	0	0	0	0	0
ANIMAL MISSING-NO NECROPSY PERFORMED	1	0	0	0	1	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

During the course of this study, 187 rats died spontaneously or were sacrificed in a moribund condition. Many of the spontaneous deaths were due to mononuclear cell leukemia and/or pituitary adenomas, both of which are commonly seen in aged Fischer 344 rats. Other animals were sacrificed because of large skin tumors, such as fibroadenomas of the mammary gland, etc. With the exception of mononuclear cell leukemia, there appears to be no increased incidence of these lesions in the fibrous glass test groups when compared to the control group of animals.

Plaque-like lesions of the pleura were the only lesions observed at necropsy that were attributed to fibrous glass exposure. These plaque-like lesions consisted of gray to tan, elevated, firm areas of various sizes on the surface of the lung lobes. These lesions occurred in 1 of 19 females from the F01 group (15 mg/m^3 > 20 micrometer fiber with binder), in 5 of 23 females from the F02 group (15 mg/m^3 > 10 micrometer fiber with binder), in 2 of 12 females and in 4 of 18 males from the F03 group (5 mg/m^3 > 10 micrometer without binder), and in 5 of 26 females from the F04 group (5 mg/m^3 < 10 micrometer without binder). The superficial lung lesions in the animals from the F04 group were "gritty" or "granular" in character.

There were many additional lesions recorded at necropsy in a variety of organs, all considered to be spontaneous due to their nature, incidence, or severity, or due to a similar incidence between the control group (F05) and those exposed to fibrous glass. Histomorphologic lesions induced by fibrous glass were limited to the lungs, pleura, and lymph nodes (thymic and tracheobronchial) in rats from all exposure groups.

The lung lesions consisted of small to large aggregations of macrophages containing a few to many non-polarizable needle-shaped fibers (fibrous glass), readily seen under reduced light and located in peribronchiolar, peribronchial, or perivascular areas as well as within alveoli and in pleural and subpleural locations.

In many animals, there was granulomatous inflammation of the lung and pleura that was minimal to severe and apparently associated with fibrous glass deposition. This inflammatory response consisted of fibrous glass-laden macrophage aggregates that were surrounded by varying numbers of lymphocytes, plasma cells, and, at times, neutrophils. There were no obvious differences

in the lobar distribution of these pulmonary lesions in the affected rats. The fibrous glass-containing macrophages, in lungs of virtually all rats, occupied less than 5 percent of the total area of the lung sections.

The thymic and tracheobronchial lymph nodes contained various amounts of fibrous glass fibers, usually in the medulla of the lymph node.

Although fibrous glass-laden macrophages occurred in pleural and subpleural locations and were present in thymic and tracheobronchial lymph nodes, there was no evidence of translocation of fibrous glass fibers to other organs in these rats.

There were substantial variations in qualitative and quantitative fibrous glass-related changes among the various exposure groups in the lungs and thymic and tracheobronchial lymph nodes. These changes were least pronounced in the F01 group, became progressively more pronounced in the F02 and F03 groups, and were most pronounced in the F04 group. Table 43 depicts the numbers of animals affected per exposure group and the qualitative severities of the fibrous glass-induced lesions in the lung and lymph nodes (thymic and tracheobronchial).

Four of 20 male rats from the F04 group had mesotheliomas that primarily involved the testis (no other early death animals had this lesion). However, we believe that this neoplastic process was spontaneous because this tumor commonly occurs in aged Fischer 344 rats and there was no evidence of fibrous glass about or within (translocation) the serosal surfaces of the testis.

Many early death rats in this study had mononuclear cell leukemia (Fischer rat leukemia) are depicted in Table 44. The male rats in the F05 (control) group appeared to have a lower incidence of mononuclear cell leukemia when compared to the male and female rats in the other test groups.

There were many additional lesions seen microscopically in a variety of organs, all of which were considered to be spontaneous due to their nature, incidence, or severity, or due to a similar incidence between the control group and those exposed to fibrous glass.

TABLE 43. NUMBER OF RATS WITH FIBROUS-GLASS INDUCED LESIONS BY EXPOSURE GROUP

Lesion	Severity	Number of Animals							
		Group F01		Group F02		Group F03		Group F04	
		Male	Female	Male	Female	Male	Female	Male	Female
Lymph node-thymic, macrophage aggregates, multifocal	Minimal	1	2	1	1	1	0	1	0
	Mild	1	2	2	5	4	5	5	5
	Moderate		2	3	1	4	2	7	9
	Severe					0	1	1	1
	No lesion	15	15	13	16	9	3	6	11
Lymph node-tracheobronchial, macrophage aggregates, multifocal/diffuse/focal	Minimal	1	0			1	2	5	4
	Mild			1	2	5	1	10	6
	Moderate	0	1			1	0	0	1
	Severe								
	No lesion	16	18	18	21	11	9	4	14
Lung, macrophage aggregates, multifocal	Minimal	15	15	8	11	1	5	3	1
	Mild	0	2	10	8	15	7	16	23
	Moderate					1	0	1	1
	Severe								
	No lesion	2	2	1	4	1	0	0	1
Lung, pneumonia, granulomatous, multifocal	Minimal			0	1	6	5	5	8
	Mild			1	0	6	2	13	13
	Moderate							1	1
	Severe								
	No lesion	17	19	19	23	6	5	1	4
Pleura, pleuritis, granulomatous, multifocal/focal	Minimal	1	1	0	2	4	2	4	7
	Mild	1	1	2	0	3	5	13	10
	Moderate					1	0	0	3
	Severe								
	No lesion	15	17	17	21	10	5	3	6

TABLE 44. MONONUCLEAR CELL LEUKEMIA (M.C.L.) IN THE SPLEEN OF EARLY DEATH RATS

Group	M.C.L. (Males) / Total Examined	% M.C.L. Males	M.C.L. (Females) / Total Examined	% M.C.L. Females	M.C.L. (Males + Females) / Total Examined	% M.C.L. Males + Females
F01	9/17	53.9	14/19	73.7	23/36	63.9
F02	10/19	52.6	11/23	47.8	21/42	52.6
F03	9/18	50.0	5/12	41.7	14/30	46.7
F04	13/20	65.0	12/25	48.0	25/45	55.0
F05	3/14	21.4	10/18	55.6	13/32	40.6

Scheduled Sacrifice Rats

Observations recorded during necropsy are shown for individual animals in Tables I-21 through I-25 and are summarized in Table 45. Microscopic lesions are shown for individual animals in Tables I-26 through I-30 and are summarized in Table 46.

A total of 313 rats were sacrificed by group, beginning with the F01 group (15 mg/m^3 > 20 micrometer fiber with binder), terminated on April 16, 1981, and ending with the control group (F05), terminated on April 22, 1981. Plaque-like lesions of the pleura were the only lesions observed at necropsy attributed to fibrous glass exposure. Essentially no gross lesions were observed in the respiratory tracts of rats from the control group (F05) or in rats from the F01 group (Figure 47).

Plaque-like lesions of the pleura occurred in 25 of 27 females and in all 31 males from the F02 group (15 mg/m^3 > 10 micrometer fiber with binder). These lesions were multifocal, gray to tan, elevated, firm plaques that measured 1 to 6 or more millimeters in diameter. They were on the surface of the lung lobes and primarily involved the dorsal aspect of the diaphragmatic lobes. In one male rat (Pathology Number 804717), there were extensive fibrous adhesions between the left diaphragmatic lung lobe and both the diaphragm and adjacent thoracic wall.

Plaque-like lesions of the pleura occurred in 34 of 38 females and in 27 of 32 males from the F03 group (5 mg/m^3 > 10 micrometer plain fiber). These pulmonary lesions were similar those seen in the F02 group; however, they were smaller and there were fewer plaque-like lesions per lung lobe (Figure 48).

Plaque-like lesions of the pleura occurred in all 24 females and in 26 of 30 males from the F04 group (5 mg/m^3 < 10 micrometer plain fiber). Thirty-six animals (18 females and 18 males) from this group had superficial lung lesions as previously described; however, the plaque-like lesions were less extensive than those from animals in the F03 group. Most lesions were about 1 millimeter in diameter and there were often only a few plaques per lung lobe. Fourteen animals (6 females and 8 males) from this group had plaque-like lesions that were less than 1 millimeter in diameter and/or a

TABLE 45. NECROPSY SUMMARY BY GROUP AND SEX

PROJECT: G7148-14 STUDY: NIOSH SPECIES: RAT

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
ABDOMINAL CAVITY										
ASCITES	0	0	0	1	0	0	0	0	0	1
FLUID YELLOWISH GREEN	0	0	0	0	0	0	0	1	0	0
MASS PERIUTERINE BLOOD FILLED FOCAL	1	0	0	0	0	0	0	0	0	0
RIGHT WALL ADHESIONS	0	0	0	0	0	1	0	0	0	0
ABDOMINAL WALL										
URINARY BLADDER MASS	0	0	0	0	0	1	0	0	0	0
ADIPOSE TISSUE										
MESENTERIC FOCI BLACK	0	0	1	0	0	0	0	0	0	0
ADRENAL GLAND										
ENLARGED	0	0	0	0	0	0	0	0	0	1
ENLARGED TAN GREY BILATERAL	0	0	1	0	0	0	0	0	0	0
FOCUS CLEAR	0	0	0	1	0	0	0	0	0	0
SPOTS BLACK BILATERAL	0	0	0	0	0	0	0	0	1	0
LEFT ENLARGED	0	0	0	0	0	1	0	0	0	0
LEFT ENLARGED TAN	0	0	0	0	0	0	1	1	0	0
RIGHT ENLARGED	0	0	0	0	0	0	0	0	0	1
RIGHT FOCUS RED	0	0	0	1	0	0	0	0	0	0
RIGHT SPOT BLACK	0	0	0	0	0	0	0	0	1	0
RIGHT SPOT RED	0	0	0	0	0	0	0	0	0	1
BRAIN										
CEREBRUM VENTRAL COMPRESSED DUE TO PITUITARY TUMOR	2	0	0	0	0	0	0	0	0	0

TABLE 45. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
VENTRAL COMPRESSED DUE TO PITUITARY TUMOR	0	0	0	0	0	0	3	1	1	0
CECUM										
CONGESTED	0	0	0	0	0	0	0	0	1	1
CONGESTED DIFFUSE	0	0	0	0	0	0	0	0	1	1
RED	4	0	1	0	1	0	0	0	0	0
COLON										
NEMATODIASIS	0	0	0	0	0	2	0	0	0	0
RED SEGMENT	0	0	0	0	0	1	0	0	0	0
EPIDIDYMIS										
RED BILATERAL	0	0	0	0	0	1	0	0	0	0
EYE										
OPAQUE BILATERAL	0	0	0	1	1	0	0	0	0	0
LEFT MICROPHTHALMIA	0	0	0	0	1	0	0	0	0	0
LEFT OPAQUE	0	0	0	0	0	0	0	1	0	0
RIGHT OPAQUE	0	0	0	0	0	2	0	2	1	1
FIBULA										
RIGHT FRACTURE	0	0	0	0	0	0	1	0	0	0
FOOT										
RIGHT CONTRACTURES	0	0	0	0	0	0	1	0	0	0
KIDNEY										
GRANULAR SURFACE	0	0	0	0	0	1	0	1	0	0
GRANULAR SURFACE BILATERAL	0	0	2	3	0	1	0	1	1	2

TABLE 45. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
LEFT ENLARGED	0	0	0	0	0	0	0	1	0	0
LEFT GRANULAR SURFACE	0	1	0	0	0	0	0	0	0	0
LEFT CORTICAL CYST FOCAL	0	0	0	0	0	0	0	1	0	0
RIGHT PITTED SURFACE	0	0	1	0	0	0	0	0	0	0
RIGHT GRANULAR SURFACE	0	0	0	1	0	0	0	0	0	0
LIVER										
ENLARGED	0	0	0	0	0	0	1	0	0	1
NODULES TAN	0	0	0	0	0	0	1	0	0	0
ACCENTUATED LOBULAR PATTERN	0	0	1	0	0	0	0	0	1	0
MOTTLED SURFACE	1	3	4	6	4	6	2	4	6	3
ANTERIOR RIGHT LOBE FOCUS YELLOW	0	1	0	0	0	0	0	0	0	0
LEFT LATERAL AND MEDIAN LOBE FOCI SMALL WHITE	0	0	0	0	0	0	1	0	0	0
LEFT LATERAL LOBE FOCUS GREY	0	0	0	0	1	0	0	0	0	0
LEFT LATERAL LOBE FOCUS RED	0	0	0	0	0	1	0	0	0	0
LEFT LATERAL LOBE FOCUS TAN	1	0	0	0	0	0	0	0	0	0
LEFT LATERAL LOBE FOCUS WHITE	0	1	0	0	0	0	0	0	0	0
LEFT LATERAL LOBE NODULE RED	0	0	0	0	0	0	0	0	1	0
LEFT LATERAL LOBE NODULE RED FIRM	0	0	0	1	0	0	0	0	0	0
LEFT LATERAL LOBE NODULE YELLOW	0	0	0	0	0	0	0	0	1	0
LEFT LATERAL LOBE FOCUS YELLOW	2	0	0	0	0	0	0	0	1	0
LEFT LATERAL LOBE SPOT RED	0	0	0	0	0	1	0	0	0	0
LEFT LATERAL LOBE FOCI YELLOW MULTIFOCAL	1	0	0	0	0	0	0	0	0	0

TABLE 45. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
LEFT LATERAL LOBE MOTTLED SURFACE	0	0	0	1	0	0	0	0	0	0
LEFT LATERAL LOBE MARGIN FOCUS RED	0	0	0	0	0	0	1	0	0	0
LEFT LATERAL LOBE VENTRAL SURFACE NODULE WHITE	0	0	1	0	0	0	0	0	0	0
MEDIAN LOBE FOCI WHITE	0	0	1	0	0	0	0	0	0	0
MEDIAN LOBE FOCUS	0	0	0	0	0	0	0	1	0	0
MEDIAN LOBE FOCUS TAN	0	0	0	0	0	0	1	0	0	1
MEDIAN LOBE FOCUS WHITE	1	0	0	0	0	0	0	0	0	0
MEDIAN LOBE MASS	0	0	0	0	0	1	0	0	0	0
MEDIAN LOBE MASS RED	1	0	0	0	0	0	0	0	0	0
MEDIAN LOBE MASS SOLID	0	0	0	0	0	1	0	0	0	0
MEDIAN LOBE MASS SOLID GREY	0	0	0	0	0	1	0	0	0	0
MEDIAN LOBE FOCI WHITE MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
MEDIAN LOBE FOCUS YELLOW	1	2	0	0	2	1	0	0	0	0
MEDIAN LOBE NODULES HIATAL	0	0	0	0	0	0	0	0	2	0
MEDIAN LOBE NODULE HIATAL	1	0	2	0	0	0	2	0	0	0
MEDIAN LOBE MASS YELLOW	0	0	0	2	0	0	0	0	0	0
MEDIAN LOBE RIGHT SIDE FOCI TAN	0	0	0	0	0	0	0	1	0	0
LUNG										
CONGESTED	0	1	0	0	0	0	0	0	1	0
FOCI RED	0	0	1	0	0	0	0	0	0	0
FOCI BLACK MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
FOCI RED MULTIFOCAL	0	0	0	0	1	2	0	0	0	0

TABLE 45. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
ALL LOBES FOCI BROWN	0	0	0	2	0	0	0	0	0	0
ALL LOBES FOCI TAN	0	0	0	0	0	0	1	0	0	0
LEFT DIAPHRAGMATIC LOBE MASS TAN	0	0	0	0	0	0	0	1	0	0
LEFT DIAPHRAGMATIC LOBE MARGIN WHITE	0	1	0	0	0	0	0	0	0	0
LEFT DIAPHRAGMATIC LOBE PLEURA ADHESIONS TO THORACIC CAVITY	0	0	0	0	0	0	0	0	0	1
PLEURA SPOTS	0	0	0	0	0	0	0	0	1	0
PLEURA PLAQUES GREY MULTIFOCAL	0	0	32	25	24	26	0	0	25	31
PLEURA PLAQUES WHITE TAN MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
PLEURA PLAQUES TAN MULTIFOCAL	0	0	1	1	0	0	0	0	0	0
RIGHT APICAL LOBE FOCUS RED	0	0	0	0	0	0	1	0	0	0
RIGHT APICAL LOBE FOCUS YELLOW	1	0	0	0	0	0	0	0	0	0
RIGHT DIAPHRAGMATIC LOBE FOCUS WHITE	2	0	0	0	0	0	0	0	0	0
RIGHT DIAPHRAGMATIC LOBE MASS ROUND SOLID	0	0	0	0	0	1	0	0	0	0
RIGHT DIAPHRAGMATIC LOBE MASS TAN SOLID	0	0	0	0	0	0	0	1	0	0
RIGHT DIAPHRAGMATIC LOBE ADHESION TO DIAPHRAGM SOLID GREY YELLOW	0	0	0	0	0	1	0	0	0	0
RIGHT DIAPHRAGMATIC LOBE FOCUS YELLOW	0	1	0	0	0	0	0	0	0	0
RIGHT DIAPHRAGMATIC LOBE MARGIN FOCUS WHITE	1	0	0	0	0	0	0	0	0	0
RIGHT DIAPHRAGMATIC LOBE MARGIN WHITE	2	0	0	0	0	0	0	0	0	0
RIGHT DIAPHRAGMATIC LOBE PLEURA PLAQUES	0	0	1	0	0	0	0	0	0	0

TABLE 45. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
RIGHT DIAPHRAGMATIC LOBE PLEURA PLAQUES GREY FOCAL	1	0	0	0	0	0	0	0	0	0
RIGHT INTERMEDIATE LOBE NODULAR PINK GREY FIRM	0	0	0	0	0	0	0	0	0	1
RIGHT LATERAL LOBE PLEURA FOCUS BROWN	0	0	0	0	0	0	0	0	1	0
LYMPH NODE										
MANDIBULAR ENLARGED TAN	0	0	0	0	0	1	0	0	0	0
MANDIBULAR RED	0	0	0	0	0	0	0	0	0	1
MESENTERIC ENLARGED TAN	0	0	0	0	0	0	1	0	2	0
SACROLUMBAR ADHESIONS	0	0	0	0	0	0	0	1	0	0
SACROLUMBAR ENLARGED YELLOW	0	0	0	0	0	0	0	1	0	0
SUBMANDIBULAR LEFT ENLARGED RED	0	0	0	0	0	0	0	1	0	0
THORACIC ENLARGED TAN	0	0	0	0	0	0	0	0	1	0
MESENTERY										
MESOTHELIOMA	0	0	0	0	0	0	0	1	0	0
FAT NECROSIS FOCAL	0	0	1	0	0	0	0	0	0	0
EDEMATOUS TAN	0	0	0	0	0	0	0	0	1	0
FAT NECROSIS RED FOCUS	0	1	0	0	0	0	0	0	0	0
GREATER OMENTUM MASS FAT NECROSIS YELLOW	0	0	0	0	0	0	1	0	0	0
RIGHT ABDOMINAL AREA ADHESIONS	0	0	0	0	0	1	0	0	0	0
RIGHT ABDOMINAL AREA FAT NECROSIS YELLOW	0	0	0	1	0	0	0	0	0	0
RIGHT ABDOMINAL AREA FAT NECROSIS FOCAL YELLOW	0	0	0	0	1	0	0	0	0	0

TABLE 45. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
TESTICULAR FAT MASS YELLOW SOLID	0	0	0	0	0	0	0	1	0	0
ORAL CAVITY										
HARD PALATE PAPILLARY SURFACE MASS ROUND RAISED	0	0	0	0	0	0	0	0	1	0
OVARY										
LEFT CYSTIC	0	0	0	0	0	0	1	0	1	0
RIGHT CYSTIC	1	0	3	0	1	0	2	0	2	0
RIGHT FOCI RED MULTIFOCAL	0	0	0	0	1	0	0	0	0	0
PANCREAS										
MASS WHITE	0	0	0	1	0	0	0	0	0	0
NODULE GREY	0	0	0	0	0	1	0	0	0	0
PITUITARY GLAND										
CYST FOCAL	0	0	0	0	0	0	0	1	0	0
ENLARGED	0	0	1	0	0	1	2	1	0	0
ENLARGED RED	8	5	9	4	9	3	8	1	9	1
ENLARGED TAN	1	1	1	0	0	0	0	0	0	0
ENLARGED RED CYSTIC	0	0	0	0	0	0	1	1	1	1
ENLARGED RED SPOT	0	0	0	0	0	0	1	0	0	0
FOCI BLACK	0	0	0	0	1	0	0	0	0	0
FOCI RED	0	0	0	0	0	1	0	0	0	0
FOCI WHITE	1	0	0	0	0	0	0	0	0	0
FOCUS BLUE	0	0	0	1	0	0	0	0	0	0
FOCUS RED	0	0	0	0	1	0	0	0	0	0

TABLE 45. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
FOCUS BLACK	4	5	4	2	3	0	1	2	4	2
ENLARGED FOCUS BLACK	0	0	0	0	0	0	0	0	0	1
ENLARGED FOCUS RED	0	0	0	0	0	0	0	0	1	0
PURPLE	0	0	0	1	0	0	0	0	0	0
RED	1	0	0	0	0	0	0	0	0	0
RED HEMORRHAGIC	0	0	0	0	0	0	0	0	1	0
ENLARGED CYST	0	1	0	0	0	0	1	0	0	0
LEFT LOBE CYST	0	0	0	0	0	0	0	0	0	1
SEMINAL VESICLE										
ENLARGED	0	1	0	0	0	0	0	0	0	1
ENLARGED YELLOW	0	1	0	0	0	0	0	0	0	0
SMALL	0	0	0	0	0	0	0	0	0	1
RIGHT YELLOWISH	0	0	0	0	0	0	0	0	0	1
SEROSA										
ABDOMINAL GRANULAR DIFFUSE	0	0	0	1	0	0	0	0	0	0
LEFT TESTIS AREA FAT NECROSIS YELLOW MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
SKIN										
INGUINAL AREA LEFT LEG MASS SOLID TAN RED	0	0	0	0	0	0	0	0	1	0
INGUINAL AREA RIGHT LEG MASS SOLID TAN RED	0	0	0	0	0	0	0	0	1	0
LEFT AXILLARY AREA MASS SOLID/CYSTIC AREAS	0	1	0	0	0	0	0	0	0	0

TABLE 45. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
LEFT CERVICAL AREA MASS SOLID FIRM	0	0	1	0	0	0	0	0	0	0
LEFT CERVICAL AREA MASS ULCERATED FIRM SOLID	0	0	0	0	0	1	0	0	0	0
LEFT INGUINAL AREA MASS SOLID ULCERATED	0	0	0	0	0	0	0	0	1	0
LEFT INGUINAL AREA MASS ULCERATED SOLID/CYSTIC CASEATED	0	1	0	0	0	0	0	0	0	0
LEFT LATERAL ABDOMINAL AREA MASS SOLID FIRM WHITE	1	0	0	0	0	0	0	0	0	0
LEFT LATERAL ABDOMINAL AREA MASS ULCERATED SURFACE	0	0	1	0	0	0	0	0	0	0
LEFT LATERAL ABDOMINAL AREA SUBCUTIS MASS	0	0	0	0	0	0	0	1	0	0
LEFT THORACIC AREA MASS SOLID FIRM	0	0	1	0	0	0	0	0	0	0
LEFT THORACIC AREA MASS SOLID SOFT	0	0	0	0	0	1	0	0	0	0
RIGHT AXILLARY AREA MASS SOLID FIRM	0	0	0	0	1	0	0	0	0	0
RIGHT AXILLARY AREA EPIDERMIS TUMOR CRUSTY SURFACE PAPILLOMA LIKE	0	0	0	0	0	0	0	1	0	0
RIGHT CERVICAL AREA MASS WHITE SOFT	0	0	0	1	0	0	0	0	0	0
RIGHT INGUINAL AREA MASS SOLID FIRM	0	0	1	0	0	0	0	0	0	0
RIGHT INGUINAL AREA MASS SOLID SOFT	0	0	1	0	0	0	0	0	0	0
RIGHT INGUINAL AREA MASS ULCERATED SOLID CYSTIC	0	0	0	0	0	0	1	0	0	0
RIGHT INGUINAL AREA MASS SOLID CASEATED CYST	0	0	0	1	0	0	0	0	0	0
RIGHT INGUINAL AREA SOLID CYSTIC	0	0	1	0	0	0	0	0	0	0
RIGHT INGUINAL AREA MASS SUBCUTICULAR SOLID SOFT	0	0	0	0	0	0	0	1	0	0

TABLE 45. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
RIGHT LATERAL ABDOMINAL AREA MASS ULCERATED FIRM	0	0	0	0	0	0	0	0	0	1
RIGHT LATERAL THORACIC AREA MASS SUBCUTICULAR SOLID FIRM	0	0	0	0	1	0	0	0	0	0
RIGHT THORACIC AREA MASS SOLID FIRM WHITE	0	1	0	0	0	0	0	0	0	0
SUBCUTIS LEFT ABDOMINAL AREA MASS SOLID LOBULAR	0	0	1	0	0	0	0	0	0	0
SUBCUTIS LEFT ABDOMINAL AREA MASS FIRM WHITE	0	0	0	0	0	0	0	0	0	1
SUBCUTIS LEFT AXILLARY AREA MASS SOLID CYSTIC	0	0	0	0	0	0	1	0	0	0
SUBCUTIS LEFT AXILLARY AREA SOLID FIRM	0	0	0	0	0	1	0	0	0	0
SUBCUTIS LEFT INGUINAL AREA MASS TAN SOLID SOFT	0	0	0	0	0	0	0	0	1	0
SUBCUTIS LEFT THORACIC AREA MASS SOFT SOLID TAN SOFT	0	0	1	0	0	0	0	0	0	0
SUBCUTIS LEFT THORACIC AREA MASS SOLID TAN ADHERENT TO RIBS	0	0	0	0	0	0	1	0	0	0
SUBCUTIS MIDABDOMINAL AREA MASS ULCERATED SOLID	0	0	0	1	0	0	0	0	0	0
SUBCUTIS RIGHT AXILLARY AREA MASS SOLID AND CYSTIC	0	0	0	0	0	0	1	0	0	0
SUBCUTIS RIGHT INGUINAL AREA TAN SOLID FIBROUS	0	0	0	0	0	0	0	0	1	0
SUBCUTIS RIGHT INGUINAL AREA MASS YELLOW SOLID	0	0	0	0	0	0	0	0	0	1
SUBCUTIS RIGHT INGUINAL AREA MASS FIRM WHITE	0	0	0	1	0	0	0	0	0	0

TABLE 45. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
SUBCUTIS RIGHT LATERAL ABDOMINAL AREA MASS SOLID	0	0	0	0	0	0	0	1	0	0
SUBCUTIS RIGHT LATERAL ABDOMINAL AREA MASS SOLID MULTILOBULATED	0	0	0	0	0	0	1	0	0	0
SUBCUTIS VENTRAL CAUDAL ABDOMINAL ARE A MASS SOLID	0	0	0	0	0	0	1	0	0	0
SUBCUTIS VENTRAL THORACIC AREA MASS S OLID SOFT	0	0	0	0	0	0	0	0	0	1
VENTRAL ABDOMINAL AREA MASS ULCERATED	0	0	0	0	0	1	0	0	0	0
VENTRAL CERVICAL AREA EDEMATOUS	0	0	0	0	0	0	0	0	1	0
SPLEEN										
ENLARGED	1	6	8	8	2	11	4	8	6	10
NODULES TAN	0	0	0	0	0	0	1	0	0	0
SMALL	0	0	1	0	1	0	0	0	0	0
WHITISH AREA	0	0	0	0	0	0	0	1	0	0
STOMACH										
CARDIAC FUNDIC LINE NODULE WHITE FIRM	0	0	0	0	0	0	0	1	0	0
CARDIAC FUNDIC MUCOSA THICKENED RIDGE S PAPILLARY KERATINOUS	0	0	0	0	0	1	0	0	0	0
FUNDIC AREA MUCOSA NODULE TAN FIRM	0	0	0	1	0	0	0	0	0	0
FUNDIC AREA MUCOSA NODULE WHITE FIRM FOCAL	0	0	0	0	0	1	0	0	0	0
MUCOSA RED	0	0	0	0	0	1	0	0	0	0
SUBCUTIS										

TABLE 45. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
LEFT AXILLARY AREA MASS TAN SOFT	0	0	0	0	0	0	1	0	0	0
TAIL										
NODULE	0	0	0	0	1	0	0	0	0	0
KERATIN HORN	0	0	1	0	0	0	0	0	0	0
TESTIS										
NODULES BILATERAL	0	30	0	16	0	28	0	0	0	0
NODULES TAN MULTIFOCAL BILATERAL	0	0	0	1	0	0	0	0	0	0
NODULES WHITE MULTIFOCAL	0	0	0	0	0	0	0	0	0	2
NODULES WHITE MULTIFOCAL BILATERAL	0	0	0	0	0	0	0	0	0	2
SMALL	0	0	0	0	0	0	0	0	0	1
SMALL BILATERAL	0	1	0	0	0	0	0	1	0	1
GRANULAR YELLOW BILATERAL	0	0	0	0	0	0	0	0	0	1
NODULES SMALL BILATERAL	0	0	0	0	0	0	0	1	0	0
NODULES WHITE BILATERAL	0	0	0	14	0	0	0	31	0	25
LEFT CYSTIC	0	0	0	0	0	1	0	0	0	0
LEFT LARGE	0	1	0	1	0	1	0	1	0	1
LEFT LARGE NODULES WHITE	0	1	0	0	0	0	0	0	0	0
LEFT LARGE CYSTIC	0	1	0	0	0	0	0	0	0	0
LEFT NODULES	0	1	0	0	0	2	0	1	0	0
LEFT SMALL	0	3	0	0	0	2	0	2	0	0
LEFT SMALL FLACCID	0	1	0	0	0	0	0	0	0	0
RIGHT HEMORRHAGIC	0	0	0	0	0	0	0	1	0	0

TABLE 45. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
RIGHT LARGE	0	3	0	0	0	0	0	2	0	0
RIGHT NODULES	0	1	0	0	0	0	0	1	0	0
RIGHT NODULES WHITE	0	1	0	0	0	0	0	0	0	0
RIGHT SMALL	0	3	0	2	0	3	0	2	0	1
RIGHT SMALL NODULES	0	1	0	0	0	0	0	0	0	0
THYMUS										
LARGE TAN FIRM	0	0	0	1	0	0	0	0	0	0
THYROID GLAND										
LEFT LARGE RED	0	0	0	1	0	1	0	0	1	0
LEFT LARGE TAN	0	0	1	0	0	0	0	0	0	0
LEFT LARGE TAN SOLID	0	0	0	0	0	0	0	1	0	0
RIGHT LARGE	0	0	0	0	0	1	0	1	0	0
RIGHT LARGE RED	0	1	0	0	0	0	0	0	0	1
RIGHT LARGE TAN	0	0	0	0	0	0	0	1	0	0
TUNICA VAGINALIS										
TESTIS GRANULAR DIFFUSE	0	0	0	1	0	0	0	0	0	0
UTERINE HORN										
DILATED	0	0	1	0	0	0	0	0	0	0
DILATED SEGMENTAL	1	0	0	0	0	0	0	0	0	0
DILATED BILATERAL	0	0	1	0	0	0	0	0	0	0
DILATED CYSTIC BILATERAL	0	0	0	0	0	0	1	0	0	0
LARGE BILATERAL	0	0	0	0	1	0	0	0	0	0

TABLE 45. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND OBSERVATION										
LEFT DILATED RED	1	0	0	0	0	0	0	0	0	0
LEFT DILATED FOCAL	0	0	0	0	1	0	0	0	1	0
LEFT DILATED SEGMENTAL	1	0	0	0	0	0	0	0	0	0
LEFT CYSTIC APICAL WALL THICKENED	0	0	0	0	0	0	1	0	0	0
LEFT LARGE	0	0	0	0	1	0	0	0	0	0
LEFT LARGE RED	0	0	1	0	0	0	0	0	0	0
LEFT MASS	0	0	1	0	0	0	0	0	0	0
LEFT LARGE THICKENED WALL SOLID	0	0	0	0	0	0	1	0	0	0
LEFT ANTERIOR DILATED RED	1	0	0	0	0	0	0	0	0	0
RIGHT DILATED	1	0	0	0	0	0	0	0	1	0
RIGHT DILATED RED	0	0	1	0	0	0	0	0	1	0
RIGHT DILATED FOCAL	0	0	0	0	0	0	0	0	1	0
RIGHT LARGE FOCAL	0	0	0	0	1	0	0	0	0	0
RIGHT LARGE RED CYSTIC SOLID	0	0	0	0	0	0	0	0	1	0
RIGHT APICAL AREA LARGE	0	0	1	0	0	0	0	0	0	0
UTEROCERVIX										
LARGE	0	0	0	0	0	0	0	0	1	0

TABLE 46. HISTOPATHOLOGY SUMMARY BY GROUP AND SEX

PROJECT: G7188-14 STUDY: NIOSH SPECIES: RAT

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
AUDITORY CANAL	[0]	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[0]	[0]
OTITIS MEDIA SUPPURATIVE DIFFUSE UNILATERAL	0	0	0	0	0	0	1	0	0	0
EAR CANAL	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[0]
OTITIS EXTERNA SUPPURATIVE DIFFUSE UNILATERAL	0	0	0	0	0	1	0	0	0	0
ADIPOSE TISSUE	[1]	[0]	[0]	[1]	[0]	[0]	[0]	[1]	[0]	[0]
LIPOMA	0	0	0	1	0	0	0	0	0	0
MESENTERIC STEATITIS CHRONIC DIFFUSE	0	0	0	0	0	0	0	1	0	0
PERIRENAL STEATITIS GRANULOMATOUS MULTIFOCAL	1	0	0	0	0	0	0	0	0	0
MESENTERY	[0]	[1]	[2]	[1]	[1]	[0]	[1]	[0]	[2]	[1]
FAT NECROSIS CHRONIC FOCAL	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	0	0	0	0	0	0	2	0
STEATITIS CHRONIC ACTIVE FOCAL	0	1	0	0	0	0	0	0	0	0
STEATITIS CHRONIC FOCAL	0	0	0	0	0	0	1	0	0	0
STEATITIS CHRONIC MULTIFOCAL	0	0	1	0	0	0	0	0	0	1
STEATITIS GRANULOMATOUS FOCAL	0	0	1	0	0	0	0	0	0	0
STEATITIS SUBACUTE DIFFUSE	0	0	0	0	1	0	0	0	0	0
ARTERY-PULMONARY	[0]	[6]	[0]	[0]	[1]	[1]	[1]	[3]	[0]	[1]
MINERALIZATION DYSTROPHIC FOCAL	0	3	0	0	1	1	1	1	0	0
MINERALIZATION DYSTROPHIC MULTIFOCAL	0	3	0	0	0	0	0	2	0	1
HEART	[31]	[36]	[38]	[32]	[24]	[30]	[31]	[33]	[27]	[31]

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
AORTA MINERALIZATION DYSTROPHIC FOCAL	0	0	0	1	0	0	0	1	0	0
FIBROPROLIFERATIVE DISEASE MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	3	7	9	4	12	3	5	6	5
MYOCARDIUM MINERALIZATION DYSTROPHIC FOCAL	0	0	0	1	0	0	0	0	0	0
MYOCARDIUM MONONUCLEAR CELL LEUKEMIA	0	0	0	0	0	0	0	0	1	0
MYOCARDIUM MYOCARDITIS ACUTE MULTIFOCAL	1	0	0	0	0	0	0	0	0	0
MYOCARDIUM MYOCARDITIS CHRONIC MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
MYOCARDIUM MYOCARDITIS SUBACUTE DIFFUSE	0	1	2	1	2	2	1	0	0	1
MYOCARDIUM MYOCARDITIS SUBACUTE MULTIFOCAL	30	34	34	26	19	20	29	32	23	25
CECUM	[2]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]
COLON	[31]	[36]	[38]	[32]	[23]	[30]	[30]	[33]	[27]	[31]
MESOTHELIOMA	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	1	3	4	0	3	1	1	4	0
NEMATODIASIS	4	5	4	4	2	5	1	3	2	3
DUODENUM	[0]	[0]	[0]	[0]	[0]	[0]	[1]	[1]	[1]	[0]
ESOPHAGUS	[31]	[36]	[38]	[32]	[24]	[30]	[31]	[33]	[27]	[31]
ESOPHAGITIS SUBACUTE FOCAL	0	0	2	0	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	1	4	0	2	0	0	2	1
NEMATODIASIS	1	0	0	0	0	0	0	1	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
ILEUM	[31]	[35]	[38]	[31]	[22]	[28]	[29]	[32]	[27]	[31]
ILEITIS SUPPURATIVE FOCAL	0	0	0	1	0	0	0	0	0	0
MESOTHELIOMA	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	1	1	3	0	1	1	0	4	0
NEMATODIASIS	0	0	0	0	0	0	1	0	0	0
LIVER	[31]	[36]	[37]	[32]	[24]	[30]	[31]	[33]	[27]	[31]
BILE DUCT CHOLANGITIS GRANULOMATOUS FOCAL	0	0	0	0	0	0	0	1	0	0
BILE DUCT HYPERPLASIA MULTIFOCAL	1	14	1	12	0	6	0	14	1	12
BILE DUCT HYPERPLASIA WITH FIBROSIS MULTIFOCAL	1	9	1	2	0	0	0	3	0	3
EXTRAMEDULLARY HEMATOPOIESIS DIFFUSE	0	0	0	0	1	0	0	0	0	0
FOCUS OF CELLULAR ALTERATION BASOPHILIC TYPE FOCAL	0	1	3	0	0	4	0	0	4	0
FOCUS OF CELLULAR ALTERATION BASOPHILIC TYPE MULTIFOCAL	1	1	3	1	1	2	0	0	1	0
FOCUS OF CELLULAR ALTERATION CLEAR CELL TYPE FOCAL	1	0	0	0	0	0	0	1	0	0
HEPATITIS GRANULOMATOUS FOCAL	1	0	2	0	0	0	0	0	1	0
HEPATITIS GRANULOMATOUS MULTIFOCAL	8	0	6	4	11	0	12	1	10	3
HEPATITIS SUBACUTE FOCAL	3	1	0	0	3	0	0	1	0	0
HEPATITIS SUBACUTE MULTIFOCAL	12	11	8	4	2	4	9	7	2	1
HEPATITIS SUPPURATIVE FOCAL	0	0	0	1	0	0	1	0	0	0
HEPATITIS SUPPURATIVE MULTIFOCAL	0	0	0	1	0	0	1	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
HEPATOCELLULAR CARCINOMA	0	0	0	2	0	2	0	0	0	0
HEPATOCYTES VACUOLAR CHANGE FOCAL	0	0	0	2	0	0	0	0	0	0
LIPOIDAL DEGENERATION FOCAL	0	1	0	0	0	0	0	0	0	1
MONONUCLEAR CELL LEUKEMIA	1	7	10	11	5	12	6	8	8	8
NECROSIS ACUTE FOCAL	0	0	0	1	0	0	0	0	0	0
NEOPLASTIC NODULE FOCAL	1	1	0	2	0	0	0	0	0	0
ORAL CAVITY	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[1]	[0]
GINGIVA PAPILLOMA	0	0	0	0	0	0	0	0	1	0
PANCREAS-EXOCRINE	[31]	[36]	[38]	[31]	[24]	[29]	[31]	[33]	[27]	[31]
ATROPHY LOBULAR DIFFUSE	0	0	1	0	0	2	1	0	0	1
ATROPHY LOBULAR FOCAL	0	5	3	1	0	4	1	8	0	4
ATROPHY LOBULAR MULTIFOCAL	3	4	0	7	1	1	1	3	2	5
MESOTHELIOMA	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	1	5	8	1	8	2	1	6	4
PANCREATITIS LYMPHOCYTIC MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
PANCREATITIS SUBACUTE FOCAL	2	3	1	1	1	1	2	3	6	0
PANCREATITIS SUBACUTE MULTIFOCAL	0	3	4	4	4	5	5	1	2	3
SALIVARY GLAND	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[1]	[1]
MONONUCLEAR CELL LEUKEMIA	0	0	0	0	0	0	0	0	1	0
STOMACH	[31]	[36]	[38]	[32]	[24]	[30]	[30]	[33]	[27]	[31]
FIBROSARCOMA FOCAL	0	0	0	0	0	1	0	0	0	0
GLANDULAR PORTION ADENOMA FOCAL	0	0	0	0	0	0	0	0	0	1

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
GLANDULAR PORTION CHORISTOMA FOCAL	0	0	0	0	0	0	0	0	0	1
GLANDULAR PORTION DEVELOPMENTAL ANOMALY FOCAL	0	0	0	0	0	0	0	0	0	1
GLANDULAR PORTION GASTRITIS ACUTE FOCAL	0	0	0	1	0	0	0	0	0	0
GLANDULAR PORTION GLANDULAR ECTASIA MULTIFOCAL	5	1	10	11	8	15	12	16	17	19
GLANDULAR PORTION KERATIN CYST FOCAL	0	0	0	0	0	0	0	1	0	0
MONONUCLEAR CELL LEUKEMIA	0	1	1	3	0	5	0	1	6	1
NONGLANDULAR PORTION EPITHELIAL HYPERPLASIA MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
NONGLANDULAR PORTION GLANDULAR ECTASIA MULTIFOCAL	0	0	0	0	0	0	1	0	0	0
TOOTH	[101]	[113]	[6]	[6]	[3]	[6]	[8]	[11]	[5]	[8]
INCISOR PERIODONTITIS ACUTE MULTIFOCAL UNILATERAL	1	0	0	0	0	1	0	0	0	0
INCISOR PERIODONTITIS GRANULOMATOUS FOCAL UNILATERAL	0	0	0	0	0	0	0	1	0	0
INCISOR PERIODONTITIS SUBACUTE DIFFUSE UNILATERAL	1	3	0	0	0	1	1	1	1	0
INCISOR PERIODONTITIS SUBACUTE DIFFUSE UNILATERAL HAIR SHAFTS AND OTHER FOOD DEBRIS	0	0	0	0	0	0	0	0	0	1
INCISOR PERIODONTITIS SUBACUTE FOCAL	0	0	0	0	0	1	0	0	1	0
INCISOR PERIODONTITIS SUBACUTE FOCAL UNILATERAL	0	0	0	0	0	1	2	1	1	3
INCISOR PERIODONTITIS SUBACUTE FOCAL UNILATERAL FOREIGN OBJECT	0	0	0	0	0	0	0	0	0	1

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
INCISOR PERIODONTITIS SUBACUTE MULTIFOCAL BILATERAL	1	1	0	0	0	0	0	0	2	0
INCISOR PERIODONTITIS SUBACUTE MULTIFOCAL UNILATERAL	4	7	2	1	0	0	4	5	0	3
INCISOR PERIODONTITIS SUPPURATIVE DIFFUSE UNILATERAL	1	0	0	0	0	0	0	0	0	0
INCISOR PERIODONTITIS SUPPURATIVE FOCAL UNILATERAL	0	0	2	0	0	0	0	0	0	0
INCISOR PERIODONTITIS SUPPURATIVE MULTIFOCAL UNILATERAL	0	0	0	3	0	0	1	0	0	0
INCISOR PULPITIS CHRONIC ACTIVE FOCAL UNILATERAL	2	0	0	1	0	0	0	1	0	0
INCISOR PULPITIS CHRONIC FOCAL	0	0	0	0	1	1	0	0	0	0
INCISOR PULPITIS CHRONIC FOCAL UNILATERAL	1	0	2	2	2	1	0	2	0	0
INCISOR PULPITIS SUBACUTE FOCAL UNILATERAL	0	0	0	3	0	1	0	0	0	0
INCISOR PULPITIS SUPPURATIVE DIFFUSE UNILATERAL	1	0	0	0	0	0	1	0	0	0
INCISOR PULPITITIS CHRONIC FOCAL UNILATERAL	1	0	1	0	0	0	0	0	0	0

( ) = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

PROJECT: G7188-14 STUDY: NIOSH SPECIES: RAT

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
ADRENAL GLAND	[31]	[36]	[38]	[31]	[23]	[30]	[31]	[33]	[27]	[31]
ADENOMA FOCAL UNILATERAL	0	0	0	1	0	0	0	0	0	0
ANGIECTASIS FOCAL UNILATERAL	1	0	0	0	0	0	0	0	0	0
ANGIECTASIS MULTIFOCAL BILATERAL	14	6	22	11	13	13	16	13	15	7
ANGIECTASIS MULTIFOCAL UNILATERAL	6	2	3	5	7	4	9	5	4	6
CORTEX ADENOMA FOCAL UNILATERAL	1	0	1	0	0	0	0	0	0	0
CORTEX HYPERPLASIA FOCAL	0	0	0	0	0	0	1	0	0	0
CORTEX LIPOIDAL DEGENERATION FOCAL BILATERAL	2	0	0	0	1	0	0	0	0	0
CORTEX LIPOIDAL DEGENERATION FOCAL UNILATERAL	5	3	6	2	2	0	5	2	3	2
CORTEX LIPOIDAL DEGENERATION MULTIFOCAL BILATERAL	1	0	1	0	0	0	1	0	0	0
CORTEX LIPOIDAL DEGENERATION MULTIFOCAL UNILATERAL	3	0	2	0	2	0	2	0	1	0
ECTASIA MULTIFOCAL BILATERAL	0	0	0	0	0	0	1	0	0	0
MESOTHELIOMA BILATERAL	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA BILATERAL	0	1	6	7	3	8	2	1	4	5
MONONUCLEAR CELL LEUKEMIA UNILATERAL	0	1	0	0	0	0	0	1	0	0
PHEOCHROMOCYTOMA	0	0	0	0	0	0	1	0	0	0
PHEOCHROMOCYTOMA BILATERAL	0	1	0	0	0	2	0	0	0	0
PHEOCHROMOCYTOMA UNILATERAL	0	3	1	0	2	3	1	2	0	2
PANCREATIC ISLET	[31]	[36]	[38]	[31]	[24]	[29]	[31]	[33]	[27]	[31]

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
ISLET CELL ADENOMA	3	1	2	1	0	2	1	2	0	2
ISLET CELL CARCINOMA	0	2	0	1	0	2	0	4	0	1
PARATHYROID GLAND	[26]	[29]	[28]	[24]	[16]	[26]	[29]	[29]	[25]	[23]
ADENOMA UNILATERAL	0	0	0	0	0	1	0	0	0	0
PITUITARY GLAND	[31]	[36]	[37]	[31]	[22]	[29]	[31]	[32]	[27]	[31]
ADENOMA	13	11	18	13	15	8	14	6	13	4
CYST FOCAL	0	4	0	0	0	0	0	0	0	0
HEMATOCYST FOCAL	0	0	0	0	0	0	0	1	0	0
HEMATOCYST MULTIFOCAL	0	0	0	0	0	0	1	0	0	0
HEMORRHAGE CHRONIC MULTIFOCAL	0	0	1	0	0	0	0	0	0	0
INFARCT SUBACUTE FOCAL	0	1	0	0	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	1	3	2	0	3	2	0	4	3
PARS DISTALIS ADENOMA FOCAL	0	1	0	0	0	0	0	0	0	1
PARS DISTALIS CYST	0	0	0	0	0	0	0	1	0	0
PARS DISTALIS CYST FOCAL	0	0	1	3	1	3	0	2	2	3
PARS DISTALIS CYST MULTIFOCAL	1	0	0	0	0	1	0	0	0	0
PARS DISTALIS CYST MULTILOCULATED	0	0	0	0	0	0	0	1	0	0
PARS DISTALIS HEMATOCYST MULTIFOCAL	0	0	0	0	0	0	0	0	2	0
PARS DISTALIS HEMORRHAGE ACUTE FOCAL	0	0	0	0	0	0	0	0	0	1
PARS DISTALIS HEMORRHAGE CHRONIC MULTIFOCAL	0	0	0	0	1	0	0	0	0	0
PARS DISTALIS HEMORRHAGE SUBACUTE MULTIFOCAL	0	0	1	0	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
PARS DISTALIS LIPIDOSIS FOCAL	0	0	0	0	1	0	0	0	0	0
PARS INTERMEDIA ADENOMA	1	0	0	0	0	0	0	0	0	0
PARS INTERMEDIA HYPERPLASIA EPITHELIAL FOCAL	1	0	0	0	0	0	0	0	0	0
PARS NERVOSA ANGIECTASIS MULTIFOCAL	0	0	0	0	0	0	0	1	0	0
THYROID GLAND	[31]	[36]	[37]	[31]	[24]	[30]	[31]	[33]	[27]	[31]
C CELL ADENOMA FOCAL UNILATERAL	0	0	1	4	0	0	0	0	0	0
C CELL CARCINOMA	0	0	1	0	0	1	0	0	0	0
C CELL CARCINOMA BILATERAL	0	0	0	0	0	0	0	1	0	0
C CELL CARCINOMA UNILATERAL	1	2	0	1	0	3	1	2	1	2
C CELL HYPERPLASIA FOCAL	0	0	0	0	0	0	0	0	1	0
C CELL HYPERPLASIA FOCAL UNILATERAL	3	7	2	2	0	4	5	6	1	7
C CELL HYPERPLASIA MULTIFOCAL BILATERAL	0	0	0	0	0	0	3	0	2	0
C CELL HYPERPLASIA MULTIFOCAL UNILATERAL	1	1	0	0	1	1	1	1	1	1
FOLLICLE ADENOMA FOCAL UNILATERAL	0	0	0	1	0	0	0	0	0	0
FOLLICLE CYST MULTILOCULATED UNILATERAL	0	0	0	0	0	1	0	0	0	0
FOLLICLE ECTASIA FOCAL	0	0	0	0	0	0	0	1	0	0
FOLLICLE ECTASIA FOCAL UNILATERAL	0	0	0	0	0	1	1	0	0	1
FOLLICLE ECTASIA MULTIFOCAL BILATERAL	0	0	1	0	0	0	0	0	0	0
FOLLICLE ECTASIA MULTIFOCAL UNILATERAL	0	1	1	1	0	0	0	2	0	1
FOLLICLE SQUAMOUS METAPLASIA FOCAL	0	0	1	0	0	0	0	0	1	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		15 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
FOLLICLE SQUAMOUS METAPLASIA FOCAL UNILATERAL	1	0	0	1	0	0	0	0	0	0
FOLLICULAR CELL ADENOMA FOCAL UNILATERAL	0	0	0	2	1	0	0	0	0	1
FOLLICULAR CELL CARCINOMA FOCAL UNILATERAL	0	0	0	0	0	0	0	1	0	0
FOLLICULAR CELL CARCINOMA UNILATERAL	0	0	0	0	0	1	0	0	0	0
FOLLICULAR HYPERPLASIA FOCAL UNILATERAL	0	0	0	0	0	0	0	0	0	1
MONONUCLEAR CELL LEUKEMIA BILATERAL	0	0	0	0	0	1	0	0	0	0
LYMPH NODE	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[0]
LYMPHOID HYPERPLASIA DIFFUSE	0	0	0	1	0	0	0	0	0	0
MACROPHAGE AGGREGATES MULTIFOCAL FIBROUS GLASS	0	0	0	1	0	0	0	0	0	0
LYMPH NODE-MANDIBULAR	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[1]
HEMORRHAGE ACUTE DIFFUSE	0	0	0	0	0	0	0	0	0	1
LYMPHOID HYPERPLASIA DIFFUSE	0	0	0	0	0	0	0	0	0	1
MONONUCLEAR CELL LEUKEMIA	0	0	0	0	0	1	0	0	0	0
LYMPH NODE-MESENTERIC	[21]	[28]	[23]	[21]	[15]	[18]	[27]	[28]	[19]	[20]
HEMORRHAGE ACUTE DIFFUSE	0	0	0	1	0	0	0	0	0	0
HEMOSIDEROSIS DIFFUSE	0	0	0	0	0	0	1	0	0	0
HEMOSIDEROSIS MULTIFOCAL	1	0	0	0	0	0	0	0	0	0
LYMPHOID HYPERPLASIA DIFFUSE	11	10	15	10	8	8	13	11	12	4
LYMPHOID HYPERPLASIA MULTIFOCAL	0	0	0	0	0	0	1	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		.5 MG/M3-3		.5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
MACROPHAGE AGGREGATES MULTIFOCAL FIBROUS GLASS	0	0	0	0	0	0	0	2	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	1	2	2	3	2	1	4	1
LYMPH NODE-SACROLUMBAR	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[0]
LYMPHADENITIS GRANULOMATOUS DIFFUSE	0	0	0	0	0	0	0	1	0	0
LYMPH NODE-SUBMANDIBULAR	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[0]
LYMPHOSARCOMA	0	0	0	0	0	0	0	1	0	0
LYMPH NODE-THORACIC	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[1]	[0]
MONONUCLEAR CELL LEUKEMIA	0	0	0	0	0	0	0	0	1	0
LYMPH NODE-THYMIC	[1]	[1]	[15]	[11]	[15]	[26]	[4]	[3]	[8]	[10]
HEMOSIDEROSIS DIFFUSE	0	0	4	2	0	2	2	2	1	1
HEMOSIDEROSIS MULTIFOCAL	1	1	7	3	1	1	2	1	2	1
LYMPHADENITIS GRANULOMATOUS FOCAL FIBROUS GLASS	0	0	0	0	0	1	0	0	0	0
LYMPHOID HYPERPLASIA DIFFUSE	0	1	9	10	7	12	2	0	6	8
MACROPHAGE AGGREGATES FIBROUS GLASS	0	0	0	0	2	2	0	0	2	0
MACROPHAGE AGGREGATES MULTIFOCAL FIBROUS GLASS	0	0	10	11	13	21	0	2	3	9
MONONUCLEAR CELL LEUKEMIA	0	0	0	1	1	7	0	0	0	0
LYMPH NODE-TRACHEOBRONCHIAL	[31]	[36]	[36]	[32]	[23]	[27]	[31]	[32]	[25]	[30]
FIBROSARCOMA	0	0	0	1	0	0	0	0	0	0
HEMORRHAGE ACUTE DIFFUSE	0	0	0	0	0	0	0	1	0	0
HEMOSIDEROSIS DIFFUSE	15	8	3	4	0	0	9	19	2	10

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
HEMOSIDEROSIS FOCAL	4	1	0	0	0	0	1	0	2	0
HEMOSIDEROSIS MULTIFOCAL	12	20	7	8	2	2	12	14	10	10
LYMPHADENITIS GRANULOMATOUS MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
LYMPHADENITIS GRANULOMATOUS MULTIFOCAL FIBROUS GLASS	0	0	0	0	0	0	0	0	1	1
LYMPHOID HYPERPLASIA DIFFUSE	9	12	6	4	4	2	4	3	5	6
MACROPHAGE AGGREGATES FIBROUS GLASS	0	0	4	6	0	0	0	0	0	0
MACROPHAGE AGGREGATES FOCAL FIBROUS GLASS	0	0	0	1	0	2	0	0	0	0
MACROPHAGE AGGREGATES MULTIFOCAL FIBROUS GLASS	0	0	18	13	20	16	4	5	3	3
MONONUCLEAR CELL LEUKEMIA	2	4	2	1	2	8	2	1	4	1
SPLEEN	[31]	[36]	[37]	[32]	[24]	[30]	[31]	[33]	[27]	[31]
CAPSULE MESOTHELIOMA	0	0	0	0	0	0	0	1	0	0
EXTRAMEDULLARY HEMATOPOIESIS DIFFUSE	2	0	0	0	0	0	1	1	1	0
FIBROSIS FOCAL	0	0	0	0	0	1	0	0	0	0
HEMOSIDEROSIS DIFFUSE	24	5	28	23	20	18	26	21	19	21
INFARCT CHRONIC FOCAL	0	0	0	0	0	0	0	1	0	0
MESOTHELIOMA	0	0	0	0	0	0	0	0	1	0
MONONUCLEAR CELL LEUKEMIA	1	7	10	11	5	12	6	8	8	8
THYMUS	[0]	[0]	[2]	[0]	[0]	[0]	[0]	[0]	[1]	[0]
MONONUCLEAR CELL LEUKEMIA	0	0	0	0	0	0	0	0	1	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

PROJECT: G7188-14 STUDY: NIOSH SPECIES: RAT

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
MAXILLA	[1]	[1]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[1]
OSTEITIS PYOGRANULOMATOUS FOCAL HAIR SHAFT	0	0	0	0	0	0	0	0	0	1
OSTEITIS SUBACUTE MULTIFOCAL UNILATERAL	1	1	0	0	0	0	0	0	0	0
MUSCLE-SKELETAL	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[1]	[0]	[0]
FIBROSARCOMA	0	0	0	1	0	0	0	0	0	0
BRAIN	[31]	[36]	[38]	[32]	[24]	[30]	[31]	[33]	[27]	[31]
CEREBELLUM MONONUCLEAR CELL LEUKEMIA	0	2	4	5	0	5	1	0	2	1
CEREBRUM ASTROCYTOMA FIBROUS TYPE	1	0	0	0	0	0	0	0	0	0
CEREBRUM LATERAL VENTRICLES HYDROCEPHALUS BILATERAL	4	0	7	3	5	5	5	2	4	1
CEREBRUM MINERALIZATION DYSTROPHIC FOCAL	0	0	1	0	0	0	0	0	0	0
CEREBRUM MONONUCLEAR CELL LEUKEMIA	0	2	4	5	1	5	1	0	3	1
CEREBRUM PERIVASCULITIS GRANULOMATOUS FOCAL	1	0	0	0	0	0	0	0	0	0
CHOROID PLEXUS MINERALIZATION DYSTROPHIC FOCAL	0	0	0	0	0	0	1	0	0	0
MEDULLA COMPRESSION PITUITARY ADENOMA	0	0	1	0	0	0	0	0	0	0
MEDULLA HEMORRHAGE ACUTE FOCAL	1	0	1	0	0	0	0	0	0	0
MEDULLA HEMORRHAGE ACUTE FOCAL PITUITARY ADENOMA	0	0	0	0	0	0	0	0	1	0
MEDULLA MONONUCLEAR CELL LEUKEMIA	0	2	4	4	0	4	1	0	1	1
MEDULLA PITUITARY ADENOMA	0	0	1	0	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
MIDBRAIN ASTROCYTOMA FIBROUS TYPE	1	0	0	0	0	0	0	0	0	0
MIDBRAIN COMPRESSION PITUITARY ADENOMA	0	0	1	0	0	2	1	0	0	0
MIDBRAIN HEMORRHAGE ACUTE FOCAL	0	0	0	0	0	0	0	1	0	0
MIDBRAIN MONONUCLEAR CELL LEUKEMIA	0	2	3	5	1	5	1	0	3	1
MIDBRAIN PITUITARY ADENOMA FOCAL	1	0	0	0	1	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	2	0	0	0	0	0	0	0
EYE	[31]	[36]	[38]	[31]	[24]	[30]	[31]	[32]	[27]	[31]
CORNEA KERATITIS ACUTE DIFFUSE UNILATERAL	0	0	0	0	2	0	0	0	0	0
LENS CATARACTOUS CHANGE DIFFUSE UNILATERAL	0	0	0	0	0	0	0	1	0	0
LENS CATARACTOUS CHANGE FOCAL UNILATERAL	0	0	0	0	0	0	0	1	0	0
LENS CATARACTOUS CHANGE MULTIFOCAL	1	0	0	0	0	0	0	0	0	1
LENS CATARACTOUS CHANGE MULTIFOCAL BILATERAL	0	0	0	1	1	0	0	0	0	0
LENS CATARACTOUS CHANGE MULTIFOCAL UNILATERAL	0	0	0	1	0	2	2	0	1	0
LENS CATARACTOUS CHARGE MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
MICROPHTHALMIA UNILATERAL	0	0	0	0	1	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA BILATERAL	0	0	1	1	0	0	0	0	0	0
RETINA DEGENERATION DIFFUSE	1	0	0	0	0	0	0	0	1	0
RETINA DEGENERATION DIFFUSE BILATERAL	0	0	0	0	2	0	0	0	0	0
RETINA DEGENERATION DIFFUSE UNILATERAL	0	0	0	1	0	2	1	2	0	1

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
RETINA DEGENERATION SEGMENTAL UNILATERAL	0	0	1	0	0	0	0	0	0	0
SYNECHIA BILATERAL	0	0	0	0	0	0	0	1	0	0
HARDERIAN GLAND	[23]	[26]	[27]	[13]	[12]	[9]	[23]	[21]	[22]	[21]
ADENITIS GRANULOMATOUS FOCAL UNILATERAL	3	0	3	1	0	1	1	0	0	1
ADENITIS GRANULOMATOUS MULTIFOCAL BILATERAL	1	0	3	0	1	1	0	0	0	0
ADENITIS GRANULOMATOUS MULTIFOCAL UNILATERAL	0	0	1	0	1	0	0	0	0	0
ADENITIS LYMPHOCYTIC FOCAL	0	0	0	0	0	0	0	1	0	0
ADENITIS LYMPHOCYTIC FOCAL BILATERAL	0	0	0	0	0	0	0	0	0	1
ADENITIS LYMPHOCYTIC FOCAL UNILATERAL	0	6	1	0	0	1	1	1	0	2
ADENITIS LYMPHOCYTIC MULTIFOCAL	0	1	0	0	0	0	0	0	0	1
ADENITIS LYMPHOCYTIC MULTIFOCAL BILATERAL	12	10	10	5	8	6	10	6	16	9
ADENITIS LYMPHOCYTIC MULTIFOCAL UNILATERAL	8	5	9	6	2	1	8	6	5	8
MONONUCLEAR CELL LEUKEMIA BILATERAL	0	0	0	0	0	0	0	0	1	0
CERVIX	[0]	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[1]	[0]
CERVICITIS ACUTE MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
EPIDIDYMIS	[0]	[35]	[0]	[31]	[0]	[27]	[0]	[33]	[0]	[30]
EPIDIDYMITIS SUBACUTE DIFFUSE	0	0	0	0	0	0	0	1	0	0
MESOTHELIOMA	0	1	0	1	0	0	0	2	0	0
MONONUCLEAR CELL LEUKEMIA	0	1	0	0	0	0	0	0	0	2

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
SPERM GRANULOMA FOCAL	0	0	0	0	0	0	0	1	0	0
TUBULAR EPITHELIUM MINERALIZATION DYSTROPHIC MULTIFOCAL	0	4	0	1	0	1	0	0	0	2
EPIDIYMIS	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[0]	[0]	[0]
EPIDYMIS	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[0]	[1]
OVARY	[31]	[0]	[38]	[0]	[24]	[0]	[31]	[0]	[27]	[0]
CYST FOCAL UNILATERAL	0	0	1	0	1	0	3	0	2	0
MONONUCLEAR CELL LEUKEMIA BILATERAL	0	0	3	0	0	0	1	0	2	0
MONONUCLEAR CELL LEUKEMIA UNILATERAL	0	3	1	0	0	0	0	0	0	0
OOPHORITIS SUPPURATIVE DIFFUSE	0	0	0	0	0	0	1	0	0	0
OVARIAN STROMA CYST MULTILOCULATED	0	0	0	0	0	0	0	0	1	0
PROSTATE GLAND	[0]	[36]	[0]	[32]	[0]	[30]	[0]	[33]	[0]	[31]
ACINI EPITHELIAL HYPERPLASIA MULTIFOCAL	0	0	0	2	0	1	0	1	0	4
ADENOMA FOCAL	0	2	0	0	0	0	0	0	0	0
MESOTHELIOMA	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	0	1	0	1	0	0	0	1
PROSTATITIS ACUTE MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
PROSTATITIS LYMPHOCYTIC MULTIFOCAL DIFFUSE	0	1	0	0	0	0	0	0	0	0
PROSTATITIS SUBACUTE DIFFUSE	0	0	0	1	0	0	0	0	0	0
PROSTATITIS SUBACUTE FOCAL	0	0	0	1	0	0	0	0	0	0
PROSTATITIS SUBACUTE MULTIFOCAL	0	0	0	0	0	0	0	2	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
PROSTATITIS SUPPURATIVE DIFFUSE	0	0	0	1	0	5	0	0	0	0
PROSTATITIS SUPPURATIVE FOCAL	0	0	0	1	0	0	0	1	0	0
PROSTATITIS SUPPURATIVE MULTIFOCAL	0	20	0	17	0	10	0	22	0	18
SEMINAL VESICLE	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[1]	[0]	[3]
ATROPHY DIFFUSE	0	0	0	0	0	0	0	0	0	1
ECTASIA MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
SEMINAL VESICULITIS SUBACUTE DIFFUSE	0	0	0	0	0	0	0	0	0	1
TESTIS*	[0]	[36]	[0]	[32]	[0]	[30]	[0]	[33]	[0]	[31]
HEMATOCYST MULTIFOCAL	0	1	0	0	0	0	0	0	0	0
INTERSTITIAL CELL HYPERPLASIA MULTIFOCAL	0	2	0	3	0	5	0	4	0	3
INTERSTITIAL CELL TUMOR	0	0	0	0	0	0	0	1	0	0
INTERSTITIAL CELL TUMOR DIFFUSE	0	17	0	26	0	27	0	16	0	20
INTERSTITIAL CELL TUMOR FOCAL	0	3	0	0	0	2	0	3	0	2
INTERSTITIAL CELL TUMOR MULTIFOCAL	0	23	0	9	0	3	0	18	0	10
MESOTHELIOMA	0	1	0	1	0	0	0	1	0	0
SEMINIFEROUS TUBULES DEGENERATION ACUTE	0	0	0	1	0	0	0	0	0	0
SEMINIFEROUS TUBULES DEGENERATION AND INTERSTITIAL CELL TUMOR	0	1	0	0	0	0	0	0	0	0
SEMINIFEROUS TUBULES DEGENERATION DIFFUSE	0	33	0	30	0	28	0	32	0	29
SEMINIFEROUS TUBULES DEGENERATION MULTIFOCAL	0	3	0	1	0	2	0	1	0	2

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

* Total number of interstitial cell tumors may exceed the number of animals examined because the tumor in both the right and left testis may have had different distribution patterns (focal, multifocal, and diffuse).

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
UTERUS	[31]	[0]	[38]	[0]	[24]	[0]	[31]	[0]	[27]	[0]
ADENOCARCINOMA	1	0	3	0	1	0	0	0	1	0
ENDOMETRIAL GLANDS CYSTIC HYPERPLASIA FOCAL	0	0	0	0	0	0	1	0	0	0
ENDOMETRIAL GLANDS CYSTIC HYPERPLASIA MULTIFOCAL	2	0	1	0	1	0	2	0	3	0
ENDOMETRIAL GLANDS ECTASIA FOCAL	0	0	0	0	1	0	0	0	1	0
ENDOMETRIAL GLANDS ECTASIA MULTIFOCAL	1	0	1	0	1	0	0	0	1	0
ENDOMETRIAL GLANDS HYPERPLASIA MULTIF OCAL	0	0	2	0	0	0	0	0	0	0
ENDOMETRIAL STROMAL POLYP	2	0	2	0	3	0	3	0	5	0
ENDOMETRIUM ENDOMETRITIS ACUTE MULTIF OCAL	0	0	0	0	0	0	1	0	2	0
ENDOMETRIUM ENDOMETRITIS PURULENT MUL TIFOCAL	1	0	0	0	0	0	0	0	0	0
HEMATOCYST FOCAL	1	0	0	0	0	0	0	0	0	0
METRITIS ACUTE MULTIFOCAL	0	0	0	0	1	0	0	0	0	0
METRITIS SUPPURATIVE MULTIFOCAL	1	0	1	0	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	5	0	0	0	2	0	4	0
MUCOSA HYPERPLASIA MULTIFOCAL	1	0	0	0	0	0	0	0	0	0
PYOMETRA SUPPURATIVE DIFFUSE	0	0	0	0	1	0	0	0	0	0
UTERINE HORN ECTASIA	0	0	0	0	0	0	0	0	1	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

PROJECT: G7188-14 STUDY: NIOSH SPECIES: RAT

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
LARYNX	[31]	[36]	[37]	[31]	[23]	[29]	[27]	[33]	[27]	[31]
LAMINA PROPRIA MACROPHAGE AGGREGATES FOCAL FIBROUS GLASS	0	0	0	0	0	0	0	1	0	0
LARYNGITIS ACUTE FOCAL	0	1	0	0	0	0	0	2	1	1
LARYNGITIS ACUTE MULTIFOCAL	1	3	0	0	0	0	0	1	0	0
LARYNGITIS GRANULOMATOUS FOCAL	0	1	0	0	0	0	0	1	0	0
LARYNGITIS SUBACUTE FOCAL	1	0	0	0	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	1	1	0	1	1	0	0	1	0
SUBMUCOSAL GLANDS ADENITIS ACUTE FOCAL	1	0	1	1	0	2	1	1	4	4
SUBMUCOSAL GLANDS ADENITIS ACUTE MULTIFOCAL	2	1	6	5	1	5	2	4	2	5
SUBMUCOSAL GLANDS ADENITIS MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
SUBMUCOSAL GLANDS ADENITIS SUPPURATIVE MULTIFOCAL	0	0	1	0	0	0	0	0	0	0
SUBMUCOSAL GLANDS ECTASIA	0	0	1	0	0	0	0	0	0	0
SUBMUCOSAL GLANDS ECTASIA FOCAL	0	0	2	2	1	0	1	1	1	2
SUBMUCOSAL GLANDS ECTASIA MULTIFOCAL	21	12	28	22	14	21	18	19	16	24
LUNG	[31]	[36]	[38]	[32]	[24]	[30]	[31]	[33]	[27]	[31]
ALVEOLAR BRONCHIOLAR ADENOCARCINOMA FOCAL	0	0	0	0	0	1	0	2	0	1
ALVEOLAR BRONCHIOLAR ADENOMA FOCAL	0	0	1	0	0	0	1	1	0	0
BONE METAPLASTIC FOCAL	0	0	0	1	0	0	0	0	0	0
BRONCHOGENIC CARCINOMA	0	0	0	0	0	1	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
FIBROSARCOMA MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
FIBROSIS FOCAL	1	1	0	0	0	0	1	0	0	0
FIBROSIS INTERSTITIAL MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
FIBROSIS SUBPLEURAL AND INTRA-ALVEOLAR FOCAL FIBROUS GLASS	0	0	1	0	0	0	0	0	0	0
HISTIOCYTOSIS MULTIFOCAL	2	0	0	0	0	0	0	0	0	0
LYMPHOID AGGREGATE FOCAL	0	0	0	0	0	0	0	1	0	0
MACROPHAGE AGGREGATES FOCAL	0	0	0	0	0	0	0	0	0	1
MACROPHAGE AGGREGATES FOCAL FIBROUS GLASS	0	0	0	0	0	0	2	0	0	0
MACROPHAGE AGGREGATES MULTIFOCAL	0	0	0	0	2	0	1	0	0	0
MACROPHAGE AGGREGATES MULTIFOCAL FIBROUS GLASS	0	0	38	32	23	29	18	24	27	30
MONONUCLEAR CELL LEUKEMIA	2	7	9	8	5	11	3	3	6	4
OSTEOSARCOMA MULTIFOCAL	0	0	0	0	0	1	0	0	0	0
PLEURA FIBROSIS FOCAL	0	1	0	0	1	0	2	0	0	2
PLEURA FIBROSIS MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
PLEURA PLEURITIS GRANULOMATOUS FIBROUS GLASS	0	0	1	0	0	0	0	0	0	0
PLEURA PLEURITIS GRANULOMATOUS FOCAL FIBROUS GLASS	0	0	3	1	3	2	0	0	0	2
PLEURA PLEURITIS GRANULOMATOUS MULTIFOCAL	0	0	1	2	0	0	0	0	0	0
PLEURA PLEURITIS GRANULOMATOUS MULTIFOCAL FIBROUS GLASS	0	0	30	24	23	29	0	0	3	6

( ) = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
PNEUMONIA GRANULOMATOUS FIBROUS GLASS	0	0	0	1	0	0	0	0	0	0
PNEUMONIA GRANULOMATOUS FOCAL	0	2	0	0	0	0	0	0	0	0
PNEUMONIA GRANULOMATOUS FOCAL FIBROUS GLASS	0	0	1	0	0	0	3	5	0	2
PNEUMONIA GRANULOMATOUS MULTIFOCAL	0	0	2	0	1	1	1	0	0	0
PNEUMONIA GRANULOMATOUS MULTIFOCAL FIBROUS GLASS	0	0	34	31	24	30	6	8	20	24
PNEUMONIA HISTIOCYTIC FOCAL	1	0	0	0	0	0	0	0	0	0
PNEUMONIA INTERSTITIAL MULTIFOCAL	0	0	0	1	0	0	0	0	0	0
PNEUMONIA SUBACUTE FOCAL	1	1	0	0	0	0	0	0	0	1
PNEUMONIA SUBACUTE FOCAL FIBROUS GLASS	0	0	1	0	0	0	0	0	0	0
PNEUMONIA SUBACUTE MULTIFOCAL	1	0	0	0	0	0	0	0	0	0
PNEUMONITIS FOCAL SUBACUTE	0	1	0	0	0	0	0	0	0	0
PNEUMONITIS MULTIFOCAL	0	0	0	0	0	0	0	1	1	0
PNEUMONITIS SUBACUTE FOCAL	3	0	0	0	0	0	3	1	0	0
PNEUMONITIS SUBACUTE MULTIFOCAL	0	1	0	0	0	0	2	5	0	0
NASAL PASSAGE	[31]	[36]	[38]	[30]	[24]	[30]	[31]	[33]	[27]	[31]
ADENITIS ACUTE MULTIFOCAL	0	1	0	0	1	0	0	0	0	0
EPITHELIUM DYSPLASIA MULTIFOCAL	1	0	2	0	0	1	3	0	0	1
EPITHELIUM RHINITIS ACUTE FOCAL FOREIGN OBJECT POSSIBLY PLANT DEBRIS	0	0	0	1	0	0	0	0	0	0
EPITHELIUM RHINITIS ACUTE MULTIFOCAL	1	0	3	1	1	1	1	0	0	1
EPITHELIUM RHINITIS SUPPURATIVE FOCAL	0	0	0	1	1	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
EPITHELIUM SQUAMOUS METAPLASIA FOCAL	0	0	0	0	0	0	0	0	0	1
EPITHELIUM SQUAMOUS METAPLASIA MULTIFOCAL	0	0	1	0	0	0	0	0	0	0
GINGIVA GINGIVITIS CHRONIC ACTIVE MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
GINGIVA HYPERPLASIA FOCAL	0	0	0	0	0	0	0	1	0	0
LAMINA PROPRIA MINERALIZATION DYSTROPHIC FOCAL	1	0	0	0	0	0	1	0	0	0
LAMINA PROPRIA MINERALIZATION DYSTROPHIC MULTIFOCAL	10	24	26	24	15	24	11	18	23	27
LAMINA PROPRIA RHINITIS SUBACUTE FOCAL	0	0	0	0	0	1	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	1	7	6	1	8	2	1	7	2
NASAL TURBINATE MONONUCLEAR CELL LEUKEMIA	0	1	0	0	0	0	0	0	0	0
NASOLACRIMAL DUCT DACRYOSOLENITIS ACUTE DIFFUSE UNILATERAL	0	0	2	0	2	3	0	0	3	0
NASOLACRIMAL DUCT DACRYOSOLENITIS ACUTE MULTIFOCAL	0	0	0	0	0	0	1	0	0	0
NASOLACRIMAL DUCT DACRYOSOLENITIS ACUTE MULTIFOCAL BILATERAL	0	0	0	0	2	0	0	0	0	0
NASOLACRIMAL DUCT DACRYOSOLENITIS ACUTE MULTIFOCAL UNILATERAL	3	1	5	0	1	1	3	3	4	2
NASOLACRIMAL DUCT DACRYOSOLENITIS MULTIFOCAL UNILATERAL	0	0	0	0	0	0	0	0	0	1
NASOLACRIMAL DUCT DACRYOSOLENITIS SUB ACUTE DIFFUSE UNILATERAL	1	0	0	0	0	0	0	0	0	0
NASOLACRIMAL DUCT EPITHELIUM SQUAMOUS METAPLASIA MULTIFOCAL UNILATERAL	0	0	1	0	0	0	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
RHINITIS ACUTE FOCAL	0	0	0	1	0	0	0	0	0	0
RHINITIS ACUTE MULTIFOCAL	0	0	0	0	1	0	0	0	0	0
RHINITIS LYMPHOCYTIC MULTIFOCAL BILATERAL	0	0	0	0	0	0	0	0	0	1
RHINITIS PURULENT FOCAL	1	0	0	0	0	0	0	0	0	0
RHINITIS PURULENT MULTIFOCAL	0	0	0	0	1	0	1	0	0	0
RHINITIS PURULENT MULTIFOCAL MINERALIZED DEBRIS	0	0	0	0	0	0	1	0	0	0
RHINITIS SEROPURULENT MULTIFOCAL	1	0	1	0	0	0	1	0	0	1
RHINITIS SUPPURATIVE FOCAL	0	0	2	1	2	1	0	0	0	1
RHINITIS SUPPURATIVE FOCAL FOREIGN OBJECT POSSIBLY HAIR	0	0	0	0	0	1	0	0	0	0
RHINITIS SUPPURATIVE MULTIFOCAL	0	0	4	0	0	2	1	0	0	1
RHINITIS SUPPURATIVE MULTIFOCAL HAIR SHAFTS	0	0	0	0	0	1	0	0	0	0
SUBMUCOSAL GLANDS ADENITIS ACUTE	0	0	0	0	0	0	0	0	0	1
SUBMUCOSAL GLANDS ADENITIS ACUTE FOCAL	0	0	0	0	0	0	2	0	0	0
SUBMUCOSAL GLANDS ADENITIS ACUTE MULTIFOCAL	18	28	25	27	16	23	24	33	16	26
SUBMUCOSAL GLANDS ADENITIS MULTIFOCAL	0	0	1	0	0	1	0	0	0	0
SUBMUCOSAL GLANDS ECTASIA MULTIFOCAL	0	0	0	1	0	0	0	0	1	0
SUBMUCOSAL GLANDS SQUAMOUS METAPLASIA FOCAL	0	0	1	0	0	0	0	0	0	0
VOMERONASAL ORGAN ADENITIS ACUTE DIFFUSE BILATERAL	0	0	0	0	1	2	0	0	0	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
VOMERONASAL ORGAN ADENITIS ACUTE MULT IFOCAL	5	3	1	1	1	1	0	3	0	1
VOMERONASAL ORGAN ADENITIS ACUTE MULT IFOCAL BILATERAL	24	33	34	28	21	27	28	29	27	30
VOMERONASAL ORGAN ADENITIS ACUTE MULT IFOCAL UNILATERAL	0	0	1	1	0	0	0	0	0	0
VOMERONASAL ORGAN ECTASIA BILATERAL	0	0	0	0	0	0	0	1	0	0
VOMERONASAL ORGAN ECTASIA UNILATERAL	0	0	0	1	0	0	0	0	0	0
VOMERONASAL ORGAN MONONUCLEAR CELL LEUKEMIA	0	0	0	0	1	0	0	0	0	0
PARANASAL SINUS	[31]	[36]	[38]	[30]	[24]	[30]	[31]	[33]	[27]	[31]
TRACHEA	[31]	[36]	[37]	[32]	[24]	[28]	[31]	[33]	[27]	[31]
LYMPHOSARCOMA	0	0	0	0	0	0	0	1	0	0
MONONUCLEAR CELL LEUKEMIA	0	0	0	1	0	1	0	0	2	0
SUBMUCOSAL GLANDS ECTASIA FOCAL	0	0	0	0	0	1	0	0	0	0
SUBMUCOSAL GLANDS ECTASIA MULTIFOCAL	0	0	0	0	0	0	1	0	0	0
TRACHEITIS ACUTE MULTIFOCAL	0	0	0	0	0	0	1	0	1	0

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

PROJECT: G7100-14 STUDY: NIOSH SPECIES: RAT

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
EPIDERMIS	[0]	[0]	[1]	[0]	[0]	[0]	[0]	[0]	[0]	[0]
TAIL KERATIN CYST FOCAL	0	0	1	0	0	0	0	0	0	0
MAMMARY GLAND	[1]	[0]	[5]	[1]	[2]	[3]	[5]	[0]	[2]	[1]
ADENOCARCINOMA	0	0	1	0	0	0	1	0	0	0
FIBROADENOMA	1	0	4	1	2	2	4	0	2	0
MAMMARY DUCT POLYP FOCAL	0	0	0	0	0	1	0	0	0	0
MASTITIS SUBACUTE MULTIFOCAL	0	0	0	0	0	0	0	0	0	1
SKIN	[0]	[2]	[0]	[3]	[0]	[2]	[0]	[5]	[2]	[1]
BASAL CELL CARCINOMA	0	2	0	0	0	2	0	0	0	0
EPIDERMAL INCLUSION CYST FOCAL	0	0	0	1	0	0	0	1	0	1
FIBROMA	0	0	0	0	0	0	0	2	0	0
INGUINAL AREA MONONUCLEAR CELL LEUKEMIA	0	0	0	0	0	0	0	0	1	0
KERATOACANTHOMA FOCAL	0	0	0	1	0	0	0	0	0	0
NOSE DERMIS HEMORRHAGE ACUTE FOCAL	0	0	0	1	0	0	0	0	0	0
SQUAMOUS CELL CARCINOMA	0	0	0	0	0	0	0	0	1	0
KIDNEY	[31]	[36]	[38]	[32]	[24]	[30]	[31]	[33]	[27]	[31]
CHRONIC RENAL DISEASE BILATERAL	0	0	0	1	0	1	0	0	1	2
CHRONIC RENAL DISEASE DIFFUSE	0	0	0	0	0	1	0	1	0	0
CHRONIC RENAL DISEASE DIFFUSE BILATERAL	8	22	22	29	14	26	11	29	13	28
CHRONIC RENAL DISEASE MULTIFOCAL BILATERAL	16	8	12	1	7	2	12	2	7	1

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
CHRONIC RENAL DISEASE MULTIFOCAL UNILATERAL	1	0	1	0	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA BILATERAL	1	3	9	11	4	12	3	7	6	7
NEPHRITIS SUBACUTE MULTIFOCAL BILATERAL	1	0	0	0	0	0	0	0	0	0
RENAL CORTEX CYST MULTILOCULATED UNILATERAL	0	0	0	0	0	0	0	1	0	0
RENAL TUBULAR ADENOMA FOCAL UNILATERAL	0	0	0	1	0	0	0	1	0	0
RENAL TUBULES CORTICOMEDULLARY JUNCTION ECTASIA MULTIFOCAL BILATERAL	3	5	2	1	2	0	3	1	2	0
RENAL TUBULES CORTICOMEDULLARY JUNCTION ECTASIA MULTIFOCAL UNILATERAL	0	0	0	0	0	0	1	0	0	0
RENAL TUBULES ECTASIA MULTIFOCAL BILATERAL	0	1	0	0	0	0	0	0	0	0
RENAL TUBULES REGENERATION MULTIFOCAL BILATERAL	1	2	0	0	0	0	0	0	0	0
URINARY BLADDER	[31]	[36]	[38]	[32]	[24]	[29]	[30]	[32]	[27]	[31]
MESOTHELIOMA	0	0	0	1	0	0	0	0	0	0
MONONUCLEAR CELL LEUKEMIA	0	2	4	9	3	5	2	1	5	3
NEMATODIASIS	1	0	0	0	0	0	0	0	0	0
TRANSITIONAL CELL CARCINOMA	0	0	0	1	0	1	0	0	0	0
TRANSITIONAL EPITHELIUM CYSTITIS ACUTE MULTIFOCAL	0	0	0	0	0	0	0	0	1	0
TRANSITIONAL EPITHELIUM HYPERPLASIA DIFFUSE	0	0	0	0	0	0	0	0	1	0
ORGAN UNKNOWN	[0]	[1]	[1]	[1]	[0]	[0]	[1]	[0]	[0]	[2]

[ ] = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

TABLE 46. (Continued)

GROUP	0 MG/M3		5 MG/M3-3		5 MG/M3-4		15 MG/M3-1		15 MG/M3-2	
SEX	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
NUMBER IN GROUP	31	36	38	32	24	30	31	33	27	31
ORGAN AND DIAGNOSIS										
FIBROADENOMA	0	0	1	0	0	0	0	0	0	0
FIBROMA	0	1	0	0	0	0	1	0	0	2
FIBROSARCOMA	0	0	0	1	0	0	0	0	0	0

( ) = NUMBER OF ORGANS PRESENT AND ADEQUATE FOR EVALUATION

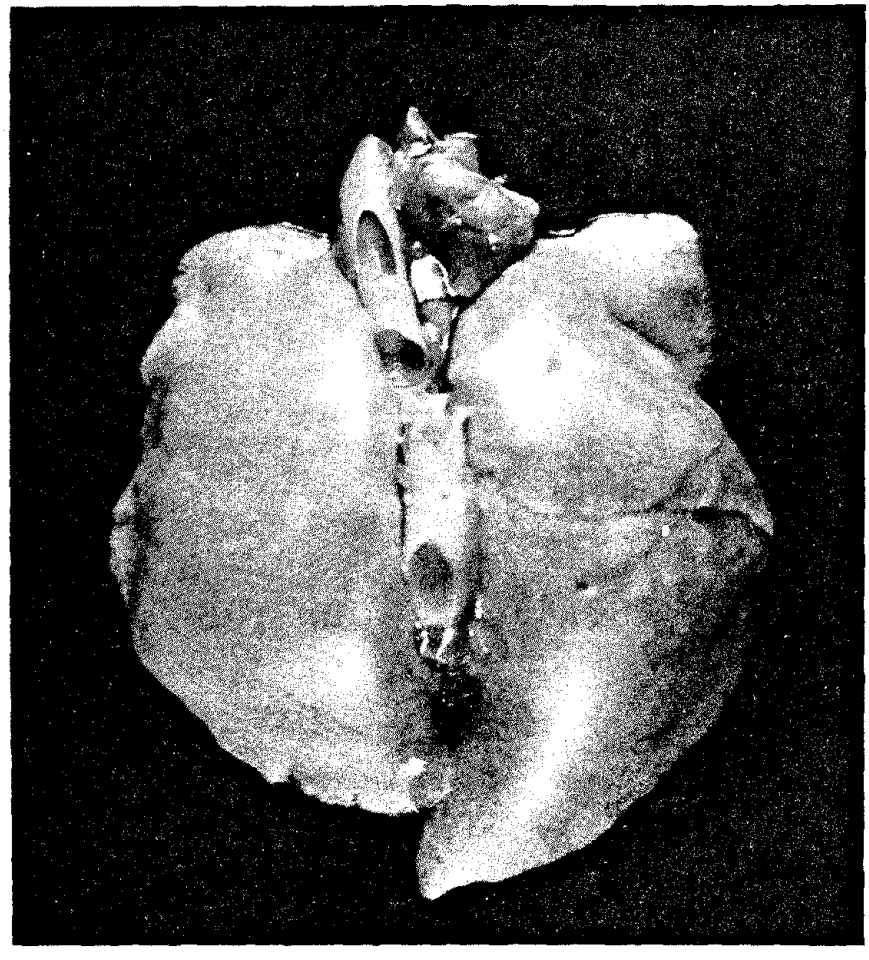


Figure 47. Lung, male rat, control group. Normal left and right lung lobes.

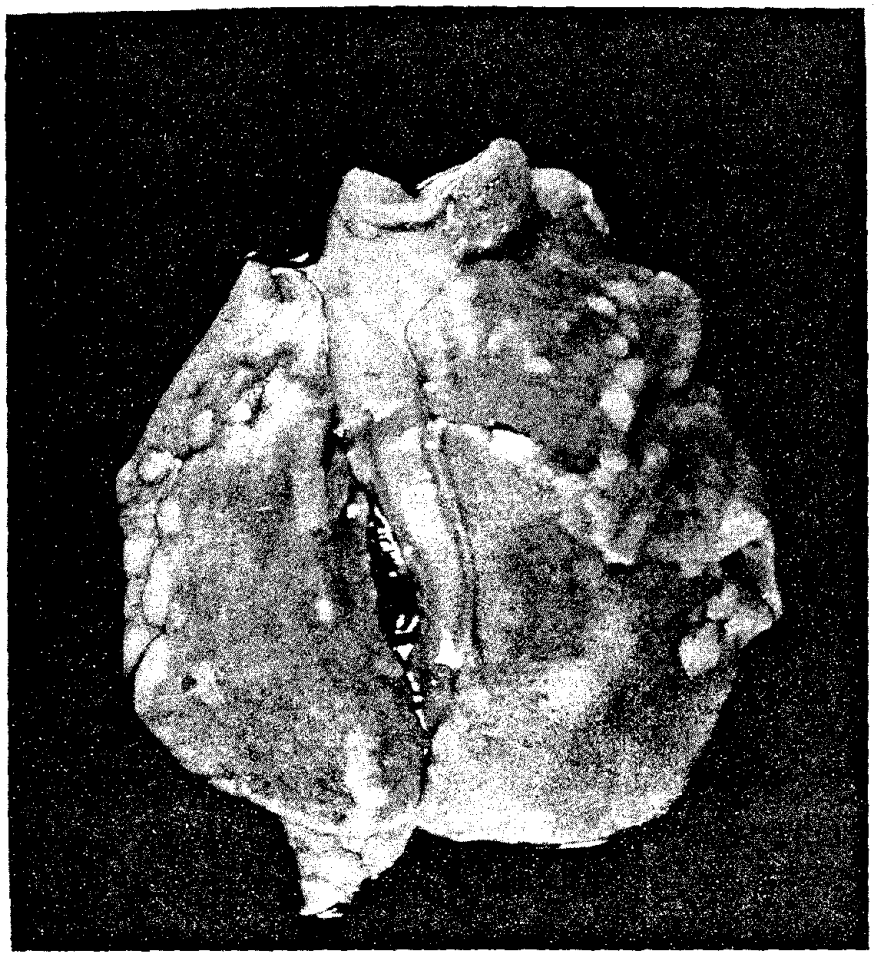


Figure 48. Lung, female rat, F03 group. All lung lobes have multifocal gray to tan, elevated, firm plagues, measuring 1 to 3 millimeters in diameter.

pleural surface that was "granular" in character. The "granular" lesions of the pleura were about equally distributed in all lung lobes in these animals (Figure 49).

There were many additional lesions recorded at necropsy in a variety of organs, all of which were considered to be spontaneous due to their nature, incidence, or severity, or due to a similar incidence between the control group (F05) and those exposed to fibrous glass.

Fibrous glass-induced histomorphologic lesions were primarily limited to the lungs, pleura, and thymic and tracheobronchial lymph nodes in rats from all exposure groups.

The lung lesions consisted of small to large aggregations of macrophages containing various amounts of nonpolarizable needle-shaped fibers (fibrous glass), readily seen under reduced light, and located in peribronchiolar, peribronchial, or perivascular areas as well as within alveoli and in pleural and subpleural locations. In many animals, there was granulomatous inflammation in the lung and pleura that was of minimal to severe intensity (Figures 50 and 51). This inflammatory response consisted of fibrous glass-laden macrophage aggregates that were surrounded by varying numbers of lymphocytes, plasma cells, and, at times, neutrophils (Figure 52). These pulmonary lesions appeared to be more severe and prevalent in the diaphragmatic areas of the lung lobes in the affected rats. The fibrous glass-containing macrophages, in lungs of virtually all rats, occupied less than 5 percent of the total area of the lung sections.

The thymic and tracheobronchial lymph nodes contained small to large aggregations of macrophages containing various amounts of fibrous glass fibers that were usually in the medulla of the lymph node (Figures 53 and 54). Granulomatous inflammation was present in some sections of lymph node in a few rats exposed to fibrous glass.

Although fibrous glass-laden macrophages occurred in pleural and subpleural locations and were present in thymic and tracheobronchial lymph nodes, there was little evidence of translocation of fibrous glass fibers in other organs in the rats in this study. However, two male rats in the F01 group had a few small macrophage aggregates laden with fibrous glass in their mesenteric lymph nodes.

Figure 49. Lung, female rat, F04 group. The pleura has a "granular" surface involving all the lung lobes.

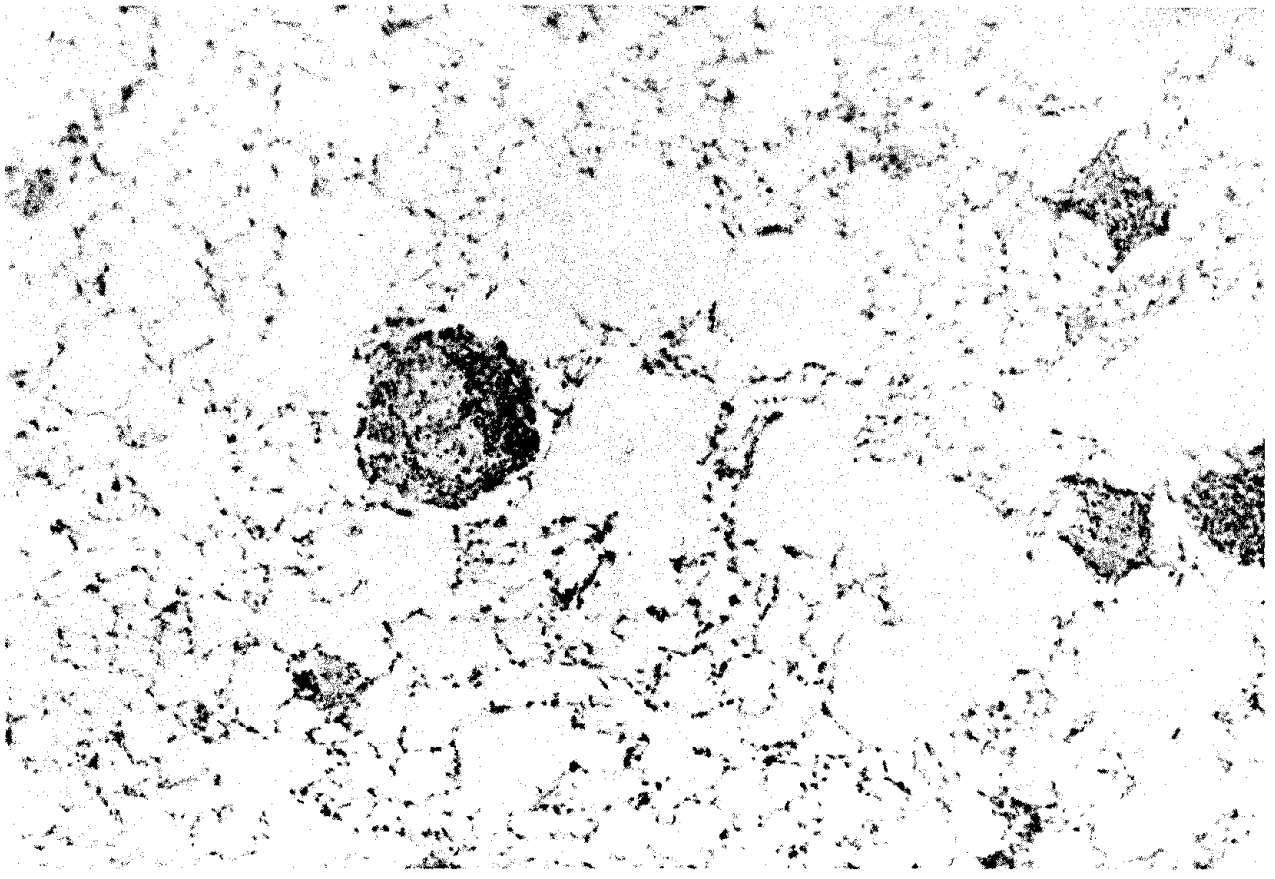


Figure 50. Lung (25X), male rat, F03 group. Many granulomas are present in the alveoli that are mild to moderate in intensity. The macrophages are laden with numerous fibrous glass particles.

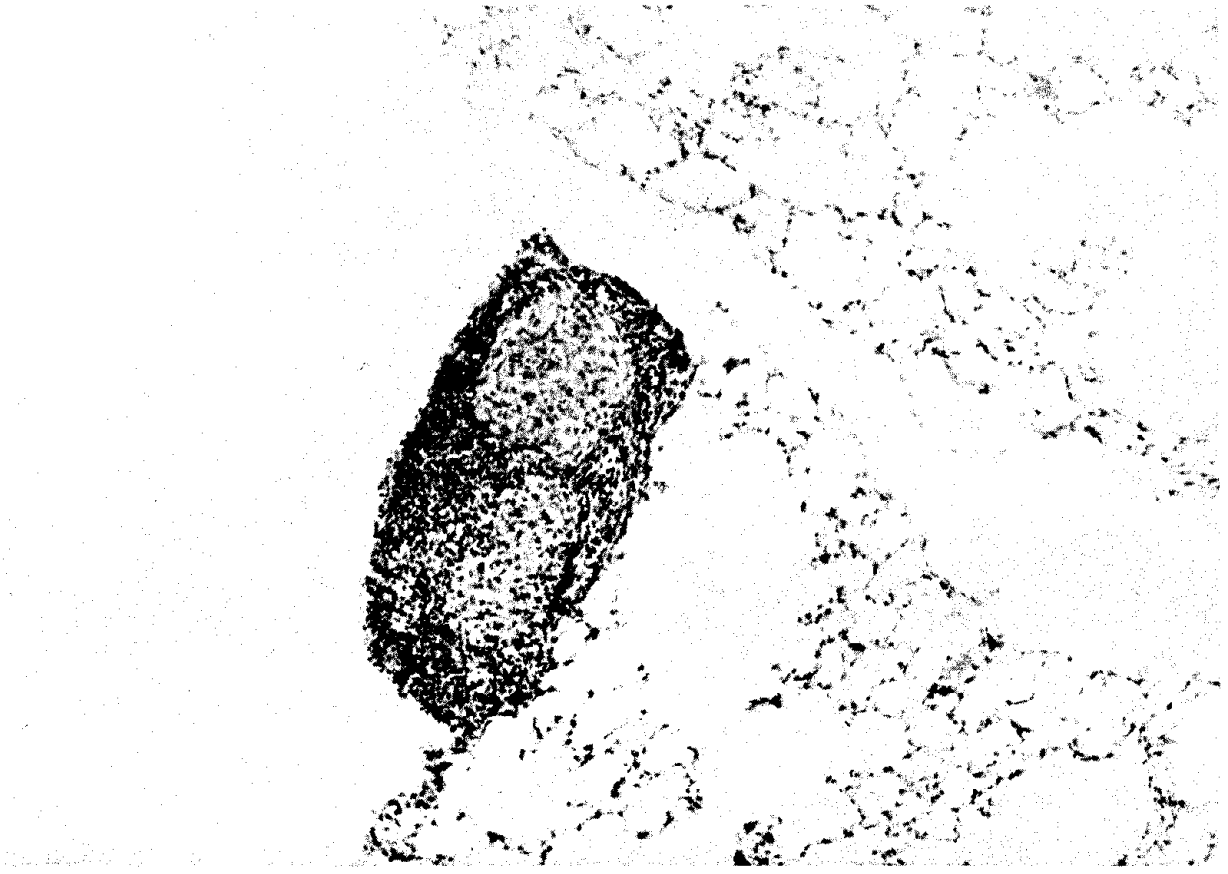


Figure 51. Lung - pleura (25X), male rat, F03 group. A granuloma is present in the pleura that is moderate in intensity. The macrophages are laden with many fibrous glass particles.

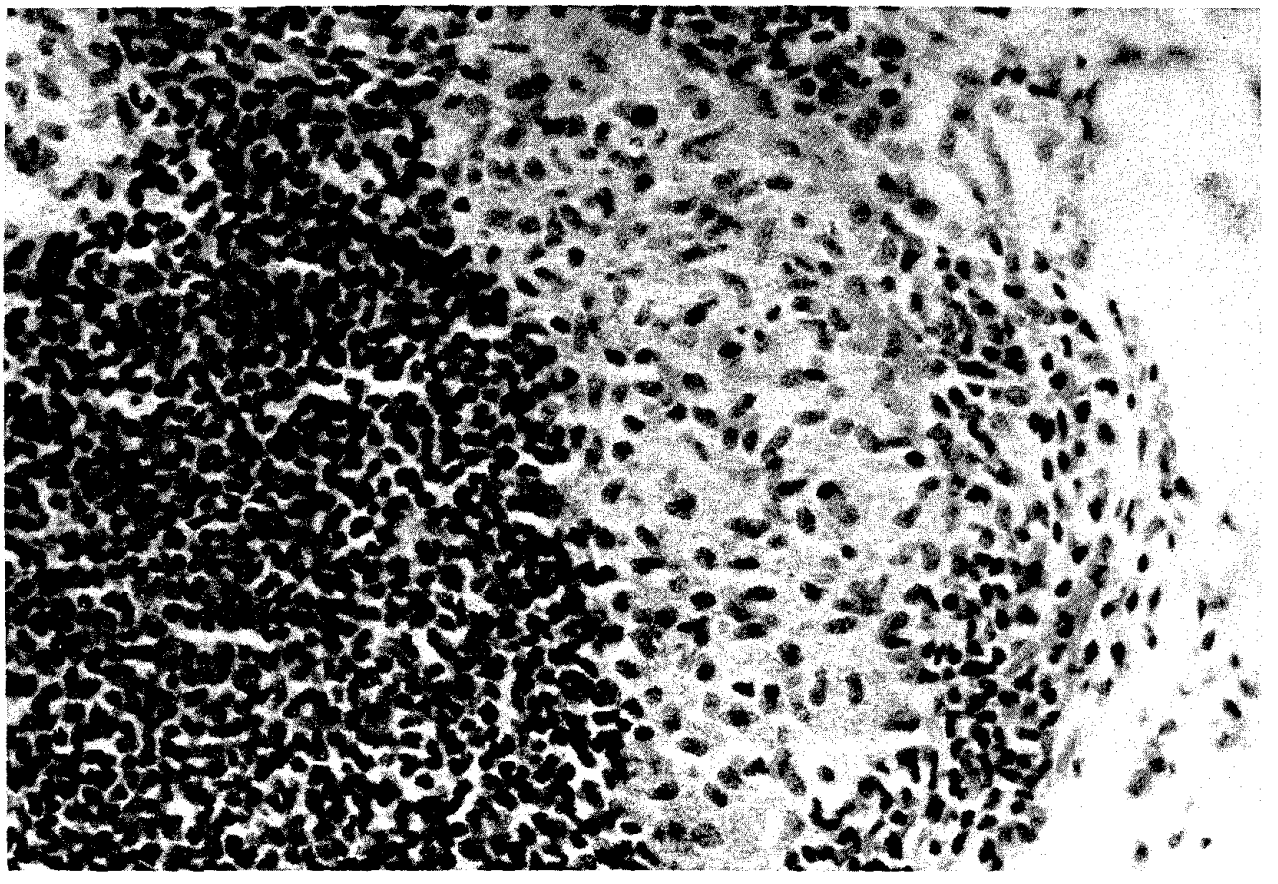


Figure 52. Lung (100X), male rat, F04 group. The granulomas are characterized by fibrous glass - laden macrophage aggregates which are surrounded by varying numbers of lymphocytes, plasma cells, and, at times, neutrophils.

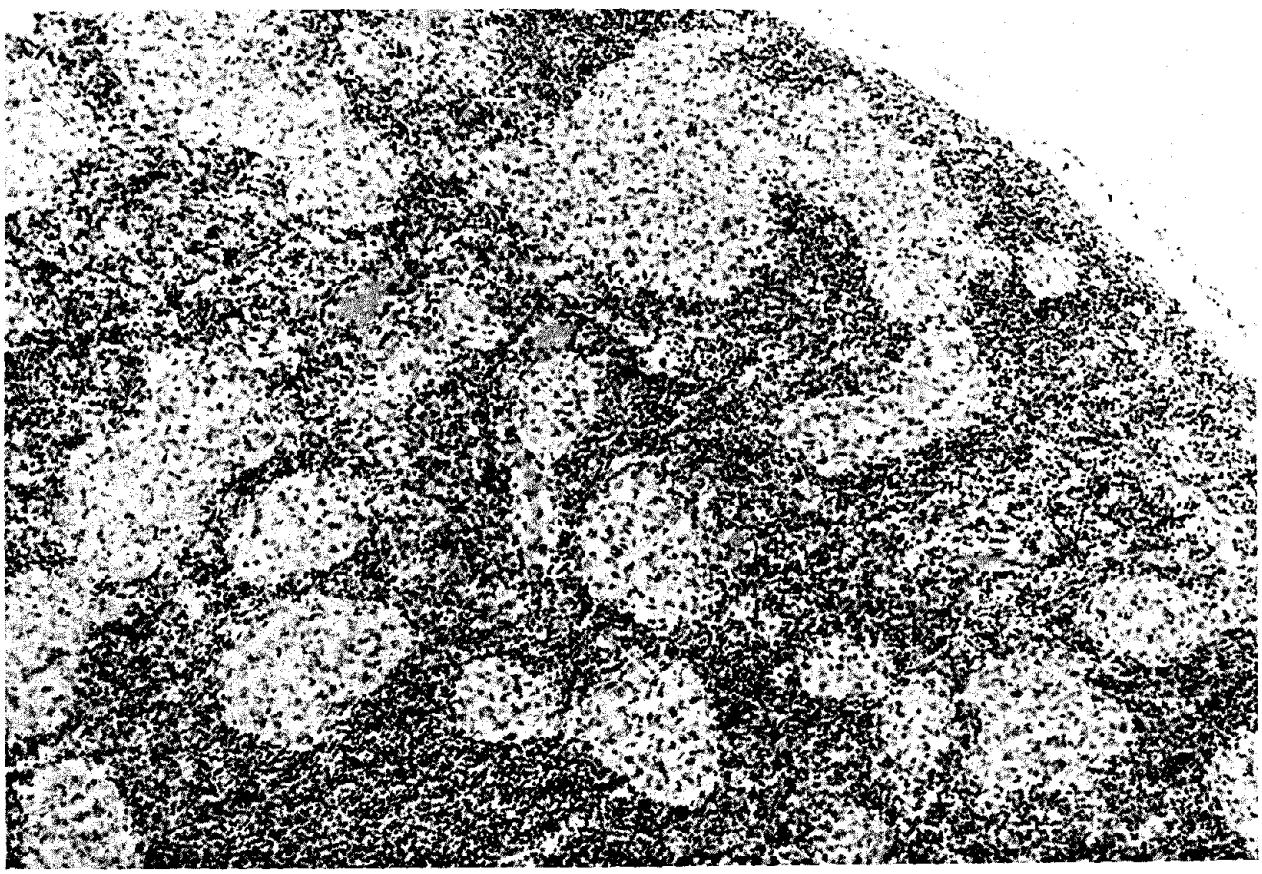


Figure 53. Thymic lymph node (25X), male rat, F04 group. Many small to large macrophage aggregates are present in the medullary area. The macrophages are laden with many fibrous glass particles.

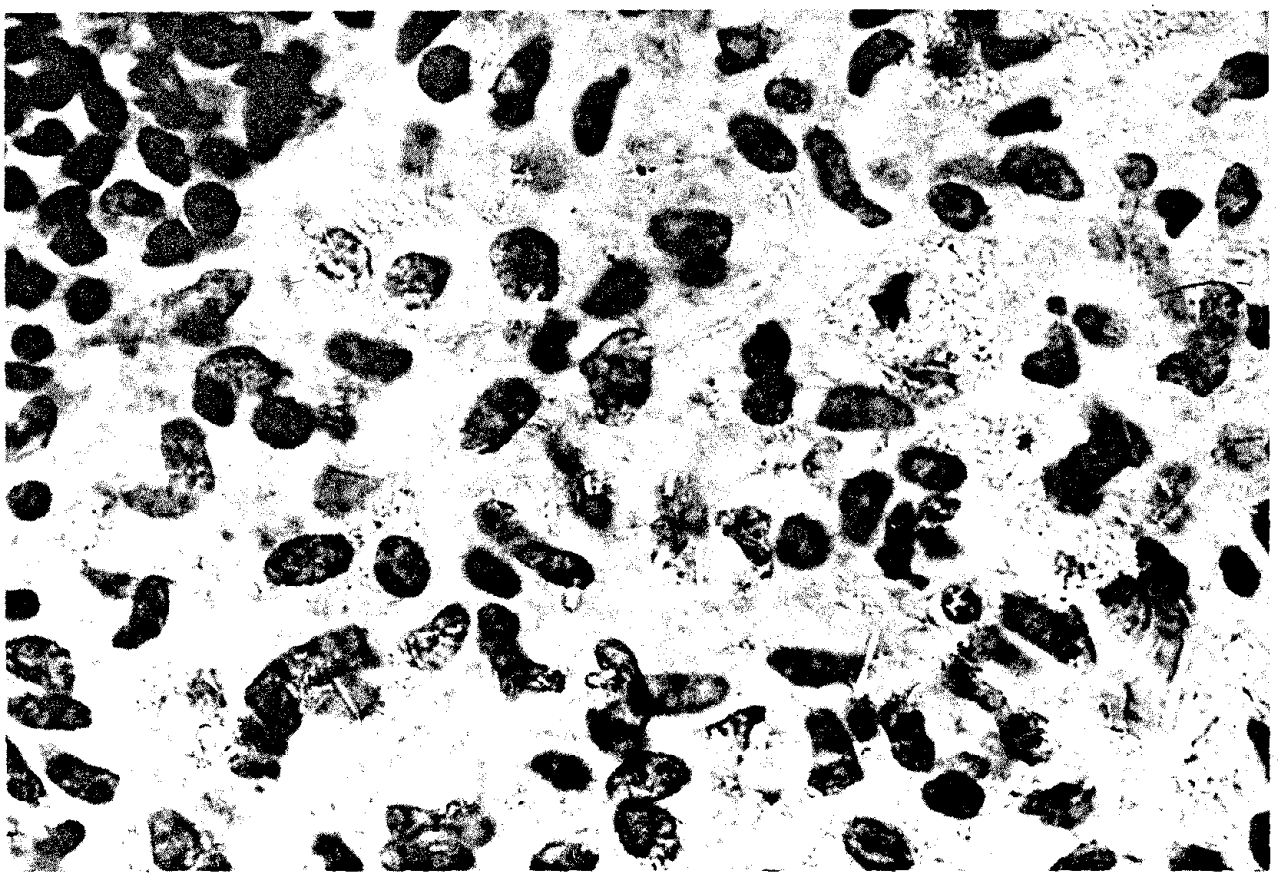


Figure 54. Thymic lymph node (250X - reduced light), male rat, F04 group. Fibrous glass particles are clearly depicted in this macrophage aggregate.

There were rather significant histomorphologic variations in qualitative and quantitative fibrous glass-related changes among the various exposure groups in the lungs and thymic and tracheobronchial lymph nodes. These changes were least pronounced in the F01 group, became progressively more pronounced in the F02 and F03 groups, and were most pronounced in the F04 group. In contrast to this, the gross changes seen in the lung lobes at the time of necropsy were most severe in the F02 group, were somewhat less severe in the F03 group, and were least severe in the F04 group, i.e., in relation to size of the plaque-like lesions of the pleura. The pleural lesions seen microscopically in many of the F04 group animals may have been relatively more significant (more lesions per unit area of pleura) than those seen in the F02 and F03 group animals because there were more lesions per unit area of pleura, i.e., the pleura was "granular" in character in many of the animals at necropsy. Hence a larger number of pleural lesions would be present per microscopic field resulting in a more "severe" lesion designation.

Table 47 depicts the numbers of animals affected per exposure group and qualitative severities of the fibrous glass-induced lesions in the lung and lymph nodes (thymic and tracheobronchial).

Many scheduled sacrifice rats in this study had mononuclear cell leukemia (Fischer rat leukemia) depicted in Table 48. Both the male and the female rats in the F05 (control) group had a lower incidence of mononuclear cell leukemia when compared to the male and female rats in the other test groups. When the males and females, early death and scheduled sacrifice, were considered together and a chi square analysis applied, the difference between the control group (F05) and each of the test groups was significant ($P < 0.05$) (Table 49).

Discussion

The response to fibrous glass inhalation was qualitatively similar in both rats and monkeys, in that the changes induced consisted of macrophage responses to the inhaled fibers. In both species there was translocation of fibers from the lung to draining lymph nodes and, with the exception of two

TABLE 47. NUMBER OF RATS WITH FIBROUS-GLASS INDUCED LESIONS BY EXPOSURE GROUP

Lesion	Severity	Number of Animals							
		Group F01		Group F02		Group F03		Group F04	
		Male	Female	Male	Female	Male	Female	Male	Female
Lymph node-thymic,	Minimal	1	0	1	0				
macrophage aggregates,	Mild	1	0	4	2	2	3	8	3
multifocal	Moderate			4	3	9	7	15	12
	Severe								
	No lesion	31	31	22	22	21	28	7	9
Lymph node-tracheobronchial,	Minimal	3	4			10	6	1	5
macrophage aggregates,	Mild	2	0	3	2	8	14	11	8
multifocal/focal	Moderate			0	1	2	2	6	7
	Severe								
	No lesion	28	27	28	24	12	16	12	4
Lung, macrophage aggregates,	Minimal	23	17	14	18	30	35	23	21
multifocal/focal	Mild	1	3	16	9	2	3	6	2
	Moderate								
	Severe								
	No lesion	9	11	1	0	0	0	1	1
Lung, pneumonia,	Minimal	10	7	19	19	17	28	10	11
granulomatous,	Mild	3	2	6	1	15	7	20	13
multifocal/focal	Moderate			1	0				
	Severe								
	No lesion	20	22	5	7	0	3	0	0
Pleura, pleuritis,	Minimal			5	3	19	27	15	12
granulomatous,	Mild			3	0	6	7	13	9
multifocal/focal	Moderate							1	2
	Severe								
	No lesion	33	31	23	24	7	4	1	1

TABLE 48. MONONUCLEAR CELL LEUKEMIA (M.C.L.) IN THE SPLEEN OF SCHEDULED SACRIFICE RATS

oup	M.C.L. (Males) / Total Examined	% M.C.L. Males	M.C.L. (Females) / Total Examined	% M.C.L. Females	M.C.L. (Males + Females) / Total Examined	% M.C.L. Males + Females
1	$\frac{8}{33}$	24.2	$\frac{6}{31}$	19.4	$\frac{14}{64}$	21.9
2	$\frac{8}{31}$	25.8	$\frac{8}{27}$	29.6	$\frac{16}{58}$	27.6
3	$\frac{11}{32}$	34.4	$\frac{10}{37}$	27.0	$\frac{21}{69}$	30.4
4	$\frac{12}{30}$	40.0	$\frac{5}{24}$	20.8	$\frac{17}{54}$	31.5
5	$\frac{7}{36}$	19.4	$\frac{1}{31}$	3.2	$\frac{8}{67}$	11.9

TABLE 49. MONONUCLEAR CELL LEUKEMIA (M.C.L.) IN THE SPLEEN OF BOTH EARLY DEATH AND SCHEDULED SACRIFICE RATS

Group	M.C.L. (Males) / Total Examined	% M.C.L. Males	M.C.L. (Females) / Total Examined	% M.C.L. Females	M.C.L. (Males + Females) / Total Examined	% M.C.L. Males + Females
F01	17/50	34.0	20/50	40.0	37/100	37.0*
F02	18/50	36.0	19/50	38.0	37/100	37.0*
F03	20/50	40.0	15/49	30.6	35/99	35.4*
F04	25/50	50.0	17/49	34.7	42/99	42.4**
F05	10/50	20.0	11/49	22.4	21/99	21.2

* $P<0.05$ by Chi s^2 test

** $P<0.01$

there was no further evidence of fiber translocation in rats or monkeys from this study. There was no evidence of fibrous glass-induced pulmonary carcinogenicity or carcinogenicity of serosal surfaces. The only question regarding carcinogenicity arose in the increase seen in the incidence of mononuclear cell leukemia in exposed vs. control rats (see discussion below). There was no evidence that the inhaled fibrous glass induced fibroplasia or any additional change other than the macrophage response in the lung or lymph nodes of either rats or monkeys. There was no evidence that the pleural adhesions observed at necropsy in one rat from the F01 group were associated with fibrous glass inhalation.

Fibrous glass-induced pulmonary lesions in monkeys were generally mild. With the exception of the F01 group (> 20 micrometer x 4 to 6 micrometer plus binder) in which the macrophage response was minimal and in which lymphoid aggregates increased mildly, there were no apparent differences in response among the fibrous glass-exposed groups. The significance of the increase in the lymphoid aggregates is unknown but the most probable explanation would be a mild stimulation from an antigen such as the binder. The response in rats increased in severity from Group F01 to Group F04 and consisted of foci of granulomatous inflammation that were not present in monkeys. It was more difficult to precisely define the response induced by the fibrous glass in monkeys because this response was generally superimposed on the lesions induced by lung mite infestations and the aggregates of macrophages often contained both lung mite debris and fibrous glass. Lung mite-induced pulmonary lesions were prominent in many monkeys from this study and were present to some degree in nearly all monkeys. Some of these lesions were similar to those that might be expected from inhaled fibers to include such changes as pleural, subpleural, and interstitial fibrosis as well as smooth muscle hyperplasia. The presence of parasite-induced lesions in the lungs of monkeys could have masked subtle changes induced by the fibrous glass. However, the nature and distribution of the fibrous glass-induced lesions and their consistency among all groups, including monkeys with minimal lung mite-associated lesions, suggests that this was not the case. There were no fibrous glass associated granulomas in monkeys as there were in rats.

The prescribed fiber diameter in Group F01 (4 to 6 micrometers) was

both species, although minimal, probably occurred as a result of the presence of smaller diameter fibers that are inevitably present to some extent in these preparations.

Results from a previous fiberglass tracheal instillation and inhalation study in rats utilized fibers measuring either 1.5 micrometers x 5 micrometers or 1.5 micrometers x 60 micrometers[1]. The shorter fibers did not induce granulomas in the lung, instead fibers were phagocytized and cleared to the draining lymph nodes; however, the longer fibers induced granulomas and were not cleared to the lymph nodes[1]. The results in rats from the study herein described did not follow that pattern entirely as the most intense pulmonary response occurred in Group F04 where the fiber length was shortest. There was translocation of fibers to the regional lymph node even in the group with the longest fibers (F01, > 20 micrometers) indicating that either particles of this length can be phagocytized and cleared or that the phagocytized and transported fibers were fractured fibers of shorter length. As previously described, the response in monkeys was similar to that described for fibers of 1.5 micrometers x 5 micrometers in rats. However, the possibility for variation in response between species and the generally mild and consistent response in monkeys does not allow for viable comparisons with Gernstein et al.[34] in rats.

It was impossible to draw conclusions concerning the relative influence of fiber diameter, fiber length, concentration, or effect of binder on animals in this study because more than one variable was changed in each group and there were insufficient numbers of groups to isolate effects of any factor. Generally, the pulmonary response in rats was greater in groups with smaller diameter fibers as would be expected. That was true in monkeys only to the extent that the larger diameter fibers in the F01 group induced a less severe response than did fibers from the other three exposure groups.

The grossly visible plaque-like foci that occurred in rats resulted from accumulations of granulomatous foci in pleural and subpleural locations. The decreasing severity of these grossly observed lesions among three of the test groups (i.e., F02 > F03 > F04) was in direct contrast to the severity observed microscopically (i.e., F04 > F03 > F02). Although the explanation for this discrepancy was not entirely obvious, it apparently resulted from a

variation in character and in pleural localization of granulomatous foci that was not directly related to the general severity of the pulmonary lesions. These lesions were limited to granulomatous foci, there was no fibrosis, and there were no growth alterations in adjacent tissues, therefore there is no evidence in these animals that any further sequelae would result beyond that observed.

There was no consistent variation in occurrence and severity of fibrous glass-induced lesions among the various lobes of the lungs in monkeys. There was, however, a generally greater severity of such lesions in posterior lobes of the lungs in rats from Groups F02 and F03, whereas there was a more even distribution among all lobes in rats from Group F04. The extent to which fiber dimension influenced distribution could not be determined in this study.

The mononuclear cell leukemia was statistically significant when each test group was individually compared to the control group. This neoplasm is commonly seen in aged Fischer 344 rats. The incidence of mononuclear cell leukemia occurring in these control rats is essentially the same as that observed in control Fischer rats from 24-month studies over the past several years at Battelle's Columbus Laboratories. The reason for the increased incidence of mononuclear cell leukemia in test groups as compared to the control group in this study is not apparent. The possibility of an exposure-related increase in incidence of this neoplasm cannot be ruled out.

Conclusions

- The only unequivocal responses induced by fibrous glass inhalation in monkeys were macrophage aggregates with phagocytized fibrous glass in the lungs and tracheobronchial lymph nodes.
- The pulmonary responses in the rat induced by fibrous glass inhalation were characterized by macrophage aggregates and granulomas which contained fibrous glass fibers. The grossly visible plague like foci resulted from accumulations of granulomatous foci in pleural and subpleural locations. These lesions were limited to granulomatous foci, there was no fibrosis and there were no growth alterations in adjacent

- There was no evidence of a fibrous glass induced fibrogenic response in either monkeys or rats.
- The most severe lesions in rats were in the F04 group (< 10 micrometers x 1 micrometer, no binder) whereas the response in the F01 group (>20 micrometers x 4 to 5 micrometers, with binder) was minimal.
- The severity of response in monkeys was similar for all exposed groups except the F01 group (>20 micrometers x 4 to 6 micrometers, with binder) in which the response was minimal. Group F01 also had monkeys which had mildly increased numbers of lymphoid nodules or aggregates in peribronchiolar and perivascular areas. The significance of the increase in the lymphoid aggregates is unknown but the most probable explanation would be a mild stimulation from an antigen such as the binder.
- The fibrous glass induced lesions were similarly distributed among all lobes of the lung in monkeys; in rats, the lesions were most prominent in posterior lobes in all but the F04 group where there was more equal distribution throughout the lung.
- The relative influence of fiber diameter, fiber length, concentration, and binder could not be evaluated due to variation of more than one factor in each animal group.
- The only evidence of translocation of fibers occurred in macrophage transport to draining pulmonary lymph nodes in many animals (rats and monkeys) and to mesenteric lymph nodes in two rats.
- The mononuclear cell leukemia was statistically significant when each test group was individually compared to the control group. The possibility of an exposure related incidence of this neoplasm cannot be ruled out.
- This study showed no evidence of pulmonary or mesothelial carcinogenicity associated with inhaled fibrous glass.

RESEARCH NEEDS

Presently, mechanistic studies are not available to explain the apparent effect of glass fiber inhalation on the incidence of mononuclear cell leukemia in Fisher 344 rats. Previous studies (Fisher and Wilson, J. Reticuloendoth. Soc., 27, 513, 1980; Wagner, J. Natl. Cancer Inst., 57, 509, 1976; Lee, et al., Environ. Res., 24, 167, 1981; and Sherwin, et al., Lab. Investig., 40, 576, 1979) have described effects of inhaled and instilled silicates on the immune response of laboratory animals and humans. Pulmonary macrophage aggregation and granuloma formation are observations common to many of the early studies and this study. It's reasonable to hypothesize that inhaled fibrous glass may have resulted in compromised immune function and an enhanced incidence of the spontaneously occurring mononuclear cell leukemia. This hypothesis is readily tested by evaluation of the immune response and tumor incidence and dissemination in Fischer 344 rats instilled with glass fibers and subsequently exposed in the transplanted tumor.

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