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TOXICOLOGY AND CARCINOGENESIS

STUDIES OF

AMOSITE ASBESTOS

(CAS NO. 12172-73-5)

IN F344/N RATS

(FEED STUDIES)

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

FOREWORD

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

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

This study was conducted under contract to the National Institute of Environmental Health Sciences, National Toxicology Program. The studies described in this Technical Report have been conducted in compliance with NTP chemical health and safety requirements and must meet or exceed all applicable Federal, state, and local health and safety regulations. Animal care and use were in accordance with the U.S. Public Health Service Policy on Humane Care and Use of Animals. All NTP toxicology and carcinogenesis studies are subjected to a data audit before being presented for peer review.

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

Special Note: This Technical Report was peer reviewed in public session and approved by the NTP Board of Scientific Counselors' Technical Reports Review Subcommittee on September 22, 1982 [see page 6]. Thereafter, the NTP adopted the policy that the experimental data and laboratory records from all NTP toxicology and carcinogenesis studies not yet printed and distributed would be audited. The audit report was reviewed by NTP staff, who determined that none of the discrepancies influenced the final interpretation of the results of these studies. The audit report is on file at the NIEHS/NTP Quality Assurance Office and is available for review.

Because printing and distribution of this Technical Report have been delayed, the format differs from that of Technical Reports peer reviewed more recently. The categories of evidence of carcinogenicity adopted by the NTP in June 1983 were not used to evaluate these data. This final Technical Report supersedes all previous drafts of this report that have been distributed.

NTP TECHNICAL REPORT
ON THE
TOXICOLOGY AND CARCINOGENESIS
STUDIES OF AMOSITE ASBESTOS
(CAS NO. 12172-73-5)
IN F344/N RATS
(FEED STUDIES)

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AMOSITE ASBESTOS

CAS No. 12172-73-5



ABSTRACT

Carcinogenesis studies of amosite asbestos alone or in combination with the intestinal carcinogen 1,2-dimethylhydrazine dihydrochloride (DMH) were conducted in male and female F344/N rats. Amosite asbestos was administered at a concentration of 1% in pelleted diet for the entire lifetime of the rats, starting with the dams of the study animals. One group of amosite asbestos-exposed rats (amosite preweaning gavage) also received chrysotile asbestos via gavage during lactation. Group sizes varied from 100 to 250. Litter size was the same, but the offspring from mothers exposed to amosite asbestos were smaller at weaning than those from nonexposed mothers and remained smaller throughout their life. The DMH was administered by gavage at a dose of 7.5 mg/kg for males and 15 mg/kg for females every 14 days, starting at 8 weeks of age, for a total of five doses. The administration of DMH did not affect body weight gain either in amosite-exposed or nonexposed animals.

The amosite-exposed rats showed enhanced survival compared with that of the nonexposed rats. DMH exposure reduced survival by approximately 1 year, although the survival of the amosite plus DMH groups was slightly greater than that of the DMH group alone.

Significant increases in the incidences of C-cell carcinomas of the thyroid gland (untreated control, 11/117; amosite, 50/246, $P < 0.05$; amosite preweaning gavage, 14/100) and of leukemia (38/117; 106/249, $P < 0.05$; 49/100, $P < 0.01$) in male rats were observed in amosite-exposed groups. However, the biologic significance of the C-cell carcinomas in relation to amosite asbestos exposure is discounted because of a lack of significance when C-cell adenomas and carcinomas were combined and because the positive effect was not observed in the amosite preweaning gavage group. The biologic significance of an increased incidence of leukemia is questionable because of a lack of statistical significance in the amosite group when evaluated by life table analysis and because no toxic lesions were observed in the target organs, i.e., gastrointestinal tract and mesothelium.

DMH caused a high incidence (62%-74%) of intestinal neoplasia in amosite-exposed and nonexposed groups. Neither an enhanced carcinogenic nor a protective effect was demonstrated by exposure to amosite asbestos.

Conclusions: Under the conditions of these feed studies, amosite asbestos was not overtly toxic, did not affect survival, and was not carcinogenic when ingested at a concentration of 1% in the diet by male or female F344/N rats. The cocarcinogenic studies using DMH were considered inadequate because of the high incidence of DMH-induced intestinal neoplasia in both the amosite asbestos-exposed and nonexposed groups.

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The NTP Technical Report on the Toxicology and Carcinogenesis Studies of Amosite Asbestos is based on the lifetime studies that began in March 1978 and ended in February/March 1981 at Hazleton Laboratories America, Inc. (Vienna, VA).

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The members of the Peer Review Panel who evaluated the draft Technical Report on amosite asbestos on September 22, 1982, are listed below. Panel members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, Panel members have five major responsibilities: (a) to ascertain that all relevant literature data have been adequately cited and interpreted, (b) to determine if the design and conditions of the NTP studies were appropriate, (c) to ensure that the Technical Report presents the experimental results and conclusions fully and clearly, (d) to judge the significance of the experimental results by scientific criteria, and (e) to assess the evaluation of the evidence of carcinogenicity and other observed toxic responses.

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**SUMMARY OF PEER REVIEW COMMENTS
ON THE TOXICOLOGY AND CARCINOGENESIS STUDIES OF
AMOSITE ASBESTOS**

On September 22, 1982, the draft Technical Report on the toxicology and carcinogenesis studies of amosite asbestos received peer review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The review meeting was held in the Conference Center, Building 101, South Campus, National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Dr. E.E. McConnell, NIEHS, introduced the studies by reviewing the experimental design, results, and proposed conclusions (was not overtly toxic, did not affect survival, and was not carcinogenic when ingested at a concentration of 1% in the diet by male or female rats). The cocarcinogenic studies using DMH were considered inadequate.

Dr. Vesselinovitch, a principal reviewer, inquired if the statistically significant increase in C-cell carcinomas of the thyroid gland in treated male rats might have been related to asbestos. (The combined incidence of thyroid gland adenomas and carcinomas was not statistically significant.)

Dr. Harper, a second principal reviewer, agreed with the conclusions as stated. Dr. Whittemore, the third principal reviewer, also agreed with the conclusions but expressed concern about whether an MTD was achieved. Dr. Schwetz also questioned the experimental design, including the use of only one dose and the preweaning gavage regimen.

Dr. J. Moore, NTP, explained that this study and other oral asbestos ingestion studies in rats represented a consensus study design developed by a group of scientists within the Department of Health, Education, and Welfare. One dose was used so as to expose a larger than usual number of animals, and the 1% dose level in the diet represented the highest dose thought reasonable to represent a tolerated dose. The preweaning gavage was added to provide exposure of animals at a time when there might be increased permeability of the gut, which could allow enhanced penetration of fibers.

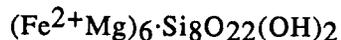
In other discussion, Dr. Scala objected to ascribing effects of asbestos on neonatal animals via lactational exposure when fibers were not measured in the milk. Dr. Whittemore moved that the report on the bioassay of amosite asbestos be accepted with the revisions as noted. Dr. Harper seconded the motion, which was approved with nine affirmative votes and one abstention (Dr. Swenberg).

I. INTRODUCTION

I. INTRODUCTION

AMOSITE ASBESTOS

CAS No. 12172-73-5



The term "asbestos" has a commercial/industrial derivation limited to naturally occurring fibrous minerals of the serpentine or amphibole series. Chrysotile is the only type of asbestos in the serpentine series, whereas the amphibole series is represented by actinolite, amosite, anthophyllite, crocidolite, and tremolite. The essential characteristic of asbestos minerals is their fibrous nature.

Excellent reviews of the carcinogenic and public health effects associated with asbestos exposure are those by Craighead and Mossman (1982), Peto and Schneiderman (1981), Selikoff (1980), the U.S. Environmental Protection Agency (EPA) (USEPA, 1980), Selikoff and Hammond (1979), and the International Agency for Research on Cancer (IARC, 1977). These studies clearly established an association between occupational inhalation exposure to chrysotile, amosite, crocidolite, and anthophyllite asbestos and an increased risk of lung cancer as well as mesotheliomas.

Large portions of the population ingest asbestos through consumption of food and water. Analyses of water samples from 365 cities found 45% to have detectable levels of various types of asbestos (Millette, 1979). Forty-one cities had asbestos concentrations in water which exceeded 10 million fibers per liter. Asbestos or asbestos-like fibers may gain access to water supplies as a result of mining (Lake Superior), from the presence of natural serpentine or amphibole deposits in watersheds (Seattle, WA, and San Francisco, CA), or, under certain conditions, through the use of asbestos-cement pipe for municipal water supplies (USEPA, 1980). For the latter, erosion of the pipe with release of fibers is associated with the "aggressiveness" of the water, a term representing a mathematical expression of pH, alkalinity, and calcium content. The EPA estimated that 68.5% of water systems in the United States utilize water that is potentially capable of eroding asbestos-cement pipe.

A number of studies have provided evidence that ingestion of asbestos in either food or water can result in the migration of asbestos fibers through the gastrointestinal mucosa and to distant organ sites in humans (Carter and Taylor, 1980), rats (Cunningham et al., 1977; Sebastien et al., 1980), and baboons (Storeygard and Brown, 1977; Patel-Mandlik, 1980). Electron microscopic studies confirmed the presence of amphibole mineral fibers in the urine of individuals who ingested water containing these fibers (Cook and Olson, 1979).

Harrington et al. (1978) failed to detect an association between the use of asbestos-cement pipe for municipal water supplies in Connecticut and the incidence of gastrointestinal cancer. In a study of cancer incidence in the San Francisco Bay area, Kanarek et al. (1980) reported a statistically significant trend for the increased incidence of several cancer types, including stomach, gallbladder, esophageal, and peritoneal cancer, when census tracts were analyzed on a gradient of low to high asbestos content in municipal water. Cooper et al. (1979) confirmed the association between asbestos concentrations in the San Francisco Bay area drinking water and cancer of the digestive tract.

Studies in animals have shown that inhalation of asbestos produces lung carcinomas and mesotheliomas in the pleural cavity (Wagner et al., 1974). Intrapleural, intratracheal, or intraperitoneal injection of asbestos also induces neoplasia in several species of laboratory animals (Stanton et al., 1981). A review of these studies is given by Levine (1981).

Asbestos (chrysotile, amosite, and crocidolite) was also cytogenic in vitro to human embryonic intestine, mouse epithelial-like colon-derived cells, and rat liver epithelial cells (Reiss et al., 1979). However, chrysotile asbestos was far more cytotoxic than were the amphibole fibers, and the effects were more pronounced in the intestine-derived cells than in those from the liver.

Asbestos also was cytotoxic to Syrian hamster peritoneal macrophages (Bey and Harrington, 1971). Using the HGPRT locus/resistance to 6-thioguanine assay system, Reiss et al. (1979) showed that these three forms of asbestos were not mutagenic. In addition, no mutagenic activity was demonstrated when chrysotile, amosite, or crocidolite asbestos was used in *Escherichia coli* or *Salmonella typhimurium* systems (Chamberlain and Tarmy, 1977). Therefore, it can be concluded that asbestos is not genotoxic but is rather an epigenetic carcinogen of the solid-state type (Weisburger and Williams, 1979).

In November 1973, the National Institute of Environmental Health Sciences and the EPA co-sponsored a symposium on the possible biologic effects of ingested asbestos (EHP, 1974). The participants at this conference concluded that a paucity of definitive data existed concerning the effects of ingested asbestos and that specific research was needed.

A subcommittee of the U.S. Department of Health, Education, and Welfare (now the U.S. Department of Health and Human Services) Committee to Coordinate Toxicology and Related Programs was established to review existing data and to prepare a draft research protocol that would be responsive to potential public health implications of ingested asbestos. This protocol was distributed widely for comment within and outside the government, and a public meeting of the Subcommittee was held on February 11, 1975. On the basis of comments received,

a revised protocol was developed which called for the use of long-term animal toxicology studies to evaluate the ingestion of several minerals for carcinogenic effects. As a result, the National Toxicology Program has investigated the carcinogenic potential of ingested chrysotile asbestos in hamsters (NTP, 1990a) and rats (NTP, 1985a), amosite asbestos in hamsters (NTP, 1985b) and rats (this report), crocidolite asbestos in rats (NTP, 1988), and tremolite in rats (NTP, 1990b). All of the studies were to encompass the lifetime of the animal, including exposure of the dams from which the study animals were derived. A single concentration of 1% asbestos in the diet was chosen because it represented the highest concentration thought to be reasonable from a biologic standpoint and one that could be tolerated in a lifetime study. Certain studies (intermediate-range chrysotile in hamsters and amosite and intermediate-range chrysotile in rats) also incorporated the intestinal carcinogen 1,2-dimethylhydrazine dihydrochloride (DMH) as part of the protocol to study the cocarcinogenic effects of asbestos. DMH is a well-known intestinal carcinogen in animals and produces epithelial neoplasms at sites of intimate exposure to asbestos.

This Technical Report presents the results of those studies undertaken to determine the effects of amosite asbestos fed to male and female F344/N rats in the diet. In addition, the studies were designed to determine if the ingestion of amosite asbestos modified the response to DMH.

II. MATERIALS AND METHODS

Study Material

Study Diets and Dose Formulations

Dose Formulations of 1,2-Dimethylhydrazine

Dihydrochloride for Gavage Administration

Study Design

Source and Specifications of Study Animals

Animal Maintenance

Safety Precautions

Clinical Examinations and Pathology

Statistical Methods

II. MATERIALS AND METHODS

Study Material

Asbestos is a general term applied to certain natural silicates when they are present in a fibrous form. Amosite is a fibrous member of the amphibole mineral group; its chemical formula is $(\text{Fe}^{2+}\text{Mg})_6\cdot\text{Si}_8\text{O}_{22}(\text{OH})_2$.

The amosite sample, identified as S-33, was purchased by the Bureau of Mines from the Atlas Asbestos Co. (Montreal, Canada). This material is from a mine in the area known as Renge, in the Transvaal, Republic of South Africa. Not a proper mineral name, amosite is a term used to describe the material from asbestos mines in South Africa.

To develop homogeneity of the sample, the amosite was processed by a single pass through an air jet mill. The high abrasive action of amosite resulted in erosion of the steel surfaces of the mill, which resulted in turn in increasing the chromium content of the milled product from 90 to 170 ppm.

The 1,200 pounds of milled amosite were packaged as 20-pound lots in virgin fiberboard drums and stored with other forms of asbestos in a special warehouse at Research Triangle Park, NC.

Each drum received a color marking unique to the mineral type. Random samples of various drums determined that the amosite was homogeneous.

The homogeneity of the samples and the physical and chemical properties of the materials were characterized by the Bureau of Mines (1980) and by the Fine Particle Laboratories, Illinois Institute of Technology Research Institute (IITRI, Special Report). Copies of these reports are available upon request from the National Toxicology Program.

Selected chemical and physical properties of amosite asbestos are presented in Tables 1 and 2 (Bureau of Mines, 1980). In an analysis of mineralogic composition, grunerite (amosite) asbestos-- $(\text{Fe}^{2+}\text{Mg})_6\cdot\text{Si}_8\text{O}_{22}(\text{OH})_2$ --was detected at a volume percent abundance of about 94 and actinolite asbestos at about 5; minor amounts of biotite, siderite, plagicolase, ziosite, glass, quartz, and other opaques were found.

Crystalline 1,2-dimethylhydrazine dihydrochloride (DMH) (greater than 97% pure) was obtained from Aldrich Chemical Co. (Metuchen, NJ) (lot no. 072967JA). Thin-layer chromatographic analysis of a 200- μg sample did not

TABLE 1. FIBER CHARACTERISTICS AND CHEMICAL INSTRUMENTAL ANALYSIS OF AMOSITE ASBESTOS

Fiber characteristics			
Surface area (m^2/g)		4.13	
Density (g/cm^3)		3.35 ± 0.026	
Measurements by transmission electron microscopy			
Fiber count (gram)		0.3466×10^{10}	
Mean length (μm)		4.37	
Range of length		0.85-995	
Median diameter		0.72	
Range of diameter		0.864-12.4	
Median fiber aspect ratio (l/d)		6.4248	
Chemical instrumental analysis (expressed as weight percent)			
Al_2O_3	0.42	MnO	2.66
CaO	0.48	Cr_2O_3	0.03
FeO	34.61	NiO	0.01
Fe_2O_3	2.24	CO_2	0.88
MgO	6.22	H_2O^-	0.15
K_2O	0.30	H_2O^+	2.30
SiO_2	50.36	Benzene-extracted organics	0.021
Na_2O	0.03		

TABLE 2. PARTICLE SIZE DISTRIBUTION OF AMOSITE ASBESTOS AND OTHER MINERALS BY PARTICLE NUMBER (a)

	Length Interval (µm)						
	0-1.99	2-3.99	4-5.99	6-7.99	8-9.99	10-19.99	20-39.99
Amosite asbestos mean width (µm)	0.28	0.38	0.45	0.45	0.48	0.52	0.51
Amosite asbestos particles per interval	57	126	88	78	52	181	184
Percent of total amosite asbestos particles	5.6	12.3	8.6	7.6	5.1	17.7	18.0
Cumulative percent amosite asbestos	5.6	17.9	26.5	34.1	39.2	56.9	74.9
Volume percent amosite asbestos (b)	--	0.1	0.3	0.4	0.4	2.4	5.0
Cumulative volume percent amosite asbestos	--	0.1	0.4	0.8	1.2	3.6	8.6
Number of other particles	11	8	1	0	1	1	0
Amosite asbestos particles per length interval, percent, by aspect ratio							
1:1-2.9:1	12	0	0	0	0	0	0
3:1-4.9:1	34	10	6	5	2	0	0
5:1-9.9:1	43	52	28	14	4	1	1
10:1-19.9:1	11	34	52	38	40	21	1
20:1-49.9:1	0	4	18	41	54	64	30
50:1-99.9:1	0	0	1	2	0	12	55
100:1-199:1	0	0	0	0	0	2	12
200:1-499:1	0	4	0	0	0	0	1
>500:1	0	0	0	0	0	0	0

(a) From Bureau of Mines (1980).

(b) Calculated from particle number data, assuming rectangular cross-section with third dimension equal to one-half measured width

detect any hydrazine or 1,1-dimethylhydrazine. Faint traces of methylazoxymethane and azoxymethane were detected by high-performance liquid chromatography (Fiala et al., 1976). Three percent of the impurities in DMH were not accounted for. The DMH was stored at 4° C.

Study Diets and Dose Formulations

The feed used was NIH 31 Rat and Mouse Ration. Amosite asbestos was incorporated to a concentration of 1% by weight into the study diet. Pilot studies determined that homogeneous mixing of amosite asbestos and feed would occur in a blender loaded by alternate layering of feed and amosite asbestos. Each batch of blended feed was analyzed for amosite asbestos concentration, pesticide contamination, and nutrient content. Results of analyses for amosite

asbestos in feed are given in Table 3. Further details are given in Table 4.

Animals were to have received 1% amosite asbestos but were inadvertently given 1% chrysotile asbestos (medium range) by gavage. That formulation was prepared by weighing out the required amount of chrysotile asbestos (medium range), a gray powder with lumps, on a Mettler balance and placing it in a beaker. Sterile water (for injection) was added to obtain the desired concentration, and then the suspension was mixed in a magnetic stirrer for a short time. The suspension was administered by gavage at a dose of 0.47 mg/g body weight to groups of 100 males and females designated as the amosite preweaning (PW) gavage groups from birth to weaning (21 days).

TABLE 3. RESULTS OF ANALYSIS OF FORMULATED DIETS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS AS DETERMINED BY IRON CONTENT

Date Mixed	Determined Concentration in Feed for Target Concentration of 10,000 ppm (1%) (a)
11/21/77	10,900 ± 1,500
12/07/77	11,200 ± 1,200
02/01/78	9,500 ± 1,600
03/22/78	11,300 ± 700
05/22/78	11,400 ± 1,000
05/22/78	11,200 ± 600
07/11/78	10,400 ± 400
07/11/78	9,900 ± 500
09/14/78	10,800 ± 800
09/14/78	11,500 ± 700
10/30/78	10,000 ± 1,300
10/30/78	12,000 ± 500
12/15/78	9,500 ± 1,600
12/15/78	11,000 ± 300
02/15/79	9,100 ± 700
02/15/79	10,200 ± 900
04/02/79	9,500 ± 400
04/02/79	13,400 ± 5,900
05/09/79	9,700 ± 400
05/09/79	9,500 ± 1,000
05/09/79	10,100 ± 100
06/26/79	11,100 ± 300
06/26/79	10,600 ± 500
08/28/79	9,900 ± 100
08/28/79	9,700 ± 500
10/16/79	11,800 ± 2,100
10/16/79	11,400 ± 900
12/03/79	9,900 ± 3,500
12/03/79	8,600 ± 1,300
01/10/80	9,100 ± 600
01/10/80	9,200 ± 600
02/27/80	6,700 ± 1,700
02/27/80	6,100 ± 2,100
04/18/80	9,800 ± 2,000
05/29/80	11,000 ± 1,900
05/29/80	13,400 ± 2,600
07/18/80	11,200 ± 600
08/26/80	10,700 ± 1,000
10/13/80	11,100 ± 700
	Mean = 10,300 ± 2,700

(a) Average of five samples

TABLE 4. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS (a)

EXPERIMENTAL DESIGN	
Size of Study Groups	F ₀ --control:male,54; female,108;exposed: male, 200; female, 400; F ₁ --untreated control: 88; amosite asbestos: 250 rats of each sex; DMH--125 rats of each sex; amosite asbestos + DMH--250 rats of each sex; amosite asbestos + PW--100
Doses	Amosite asbestos 0% or 1% (10,000 ppm) in feed; DMH--7.5 mg/kg (male); 15 mg/kg (female); PW--0.47 mg/kg chrysotile asbestos
Date of First Dose	F ₀ --obtained 12/7/77, bred starting 2/22/78
Duration of Dosing	Lifetime until only 10% of the group remained
Type and Frequency of Observation	Observed 2 × d; examined clinically 1 × wk; weighed 1 × wk
Necropsy and Histologic Examinations	Necropsy performed on all animals. Tissues examined histologically: adrenal glands; bone marrow (sternum); brain; bronchial, celiac, cervical, iliac, ilioocolonic, mandibular, mesenteric, pancreatic, and renal lymph nodes; cecum; colon (carpet rolled); duodenum; esophagus; heart; ileum; jejunum; kidneys; liver; lungs and bronchi; mammary gland; pancreas; parathyroids; pituitary gland; prostate/testes or ovaries/uterus; salivary glands; small intestine; spleen; stomach; thyroid gland; tissue masses; trachea; and urinary bladder. Epididymis, eyes, nasal cavity with turbinates, seminal vesicles, and spinal cord were examined microscopically if gross lesions were observed
ANIMALS AND ANIMAL MAINTENANCE	
Strain and Species	F344/N rats
Animal Source	Charles River Breeding Laboratories (Wilmington, MA)
Study Laboratory	Hazleton Laboratories of America
Age When Placed on Study	F ₀ --15-16 wk prior to delivery of F ₁
Age When Killed	untreated controls, amosite, amosite + PW--male 141 wk, female 145 wk; DMH, amosite + DMH--male 117 wk, female 103 wk
Necropsy Dates	Lifetime study
Method of Animal Distribution	According to tables of computer-generated random numbers
Feed	NIH 31 Rat and Mouse Ration (Zeigler Bros., Inc., Gardners, PA); available ad libitum
Bedding	Sani Chips® (J.P. Murphy, Rochelle Park, NJ, and Shurfire, Baltimore, MD)
Water	Tap water ad libitum
Cages	Polycarbonate (Hazleton Systems, Aberdeen, MD); stored on Enviro-racks®
Cage Filters	Remay nonwoven polyester sheets (Nationwide Papers, Washington, DC)
Animals per Cage	F ₀ --1 for males, 2 for females during breeding; 2 for males, 1 for females after breeding; F ₁ --3
Other Chemicals on Study in the Same Room	None
Animal Room Environment	Temp--23° ± 2° C; hum--50% ± 10%; fluorescent light 12 h/d; 10-15 room air changes/h
CHEMISTRY	
Supplier	Atlas Asbestos Co., Montreal, Quebec, Canada; obtained from a mine in South Africa in an area known as Renge in the Transvaal

TABLE 4. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS (Continued)

FORMULATED DIETS

Preparation Amosite asbestos and feed mixed in a 55-ft³ Patterson-Kelly® V-blender with intensifier bar; oval, 3/8-in × 3/4-in pellets prepared with Sprout-Waldron pellet mill. Pelleted feed packaged in 25-lb aliquots in standard paper feed bags

(a) DMH--1,2-dimethylhydrazine dihydrochloride; PW--preweaning gavage

**Dose Formulations of
1,2-Dimethylhydrazine Dihydrochloride
for Gavage Administration**

Immediately before use, DMH was mixed with ice-cooled 0.2 M acetate buffer (pH 5.0) in 15-ml screw-cap, Teflon®-lined centrifuge tubes in an ice bath. Results of colorimetric analysis of the dose mixtures indicated that the concentration of DMH was usually less than 80% of the target concentration of 3.9 and 7.8 mg/ml.

Study Design

Groups of 100-250 rats of each sex were fed pelleted diets containing 0% or 1% amosite asbestos in lifetime studies (Table 5). The mothers of those in the groups that were administered amosite asbestos started receiving amosite asbestos 7-12 days before mating. Subgroups of 100 male and 100 female rats inadvertently received 0.47 mg/g chrysotile asbestos in water by gavage, 7 days per week for 3 weeks, starting at 1 day of age. These two groups were referred to as the PW gavage groups. At 9 weeks of age, subgroups of 125-175 rats (one positive control group and one amosite asbestos-exposed group) received 7.5 mg/kg (male) or 15 mg/kg (female) DMH in acetate buffer (pH 5.0) by gavage, every other week for a total of five doses. These doses were based on a pilot study (McConnell et al., 1980) which showed that DMH at these doses produced an incidence of approximately 15% intestinal neoplasia. When the survival of either of the paired groups reached 10%, both groups were killed.

**Source and Specifications of Study
Animals**

Parental Generation (F₀): Weanling F344/N (cesarean-derived) rats, which were barrier sustained and specific pathogen free, were purchased from Charles River Breeding Laboratories. These animals constituted the F₀ generation and were received December 7, 1977 (Figure 1).

On arrival, animals were taken directly to the quarantine area and acclimated to laboratory conditions for approximately 2 weeks. Twenty-four hours after arrival, eight rats of each sex were selected and killed, and pathogen burden was determined for each animal. Pathogens examined for included ectoparasites (mites, fleas, and lice), intestinal parasites (fecal flotation), and bacteria (*Mycoplasma* sp., *Salmonella* sp., *Diplococcus pneumoniae*, *Corynebacterium kutscheri*, and *Streptobacillus moniliformis*). Serologic tests were conducted for viruses (Tables C1-C3).

After approximately 2 months in quarantine (the regular 3- to 4-week quarantine period was extended because of a shortage of cages), male and female rats (15-16 weeks old) were separated on February 15, 1978, into two groups (control and exposed) according to tables of random numbers and placed on the appropriate designated diets.

After at least 7 days' exposure to the designated diets, the rats (16-17 weeks old) were placed in

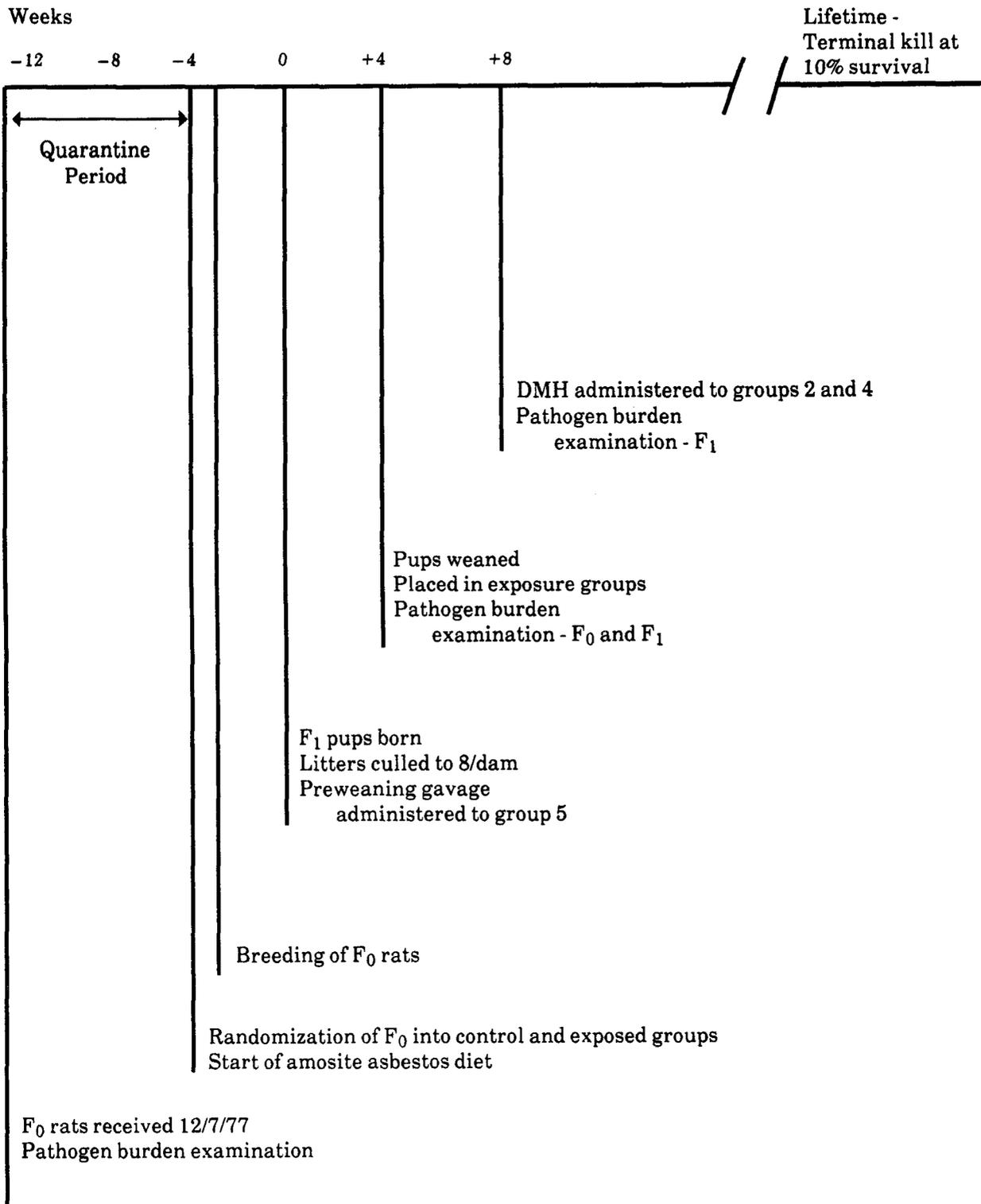


FIGURE 1. SCHEDULE OF MAJOR EVENTS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS IN RATS

TABLE 5. SUMMARY OF DISTRIBUTION OF RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Generation	Study Group	No. of Animals		Amosite		DMH (mg/kg) (a)	
		Male	Female	Percent	mg/g	Male	Female
F ₀ (b)	1 (untreated control)	250	120	0	--	--	--
	2 (amosite asbestos)	200	400	1	--	--	--
F ₁ (c)	1 (control)	117	117	0	--	--	--
	2 (DMH)	125	125	0	--	7.5	15.0
	3 (amosite asbestos)	250	250	1	--	--	--
	4 (amosite asbestos + DMH)	175	175	1	--	7.5	15.0
	5 (amosite asbestos + preweaning gavage)	100	100	1	(d) 0.47	--	--

Generation	Study Group	Birth Date (e)	Dose Date	Start of the
				Recording of Body Weights
F ₁	1 (untreated control)	3/28/78	--	5/18/78
	2 (DMH)	3/28/78	(f) 5/26/78	5/18/78
	3 (amosite asbestos)	3/28/78	--	5/18/78
	4 (amosite asbestos + DMH)	3/28/78	(f) 5/26/78	5/18/78
	5 (amosite asbestos + preweaning gavage)	3/28/78	(d) 5/26/78	5/18/78

(a) Administered five doses of 1,2-dimethylhydrazine dihydrochloride (DMH) by gavage

(b) Randomization date: 2/15/78

(c) Randomization date: 5/2/78-5/10/78

(d) Inadvertently given intermediate (medium)-range chrysotile asbestos instead of amosite asbestos by gavage

(e) Based on the average of all the birth dates of the F₁ animals

(f) Given DMH by gavage

breeding cages (one male to two females) on February 22, 1978. During the breeding period, the rats continued to be fed the same diets. Twenty days later (on the average), females were separated and housed individually in polycarbonate cages. Males were removed from the breeding cages and rehoused two per cage. After the pups were born and placed on the lifetime feeding phase of the study, nine rats (five males and four females) were selected from the F₀ generation for additional pathogen burden determinations (Tables C4-C6) to assure that the animals remained in acceptable health according to the infectious disease criteria.

Filial Generation: Litters were culled to no more than eight pups. Litters of the control and exposed groups were assigned to the corresponding control or dosed groups such that birth dates were equally distributed. Litters in which only one sex was present were excluded. After weaning at 21 days, pups from exposed or control dams were randomly assigned to various exposed (except the amosite asbestos + PW gavage group) or control groups according to a table of

random numbers. Pups assigned to the amosite asbestos + PW gavage group were administered 0.47 mg/g chrysotile asbestos in sterile water by gavage during lactation as described previously.

Animal Maintenance

The control and amosite asbestos-exposed rats were placed in separate rooms with monitored temperature and humidity and a controlled light cycle. Attempts were made to maintain the temperature at 74° ± 4° F and humidity at 50% ± 10%. Racks and filters were changed approximately once every 2 weeks. The rats were housed three per cage. Cages and bedding were replaced twice per week. Bedding samples were collected periodically for analysis (Appendix D). Control and formulated diets and tap water via automatic waterers were available ad libitum. Two water samples were collected and submitted for analysis (Appendix E). Stainless steel feed containers were changed once every 2 weeks. Sources and description of the materials used for animal maintenance are presented in Table 4.

II. MATERIALS AND METHODS

Safety Precautions

The incoming air to the animal rooms was filtered to remove particulate matter. Ten to 15 changes of room air per hour were provided. Before initiation of the study, air samples were collected and analyzed for baseline amosite asbestos concentrations (Appendix F). Additional samples were collected approximately every 6 months for analysis to assure personnel safety.

Other measures used for personnel protection included the wearing of fully protective disposable suits, gloves, boots, and bouffant caps and the use of a dust/mist respirator mask approved by the Occupational Safety and Health Administration. Personnel leaving the animal rooms were required to dispose of their protective clothing and to take showers. In addition, physical examinations, including pulmonary function tests and chest radiographs, were conducted at the initiation of the study, once per year thereafter, and at the end of the studies.

Clinical Examinations and Pathology

Rats were observed two times per day. Body weights by cage were recorded once per week for the duration of the studies. Mean body weights were calculated for each group. Moribund animals were killed, as were animals that survived to the end of the study. A necropsy was performed on all animals, including those found dead, unless the tissues were excessively autolyzed or cannibalized. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study in each group. Animals were killed when exhibiting any one of these conditions:

1. Palpable masses within the abdominal cavity (excluding retained testes).
2. Masses protruding from the rectum.
3. Rectal discharge of bright red fluid (an indication of the presence of a bleeding colonic or rectal neoplasm).
4. Large ulcerated masses in the area of the ears or on the side of the face (Zymbal gland tumors).

5. Large subcutaneous masses that were ulcerated or infected.
6. Masses that interfered with breathing and eating or that severely hampered locomotion.
7. Huge tissue masses.
8. Central nervous system signs accompanied by weight loss (head tilt, circling, incoordination, ataxia, paralysis).
9. Severe weight loss or emaciation.
10. Coma or extreme weakness.

When the remaining animals of the amosite asbestos-exposed group of either sex reached 10% of those starting the studies, that group and the corresponding control group for that sex were killed. Animals were killed by exsanguination under sodium pentobarbital anesthesia (Nembutal®, Abbott Laboratories, Inc., North Chicago, IL, or Diabutal®, Diamond Laboratories, Inc., Des Moines, IA). Final body weights were recorded, and necropsies included blood smears taken from animals killed in extremis or those killed at the end of the study and touch preparations made from any enlarged spleen or lymphoid organ.

The gastrointestinal tract, chosen as one of the target organs before these studies began, was handled in a slightly different manner than in standard long-term rodent carcinogenesis studies. Before being placed in fixative, the entire esophagus was opened and pinned with the exterior surface adjacent to cardboard. The stomach and cecum were prepared similarly. Two-centimeter lengths of duodenum and ileum and two portions of jejunum were placed unopened in fixative. The remaining small intestine was opened, washed gently with saline, and carefully examined by transillumination on a radiograph viewing box. Suspected lesions were processed separately and identified individually as to location. Likewise, the entire colon with anus was opened, examined, and pinned to cardboard (serosal surface down) before fixation. The size and location of masses were recorded. Masses greater than 1 mm in diameter were removed as separate specimens for processing. After fixation and before embedding, the colon was "carpet-rolled" starting at the posterior end, with the mucosal surface inward.

II. MATERIALS AND METHODS

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Tissues examined microscopically are listed in Table 4.

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

Statistical Methods

Data Recording: Data on this experiment were recorded in the Carcinogenesis Bioassay Data System (Linhart et al., 1974). The data elements include descriptive information on the chemicals, animals, experimental design, survival, body weight, and individual pathology results, as recommended by the International Union Against Cancer (Berenblum, 1969).

Survival Analyses: The probability of survival was estimated by the product-limit procedure of Kaplan and Meier (1958) and is presented in the form of graphs. Animals were censored from the survival analyses at the time they were found to be missing or dead from other than natural

causes; animals dying from natural causes were not censored. Statistical analyses for a possible dose-related effect on survival used the method of Cox (1972) for testing two groups for equality. All reported P values for the survival analysis are two-sided.

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

Analysis of Tumor Incidence: Three statistical methods are used to analyze tumor incidence data: life table tests, incidental tumor analysis, and Fisher exact analysis. Tests of significance include pairwise comparisons of exposed groups with controls. For studies in which administration of the study compound has little effect on survival, the results of the three alternative analyses will generally be similar. When differing results are obtained by the three methods, the final interpretation of the data will depend on the extent to which the tumor under consideration is regarded as being the cause of death. Continuity-corrected tests are used in the analysis of tumor incidence, and reported P values are one-sided. The procedures described below also were used to evaluate selected nonneoplastic lesions.

*Life Table Analyses--*The first method of analysis assumed that all tumors of a given type observed in animals dying before the end of the study were "fatal"; i.e., they either directly or indirectly caused the death of the animal. According to this approach, the proportions of tumor-bearing animals in the dosed and control groups were compared at each point in time at which an animal died with a tumor of interest. The denominators of these proportions were the total number of animals at risk in each group. These

II. MATERIALS AND METHODS

results, including the data from animals killed at the end of the study, were then combined by the Mantel-Haenszel method (1959) to obtain an overall P value. This method of adjusting for intercurrent mortality is the life table method of Cox (1972). The underlying variable considered by this analysis is time to death due to tumor. If the tumor is rapidly lethal, then time to death due to tumor closely approximates time to tumor onset. In this case, the life table test also provides a comparison of the time-specific tumor incidences.

Incidental Tumor Analyses--The second method of analysis assumed that all tumors of a given type observed in animals that died before the end of the study were "incidental"; i.e., they were merely observed at necropsy in animals dying of an unrelated cause. According to this approach, the proportions of tumor-bearing animals in dosed and control groups were compared in each of five time intervals: weeks 0-60, weeks 61-86, weeks 87-112, weeks 113-126, and beyond week 126. The denominators of these proportions were the number of animals actually ex-

amined for tumors during the time interval. The individual time interval comparisons were then combined by the previously described method to obtain a single overall result. (See Haseman, 1984, for the computational details of both methods.)

Fisher Exact Analysis--In addition to survival-adjusted methods, the results of the Fisher exact test for pairwise comparisons (Gart et al., 1979) are given in the appendix containing the analyses of tumor incidence. This test is based on the overall proportion of tumor-bearing animals and does not adjust for survival differences.

Historical Control Data: Although the concurrent control group is always the first and most appropriate control group used for evaluation, there are certain instances in which historical control data can be helpful in the overall assessment of tumor incidence. Consequently, control tumor incidences from the NTP historical control data base (Haseman et al., 1984, 1985) are included for those tumors appearing to show compound-related effects.

III. RESULTS

Establishment of Study Groups

Pathogen Burden

Clinical Signs

Body Weights and Feed Consumption

Survival

Pathology and Statistical Analyses of Results

III. RESULTS

Establishment of Study Groups

These studies were designed to evaluate the effects of ingested amosite asbestos during the entire life of the animal. When the first litters were born, therefore, the mated female rats had been on study diets for approximately 12 weeks. To minimize the chance that the mothers would reject or cannibalize their young, the litters were not handled during lactation, except for weighing and culling at birth and the administration of intermediate-range chrysotile asbestos by gavage. Litter size and survival of offspring were unaffected by the presence of amosite asbestos in the mothers' diet. The average number of live fetuses born to amosite-exposed dams was 8.5 vs. 7.7 for the control groups. Significant numbers of pups that received the preweaning (PW) asbestos gavage died. The average size of the litters in this group was 3.4 at weaning compared with 7.5 in the non-PW amosite group. The average weight at birth of the amosite-exposed pups was 4.7 g compared with 4.8 g for the controls. Fetal weights were determined by dividing the weight of each litter by the number live pups. The amosite-exposed offspring were slightly smaller at weaning than were the controls (control, 27.4 g vs. exposed, 23.2 g).

A summary of groups, number of animals, and diets for the parental (F₀) and the filial (F₁) animals is presented in Table 5.

Pathogen Burden

Microscopic examination of parental tissues for pathogen burden indicated that the parents were initially free of spontaneous disease, with the exception of mild peribronchial accumulation of lymphocytes. Examination of parental tissues subsequent to weaning of the F₁ generation gave evidence of early respiratory disease consisting of moderate peribronchial lymphoid hyperplasia and minimal perivascular lymphoid hyperplasia.

Moderate peribronchial lymphoid hyperplasia and focal hyperplasia of the bronchiolar epithelium were noted in initial samples of F₁ generation rats. The bronchiolitis with a hyperplastic response in affected bronchiolar epithelium is characteristic of Sendai virus infection, and this

conclusion was supported serologically. The disease is usually mild and self-limiting in rats as was demonstrated by the milder condition in samples obtained later in the studies and the lower Sendai serologic titer of the repeated tests (Appendix C).

Clinical Signs

A summary of clinical signs from weeks 71 to 111 is presented in Appendix G. This time period was chosen for illustration because few signs were noted before week 71 and age-related signs complicated the observations after week 111.

The incidence of clinical signs occurred at essentially similar frequencies throughout the studies in the study groups, except in those that received DMH. No distinct signs of compound-related effects were noted in any of the amosite-exposed animals during the first 52 weeks of the studies. The following representative findings were observed at generally similar frequencies in all groups: soft feces; urine stains; pale, thin, and/or hunched appearance; depression; localized alopecia or sores on head or body; rough hair coats; abnormal eyes (pale, cloudy, bloody crust, red, lacrimation, squinting, enlarged, sores, swollen, red discharge, protruding, small and/or necrotic); head tilt; salivation; localized swellings; stains on fur; bloated appearance; necrotic or abscessed tail; discharge from anus or vagina; protruding penis or vagina; small or enlarged testis; wheezing; wasting feed or decreased feed consumption; and labored respiration and/or abnormal central nervous system responses (circling, hyperactivity, loss of equilibrium, tremors, isolated occurrences of paralysis and/or ataxia).

As the study proceeded, the incidence of clinical signs increased in all groups. At intervals during which a large number of moribund animals were killed in any one particular group, the clinical signs most frequently observed were supportive of the conditions for moribund kills as outlined in the Materials and Methods section. A comparison of clinical signs observed during the same selected intervals for all groups revealed a larger number of palpable abdominal masses, tissue masses, and central nervous system signs, as well as red discharge and protruding masses from the rectum in Group 2

(DMH) and Group 4 (amosite + DMH). In addition, throughout the studies the incidences of tissue masses, nodules, and wart-like lesions of the head and ear region were greater in Groups 2 and 4. These findings were presumably due to the administration of DMH, since they were not frequently observed clinically in any of the groups not exposed to DMH.

Body Weights and Feed Consumption

Mean body weight and feed consumption values for the lifetime feeding phase of the studies are presented in Tables 6 through 8 and Figures 2 and 3. Cumulative mean body weight change relative to controls is presented in Table 9. Mean body weights were analyzed by the method of Rao (1958) at selected intervals: at birth and weeks 3, 8, 11, 15, 24, 33, and 60 for males and at birth and weeks 3, 8, 11, 16, 27, 48, and 60 for females.

The data revealed a 15% depressed mean body weight gain at weaning in rats of each sex in the amosite-exposed groups compared with that in the untreated controls. The depressed weight gain for the amosite-exposed rats was more apparent at 8 weeks of age (37% for males and 25% for females) and then paralleled that of the controls (except for DMH-exposed rats) for the remainder of the studies. Both male and female DMH-exposed groups gained less than the untreated controls. Additionally, the mean body weights of Group 5 (amosite + PW) males were

higher at all of the selected intervals when compared with those of Group 3 (amosite) males. The mean body weights of the females in Group 5 were higher than those of Group 3 females at all the intervals chosen. The mean body weight change relative to the untreated controls revealed a noticeably lower weight gain throughout the first year in Group 2 rats of each sex.

A summary of the feed consumption per rat and ratios of exposed to controls for representative weeks is presented in Appendix H. For males in Groups 2 (DMH), 3 (amosite), 4 (amosite + DMH), and 5 (amosite + PW), the mean weekly feed consumption was 101%, 102%, 104%, and 105% that by the untreated control group; for females, the weekly mean feed consumption was 100%, 102%, 107%, and 108% that by the controls. For Group 4 (amosite + DMH), the weekly mean feed consumption was 101% that by Group 2 (DMH) for males and 108% that by Group 2 for females.

Comparisons of mean total feed consumption values of the control and amosite-exposed groups from the beginning of the studies through week 52 (60 weeks of age) revealed generally higher total mean feed consumption values in the amosite-exposed groups. There was no apparent correlation between the decreased body weight gains observed in the amosite-exposed groups and feed consumption. Feed consumption by the exposed groups was generally higher than that by untreated controls.

TABLE 6. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Weeks on Study (from birth)	Control		Amosite			Amosite + PW		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors
MALE								
7	173	117	101	58	250	128	74	100
17	303	117	259	85	250	279	92	100
27	369	117	318	86	250	338	92	100
37	403	117	356	88	250	376	93	100
48	425	117	375	88	250	390	92	100
57	450	117	393	87	250	416	92	100
67	471	117	411	87	248	438	93	100
77	477	115	429	90	245	443	93	99
87	475	112	424	89	238	439	92	90
97	471	104	417	89	230	440	93	83
107	459	93	410	89	218	420	92	69
117	423	76	390	92	183	391	92	53
127	393	44	358	91	130	370	94	26
137	340	16	334	98	61	327	96	9
FEMALE								
7	123	117	91	74	250	106	86	100
17	185	117	168	91	250	176	95	100
27	212	117	192	91	247	198	93	99
37	222	117	204	92	247	211	95	99
48	241	117	221	92	247	224	93	99
57	260	117	241	93	247	247	95	98
67	295	116	271	92	246	275	93	96
77	321	112	294	92	239	294	92	94
87	334	110	298	89	230	296	89	94
97	336	100	300	89	222	303	90	91
107	340	88	306	90	199	305	90	77
117	331	65	293	89	165	287	87	59
127	326	47	282	87	109	278	85	42
137	294	27	250	85	65	269	91	18

TABLE 7. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH)

Weeks on Study (from birth)	Untreated Control		DMH			Amosite + DMH		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors
MALE								
7	173	117	226	131	125	107	62	175
17	303	117	306	101	125	254	84	175
27	369	117	372	101	125	322	87	175
37	403	117	394	98	124	354	88	175
48	425	117	417	98	117	370	87	174
57	450	117	444	99	110	396	88	170
67	471	117	459	97	91	417	89	155
77	477	115	464	97	63	425	89	113
87	475	112	457	96	51	424	89	79
97	471	104	432	92	37	402	85	61
107	459	93	419	91	23	397	86	40
FEMALE								
7	123	117	154	125	125	92	75	175
17	185	117	181	98	125	162	88	175
27	212	117	209	99	125	195	92	175
37	222	117	217	98	120	200	90	175
48	241	117	239	99	115	217	90	173
57	260	117	260	100	108	236	91	166
67	295	116	281	95	88	260	88	150
77	321	112	300	93	63	281	88	109
87	334	110	294	88	43	281	84	78
97	336	100	293	87	20	284	85	46

TABLE 8. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH) COMPARED WITH THE POSITIVE CONTROLS

Weeks on Study (from birth)	DMH		Amosite + DMH		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of DMH)	No. of Survivors
MALE					
7	226	125	107	47	175
17	306	125	254	83	175
27	372	125	322	87	175
37	394	124	354	90	175
48	417	117	370	89	174
57	444	110	396	89	170
67	459	91	417	91	155
77	464	63	425	92	113
87	457	51	424	93	79
97	432	37	402	93	61
107	419	23	397	95	40
FEMALE					
7	154	125	92	60	175
17	181	125	162	90	175
27	209	125	195	93	175
37	217	120	200	92	175
48	239	115	217	91	173
57	260	108	236	91	166
67	281	88	260	93	150
77	300	63	281	94	109
87	294	43	281	96	78
97	293	20	284	97	46

TABLE 9. CUMULATIVE MEAN BODY WEIGHT CHANGE FOR RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH)

Weeks on Study (from birth)	Cumulative Mean Body Weight Change (grams)					Weight Change Relative to Controls			
	Untreated Control	DMH	Amosite	Amosite + DMH	Amosite + PW	DMH	Amosite	Amosite + DMH	Amosite + PW
MALE									
3	59	55	67	62	65	-6.8	13.6	5.1	10.2
7	106	102	127	124	120	-3.8	19.8	17.0	13.2
16	168	157	192	185	183	-6.5	14.3	10.1	8.9
25	218	208	237	233	232	-4.6	8.7	6.9	6.4
52	283	269	302	299	299	-4.9	6.7	5.7	5.7
FEMALE									
3	31	27	36	35	32	-12.9	16.1	12.9	3.2
8	57	45	67	61	61	-21.1	17.5	7.0	7.0
19	85	72	94	92	87	-15.3	10.6	8.2	2.4
39	112	103	129	125	119	-8.0	15.2	11.6	6.3
52	146	128	158	153	146	-12.3	8.2	4.8	0.0

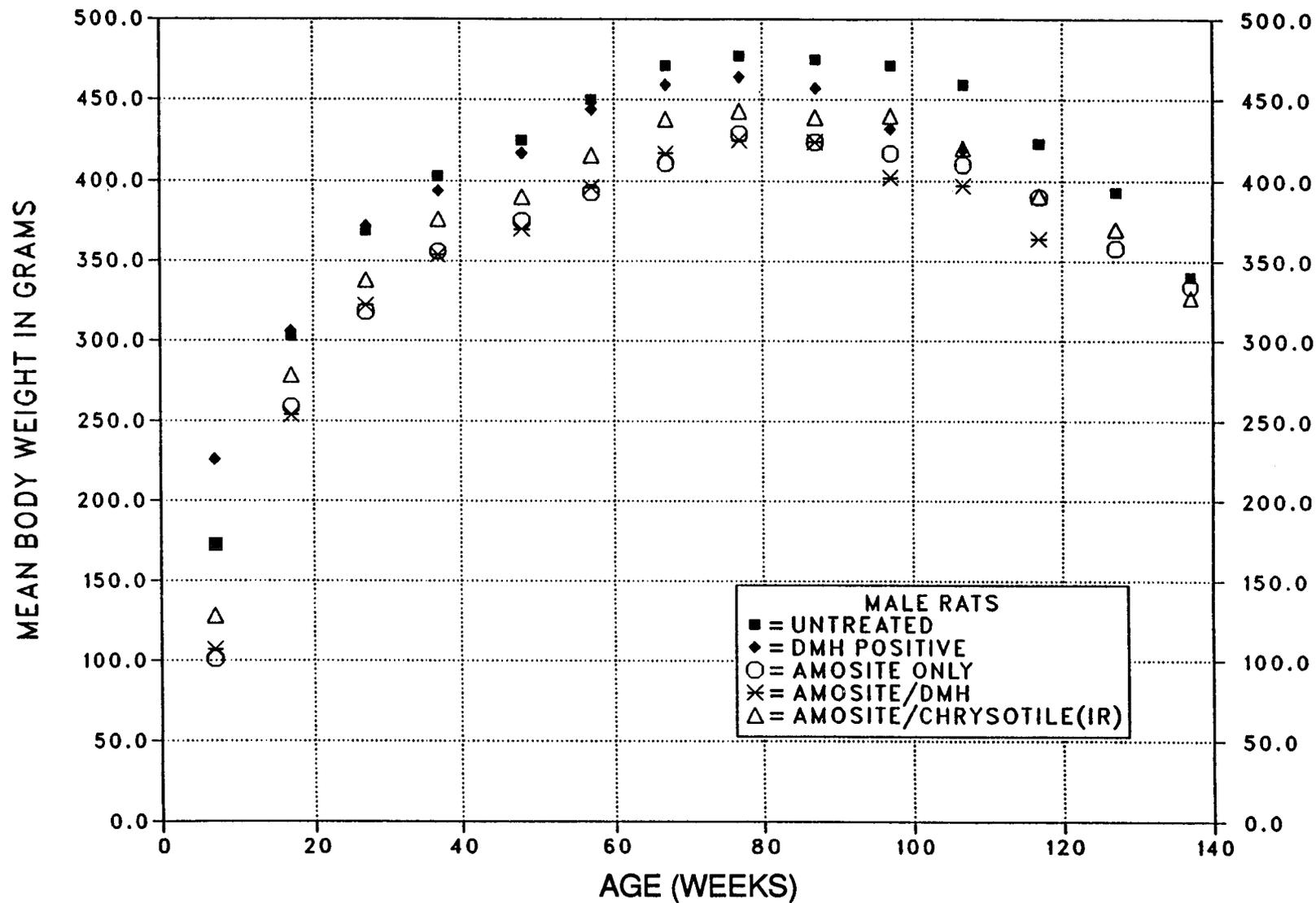


FIGURE 2. GROWTH CURVES FOR MALE RATS FED DIETS CONTAINING AMOSITE ASBESTOS IN LIFETIME STUDIES

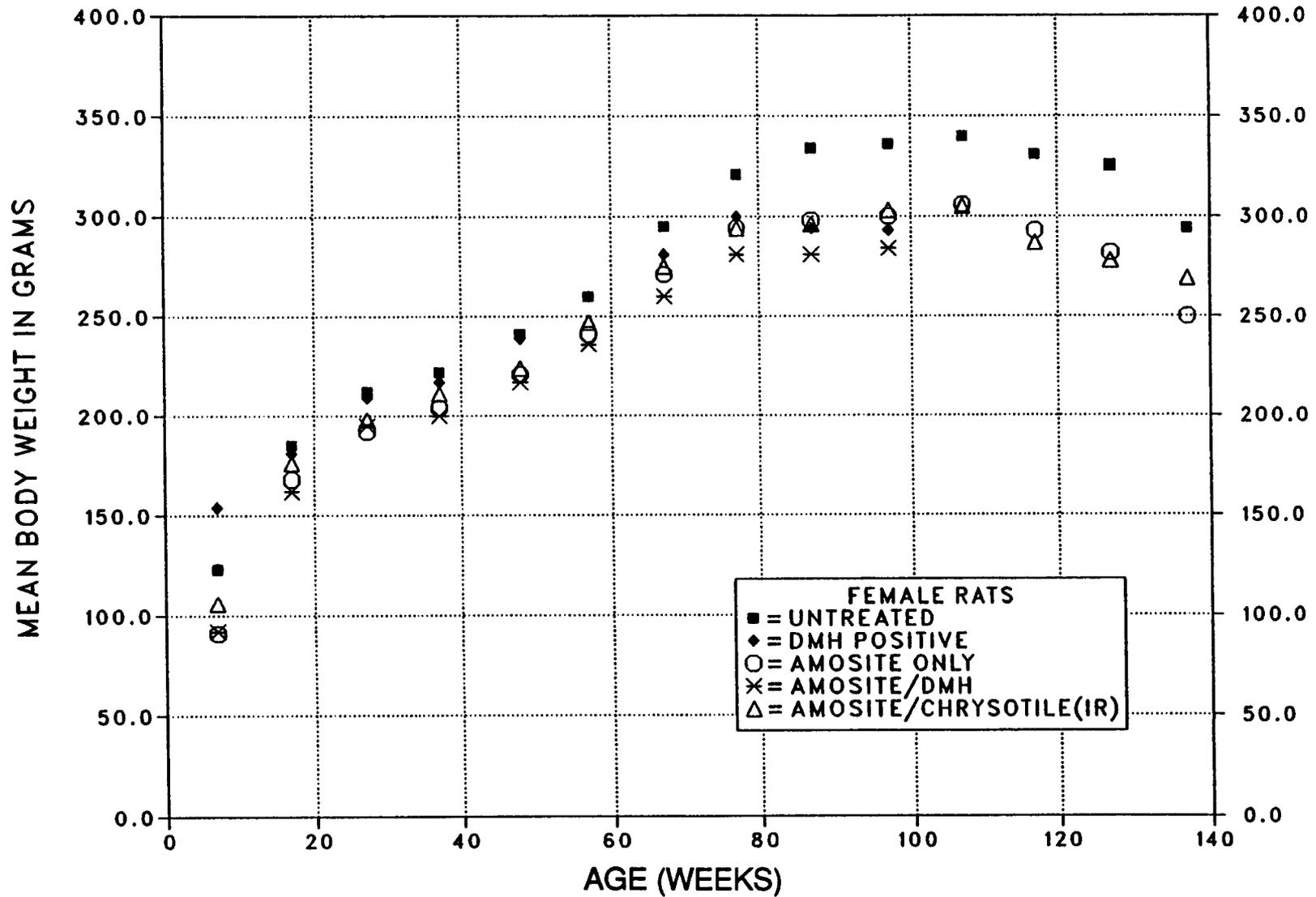


FIGURE 3. GROWTH CURVES FOR FEMALE RATS FED DIETS CONTAINING AMOSITE ASBESTOS IN LIFETIME STUDIES

III. RESULTS

Survival

Survival data are illustrated by the Kaplan and Meier curves in Figures 4 and 5. Survival relative to untreated controls at week 112 was somewhat greater for males in Group 3 (amosite) and somewhat lower in Group 5 (amosite + PW). In female rats, survival was greater than that of the untreated controls for both Groups 3

and 5. The survival of both groups of DMH-exposed rats (Groups 2 and 4) was considerably lower than that of the untreated controls. However, the survival of the amosite + DMH group was similar to that of the DMH-alone group.

Survival data at selected intervals before the final kill of all groups are summarized in Table 10.

TABLE 10. SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS AT VARIOUS TIME POINTS

Group	Age (weeks)	Male		Female	
		No. Alive/ Total No.	Survival (percent)	No. Alive/ Total No.	Survival (percent)
1 (control)	112	87/117	74	71/117	61
	126	45/117	38	50/117	43
	141	8/117	7	18/117	15
	145	--	--	13/117	11
2 (DMH)	112	16/125	13	0/125	0
	126	--	--	--	--
	141	--	--	--	--
	145	--	--	--	--
3 (amosite)	112	199/250	80	180/250	72
	126	134/250	54	115/250	46
	141	41/250	16	42/250	17
	145	--	--	30/250	12
4 (amosite + DMH)	112	32/175	18	0/175	0
	126	--	--	--	--
	141	--	--	--	--
	145	--	--	--	--
5 (amosite + PW)	112	62/100	62	69/100	69
	126	29/100	29	42/100	42
	141	8/100	8	14/100	14
	145	--	--	9/100	9

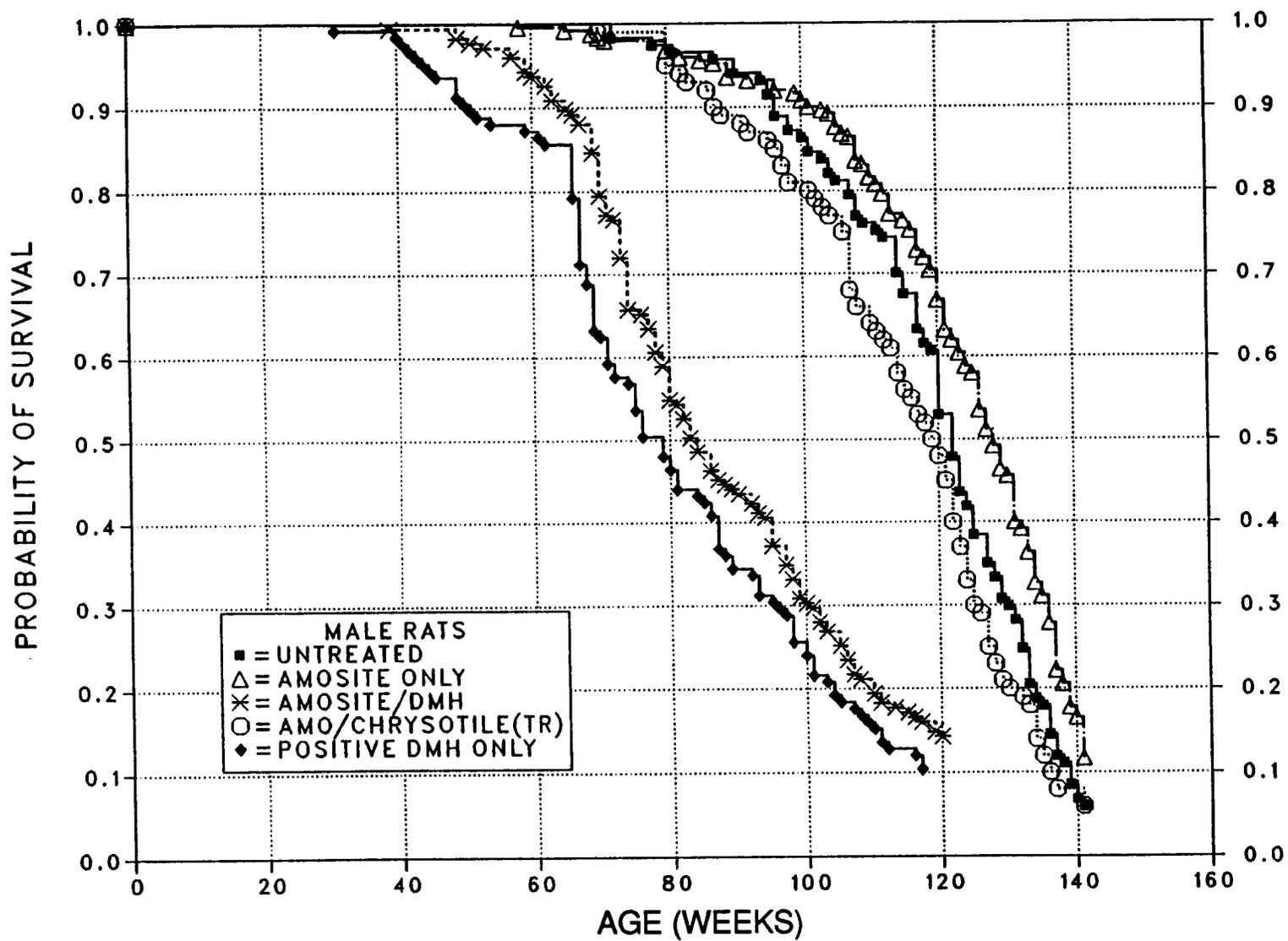


FIGURE 4. KAPLAN-MEIER SURVIVAL CURVES FOR MALE RATS FED DIETS CONTAINING AMOSITE ASBESTOS IN LIFETIME STUDIES

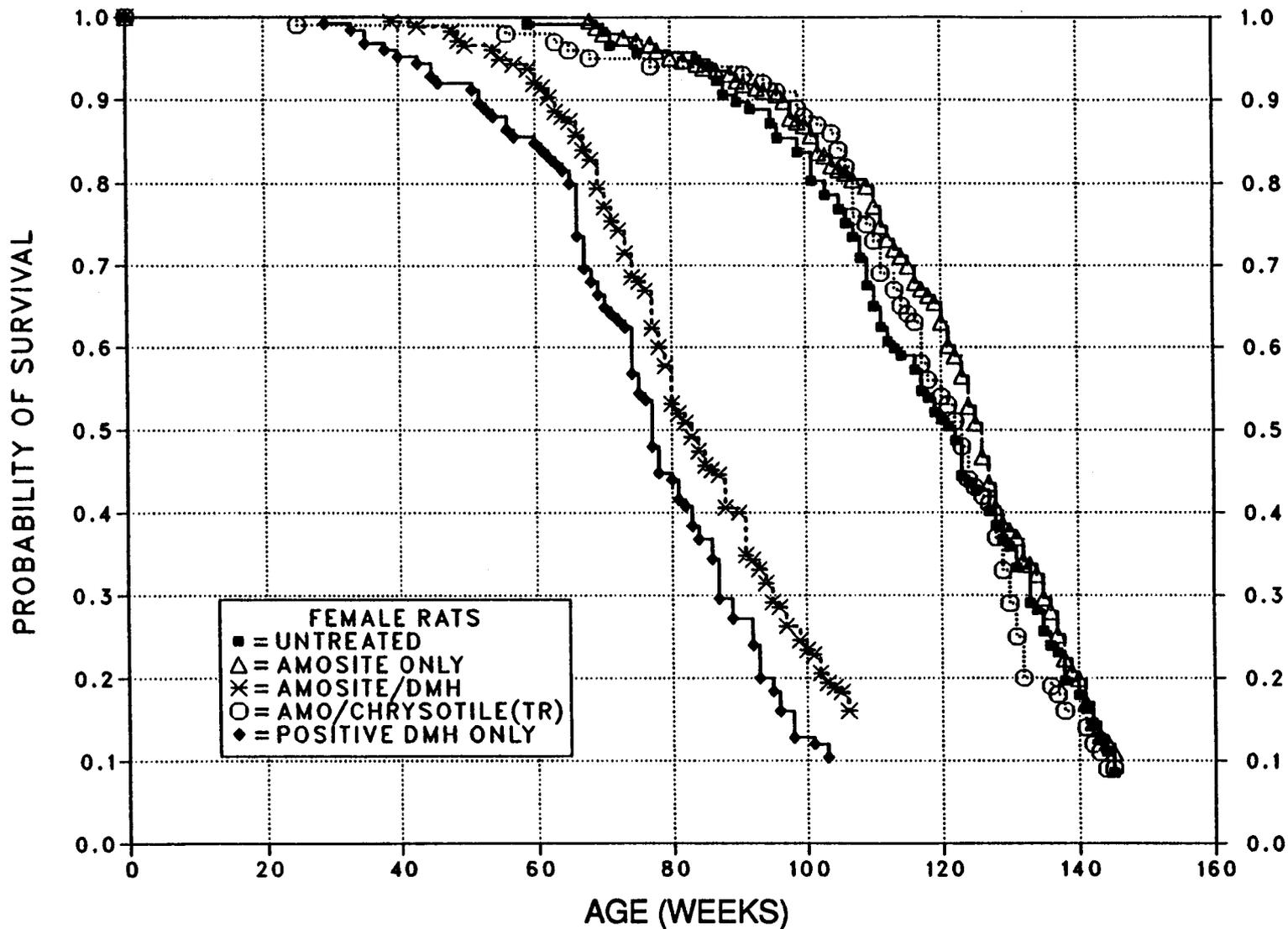


FIGURE 5. KAPLAN-MEIER SURVIVAL CURVES FOR FEMALE RATS FED DIETS CONTAINING AMOSITE ASBESTOS IN LIFETIME STUDIES

III. RESULTS

Pathology and Statistical Analyses of Results

This section describes the statistically significant or biologically noteworthy changes in the incidences of rats with neoplastic or nonneoplastic lesions. Only positive histopathologic findings based on hematoxylin- and eosin-stained sections are tabulated in the text. A few tissues were missing from occasional animals. Also, no diagnoses are given for several tissues in one male rat in Group 3 (amosite), two males in Group 4 (amosite + DMH), and one female in Group 2 (DMH) because of autolysis or cannibalization. Thus, the denominator for any particular organ, tissue, or lesion varies and does not necessarily represent the number of animals that were placed on study in each group. The severity of the lesions was graded but does not appear in the appendix tables.

Lesions in male and female rats are summarized in Appendixes A and B. Histopathologic findings on neoplasms are summarized in Tables A1 and B1. Tables A2 and B2 give the survival and

tumor status for individual male rats. Tables A3 and B3 contain the statistical analyses of those primary tumors that occurred with an incidence of at least 2% in one of the groups. The statistical analyses used are discussed in Section II (Statistical Methods) and Tables A3 and B3 (footnotes). Historical incidences of tumors in control male rats are listed in Tables A4 and B4. Findings on nonneoplastic lesions are summarized in Tables A5 and B5.

A variety of neoplasms was found in the control and various study groups, including monocytic (mononuclear cell) leukemia, endocrine tumors, testicular interstitial cell tumors, mammary gland neoplasms, and several types of skin neoplasms. Table 11 summarizes the total number of neoplasms in the amosite and amosite + PW groups compared with the number in the untreated controls. There were no obvious differences in the total incidence of benign or malignant neoplasms. Also, the average number of neoplasms per animal appears to be without relationship to exposure.

TABLE 11. INCIDENCE OF PRIMARY NEOPLASMS IN RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

	Untreated Control	Amosite	Amosite + PW
MALE			
No. of animals examined	117	250	100
Total animals with primary tumors	116 (99%)	249 (>99%)	99 (99%)
Total primary tumors	(a) 402 (3.5)	(a) 841 (3.4)	(a) 310 (3.1)
Total animals with benign tumors	115 (98%)	244 (98%)	95 (95%)
Total benign tumors	(a) 277 (2.4)	(a) 547 (2.2)	(a) 192 (2.0)
Total animals with malignant tumors	82 (70%)	201 (80%)	84 (84%)
Total malignant tumors	(a) 116 (1.4)	(a) 284 (1.4)	(a) 113 (1.3)
FEMALE			
No. of animals examined	117	250	100
Total animals with primary tumors	113 (97%)	240 (96%)	98 (98%)
Total primary tumors	(a) 316 (2.8)	(a) 663 (2.8)	(a) 247 (2.5)
Total animals with benign tumors	99 (85%)	213 (85%)	79 (79%)
Total benign tumors	(a) 204 (2.1)	(a) 419 (2.0)	(a) 152 (1.9)
Total animals with malignant tumors	74 (63%)	166 (66%)	68 (68%)
Total malignant tumors	(a) 106 (1.4)	(a) 230 (1.4)	(a) 89 (1.3)

(a) Average number of tumors per tumor-bearing animal is in parentheses.

Gastrointestinal Tract Neoplasms

The gastrointestinal tract was examined in detail as described in the Materials and Methods section. Neoplasms were classed as to morphologic type according to the following criteria (Pozharisski, 1975).

Stomach: Squamous cell papillomas occurred in the forestomach (nonglandular) as exophytic growths of epithelium resting on a proliferative connective tissue stalk. Squamous cell carcinomas were characterized by proliferating small basophilic squamous cells that were invading the lamina propria and occasionally formed keratin pearls.

Intestinal tract neoplasms: The induced primary epithelial neoplasms were separated into three major types, based on morphology and biologic behavior: adenomatous polyps, adenocarcinoma arising in an adenomatous polyp, and carcinomas.

*Adenomatous polyps--*The adenomatous polyps were exophytic lesions of the mucosa supported on a pedicle of fibrous tissue and/or elevated submucosa which appeared to extend up into the growth. The epithelial cells were usually deeply basophilic and hypertrophic and formed glands of varying sizes. Surface necrosis of these lesions was common and often was accompanied by an inflammatory response. Invasion of the pedicle was not observed. These polyps often occurred as multiple neoplasms in the large intestine.

*Adenocarcinoma arising in an adenomatous polyp--*These neoplasms were exophytic lesions of the mucosa composed of proliferating, deeply basophilic hypertrophic epithelial cells similar to those previously mentioned. In addition, they often showed disorganization, loss of relationship to the basement membrane, and abnormal mitoses. Local invasion of the pedicle was a consistent finding; however, metastases were rarely observed.

*Carcinomas--*This classification includes signet ring cell carcinoma, adenocarcinoma, mucinous cystadenocarcinoma, and carcinoma. Biologically, all were similar and were usually characterized by transmural growth that penetrated the muscular tunics and serosa and spread through-

out the coelomic cavity inducing a severe desmoplastic response. Metastasis to regional lymph nodes was common; metastasis to the lung and mediastinum occurred to a lesser extent. Grossly, in advanced cases, the loops of intestines were fused into an inseparable mass of tumor and desmoplastic tissue. Classification was based on the most prominent feature at the primary site. Signet ring cell carcinomas were composed of masses of signet ring cells. Mucinous cystadenocarcinomas were characterized by the formation of multiple large ectatic glands or spaces that were filled with mucus and cellular debris. Adenocarcinomas consisted of clusters of cells and/or glands in pools of mucus or sequestered in desmoplastic tissue. The carcinomas were anaplastic neoplasms lacking acinar formations. In some cases, there was an overlap of cell types in the same tumor, suggesting that the above morphologic types probably have the same histogenesis.

Amosite was given to two groups of male and female rats. One group (amosite group) was exposed from weaning throughout life. The second group received chrysotile asbestos (by mistake) beginning at birth by preweaning gavage and then amosite in feed from weaning throughout the lifespan (amosite + PW group).

There were no apparent exposure-related neoplasms in the digestive tract of either the amosite or amosite + PW groups (Table 12). Neoplasms of the same morphologic types (adenomatous polyp, signet ring carcinoma, and adenocarcinoma) as described in the DMH groups were observed at a low incidence in the gastrointestinal tract of both control and amosite-exposed rats. However, no specific type was increased, either at a particular location (e.g., cecum) or in the stomach or small or large intestine as a whole.

In addition, the incidences of nonneoplastic diseases of the gastrointestinal tract such as enteritis, diverticulitis, ulceration, or inflammation in general were comparable in the control and amosite-exposed rats (Table 13).

Tissues that showed an increase in neoplasms in one or both amosite groups compared with untreated controls were the thyroid gland, mammary gland, and hematopoietic system.

TABLE 12. PRIMARY EPITHELIAL NEOPLASMS OF GASTROINTESTINAL TRACT IN RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Site/Lesion	Male			Female		
	Untreated Control	Amosite	Amosite + PW	Untreated Control	Amosite	Amosite + PW
Animals examined	117	250	100	117	250	100
Total gastrointestinal	4 (4%)	7 (3%)	3 (3%)	2 (2%)	4 (2%)	3 (3%)
Total stomach	1 (1%)	2 (1%)	0 (0%)	1 (1%)	1 (<1%)	0 (0%)
Total small intestine	3 (3%)	1 (1%)	1 (1%)	0 (0%)	3 (1%)	1 (1%)
Duodenum						
Carcinoma			1 (1%)		1 (<1%)	
Jejunum						
Carcinoma	2 (2%)					1 (1%)
Adenocarcinoma arising in adenomatous polyp		1 (<1%)				
Adenomatous polyp					2 (1%)	
Ileum						
Adenomatous polyp	1 (1%)					
Total large intestine	0 (0%)	4 (2%)	2 (2%)	1 (1%)	0 (0%)	2 (2%)
Cecum						
Carcinoma						
Adenocarcinoma arising in adenomatous polyp						
Adenomatous polyp			1 (1%)			
Total colon	0 (0%)	4 (2%)	1 (1%)	1 (1%)	0 (0%)	2 (2%)
Ascending colon						
Carcinoma		1 (<1%)				
Transverse colon						
Carcinoma						1 (1%)
Descending colon						
Carcinoma						
Adenocarcinoma arising in adenomatous polyp			1 (1%)			
Adenomatous polyp		2 (1%)		1 (1%)		1 (1%)
Colon (specific portion not identified)						
Adenomatous polyp		1 (<1%)				

TABLE 13. NUMBERS OF RATS WITH NONNEOPLASTIC LESIONS OF ALIMENTARY TRACT IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS (a)

Site/Lesion	Male			Female		
	Untreated Control	Amosite	Amosite + PW	Untreated Control	Amosite	Amosite + PW
Tongue (no. examined)	117	249	100	117	250	100
Esophagus (no. examined)	115	248	100	117	246	100
Hyperkeratosis	12 (10%)	4 (2%)	12 (12%)	7 (6%)	7 (3%)	6 (6%)
Nonglandular stomach (no. examined)	117	250	100	117	250	100
Mineralization	9 (8%)	2 (1%)	1 (1%)	3 (3%)	2 (1%)	0 (0%)
Chronic inflammation	20 (17%)	57 (22%)	17 (17%)	22 (19%)	59 (24%)	18 (18%)
Ulceration	13 (11%)	25 (10%)	7 (7%)	4 (3%)	30 (12%)	10 (10%)
Necrosis	23 (20%)	41 (16%)	15 (15%)	14 (12%)	40 (16%)	12 (12%)
Hyperkeratosis	22 (19%)	41 (16%)	16 (16%)	24 (21%)	56 (22%)	17 (17%)
Acanthosis	31 (26%)	62 (25%)	21 (21%)	26 (22%)	72 (29%)	23 (23%)
Muscle degeneration	8 (7%)	3 (1%)	0 (0%)	2 (2%)	3 (1%)	0 (0%)
Glandular stomach (no. examined)	117	250	100	117	250	100
Hyperplasia	6 (5%)	0 (0%)	0 (0%)	2 (2%)	1 (<1%)	0 (0%)
Duodenum (no. examined)	117	250	100	117	249	100
Jejunum (no. examined)	117	250	100	117	249	100
Ileum (no. examined)	117	250	100	117	249	100
Colon (no. examined)	117	250	100	117	250	100
Parasitism	4 (3%)	17 (7%)	4 (4%)	2 (2%)	6 (2%)	8 (8%)
Cecum (no. examined)	117	250	100	117	250	100
Rectum (no. examined)	117	250	100	117	250	100
Anus (no. examined)	117	250	100	117	250	100

(a) Incidence of nonneoplastic lesions that occurred with a frequency of 2% or more in at least one group

Thyroid Gland: Table 14 summarizes the incidences of C-cell proliferative lesions. A significantly increased incidence of C-cell carcinomas was found in amosite-exposed male rats. This effect was not observed in amosite + PW male rats. Furthermore, the overall incidence of C-cell neoplasms (adenomas and/or carcinomas) were similar in control and exposed groups. C-Cell hyperplasia was minimally increased in amosite and amosite + PW female groups.

Hematopoietic System: A significantly increased incidence of monocytic (synonym--mononuclear cell, Fischer rat) leukemia occurred in amosite (P<0.05) and amosite + PW (P<0.01) male rats (Table 15). Statistical significance was lost for the amosite groups when evaluated using life

table analysis; however, the incidence for amosite + PW was still significant using this method. This increased incidence was not observed in exposed female rats.

Miscellaneous Neoplasms: Occasionally, a somewhat higher rate of commonly occurring neoplasms were observed in exposed groups (Tables 16 and 17). A statistically significant (P<0.05) decrease in the rate of neoplasms was observed in the pancreas (islet cell adenoma), adrenal medulla (pheochromocytoma), thyroid gland (follicular cell carcinoma), mammary gland, parathyroid gland, and preputial gland in at least one group of amosite-exposed rats compared with the controls.

TABLE 14. NUMBERS OF RATS WITH THYROID GLAND C-CELL PROLIFERATIVE LESIONS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

	Untreated Control	Amosite	Amosite + PW
MALE			
Hyperplasia	21/117 (18%)	58/246 (24%)	23/100 (23%)
Adenoma	16/117 (14%)	26/246 (11%)	11/100 (11%)
Carcinoma	11/117 (9%)	50/246 (20%)	14/100 (14%)
FEMALE			
Hyperplasia	22/116 (19%)	71/247 (29%)	26/100 (26%)
Adenoma	14/116 (12%)	37/247 (15%)	15/100 (15%)
Carcinoma	10/116 (9%)	29/247 (12%)	14/100 (14%)

*P<0.05 vs. controls (incidental tumor and Fisher exact tests)

TABLE 15. NUMBERS OF RATS WITH MONOCYTIC LEUKEMIA IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Site/Lesion	Male			Female		
	Untreated Control	Amosite	Amosite + PW	Untreated Control	Amosite	Amosite + PW
Number of animals examined	117	249	100	117	250	100
Monocytic leukemia	36 (31%)	103(41%)*	47(47%)**	39(33%)	78(31%)	33(33%)

*P<0.05 vs. controls (incidental tumor and Fisher exact tests)

**P<0.01 vs. controls (incidental tumor and Fisher exact tests)

TABLE 16. INCIDENCE OF PRIMARY NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (a)

	Untreated Control	Amosite	Amosite + PW
Integumentary system			
Squamous cell papilloma	1/117 (1%)	6/250 (2%)	5/100 (5%)
Squamous cell carcinoma	1/117 (1%)	4/250 (2%)	1/100 (1%)
Basal cell carcinoma	3/117 (3%)	7/250 (3%)	4/100 (4%)
Keratoacanthoma	4/117 (3%)	17/250 (7%)	2/100 (2%)
Sarcoma, NOS	4/117 (3%)	2/250 (1%)	5/100 (5%)
Fibroma	18/117 (15%)	33/250 (13%)	11/100 (11%)
Fibrosarcoma	7/117 (6%)	9/250 (4%)	1/100 (1%)
Lipoma	2/117 (2%)	2/250 (1%)	1/100 (1%)
Neurofibroma	3/117 (3%)	5/250 (2%)	0/100 (0%)
Lung			
Alveolar/bronchiolar carcinoma	1/117 (1%)	6/249 (2%)	4/100 (4%)
Circulatory system			
Hemangiosarcoma	1/117 (1%)	2/50 (1%)	2/100 (2%)
Liver			
Neoplastic nodule	9/117 (8%)	9/250 (4%)	5/100 (5%)
Hepatocellular carcinoma	1/117 (1%)	3/250 (1%)	3/100 (3%)
Pancreas			
Acinar cell adenoma	9/116 (8%)	19/247 (8%)	2/100 (2%)
Kidney			
Tubular cell tumor	0/117 (0%)	3/248 (1%)	2/100 (2%)
Mixed tumor	0/117 (0%)	1/249 (<1%)	2/100 (2%)
Pituitary gland			
Adenoma	24/117 (21%)	41/248 (17%)	19/99 (19%)
Carcinoma	2/117 (2%)	4/248 (2%)	2/99 (2%)
Adrenal gland			
Cortical adenoma	0/117 (0%)	5/250 (2%)	2/100 (2%)
Pheochromocytoma, benign	39/117 (33%)	† 65/250 (26%)	† 21/100 (21%)
Pheochromocytoma, malignant	3/117 (3%)	5/250 (2%)	0/100 (0%)
Thyroid gland			
Follicular cell adenoma	4/117 (3%)	13/246 (5%)	8/100 (8%)
Follicular cell carcinoma	7/117 (6%)	10/246 (4%)	4/100 (4%)
Parathyroid gland			
Adenoma	4/110 (4%)	† 1/234 (<1%)	1/99 (1%)
Pancreatic islet			
Islet cell adenoma	14/116 (12%)	17/247 (7%)	† 4/100 (4%)
Islet cell carcinoma	3/116 (3%)	5/247 (2%)	4/100 (4%)
Preputial gland			
Squamous cell carcinoma	0/117 (0%)	1/250 (0%)	† 0/100 (0%)
Testis			
Interstitial cell tumor	111/117 (95%)	240/249 (96%)	92/100 (92%)
Cerebrum			
Astrocytoma	2/117 (2%)	2/250 (1%)	2/100 (2%)
Zymbal gland			
Carcinoma	1/117 (1%)	7/250 (3%)	3/100 (3%)
All sites			
Malignant mesothelioma	2/117 (2%)	9/250 (4%)	3/100 (3%)
Mammary gland			
Adenoma	3/117 (3%)	4/250 (2%)	0/100 (0%)
Fibroadenoma	17/117 (15%)	27/250 (11%)	† 1/100 (1%)
Adenocarcinoma	1/117 (1%)	1/250 (<1%)	0/100 (0%)

(a) Incidence of neoplasms (other than those already noted) that occurred with an incidence of at least 2% in at least one group.
† P < 0.05 (decrease) relative to controls (incidental tumor and Fisher exact test)

TABLE 17. SUMMARY OF PRIMARY NEOPLASM INCIDENCE IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (a)

	Untreated Control	Amosite	Amosite + PW
Integumentary system			
Squamous cell papilloma	2/117 (2%)	3/250 (1%)	0/100 (0%)
Sarcoma, NOS	0/117 (0%)	6/250 (2%)	1/100 (1%)
Fibroma	7/117 (6%)	8/250 (3%)	3/100 (3%)
Fibrosarcoma	3/117 (3%)	5/250 (2%)	1/100 (1%)
Lipoma	3/117 (3%)	2/250 (1%)	0/100 (0%)
Liver			
Neoplastic nodule	4/117 (3%)	10/250 (4%)	4/100 (4%)
Pancreas			
Acinar cell adenoma	2/116 (2%)	0/249 (0%)	0/100 (0%)
Pituitary gland			
Adenoma	50/117 (43%)	107/249 (43%)	39/100 (39%)
Carcinoma	2/117 (2%)	11/249 (4%)	3/100 (3%)
Adrenal gland			
Cortical adenoma	3/117 (3%)	13/249 (5%)	4/100 (4%)
Pheochromocytoma	17/117 (15%)	27/249 (11%)	† 6/100 (6%)
Thyroid gland			
Follicular cell adenoma	2/116 (2%)	10/247 (4%)	3/100 (3%)
Follicular cell carcinoma	7/116 (6%)	† 3/247 (1%)	2/100 (2%)
Pancreatic Islets			
Islet cell adenoma	2/116 (2%)	7/249 (3%)	1/100 (1%)
Islet cell carcinoma	3/116 (3%)	7/249 (3%)	0/100 (0%)
Clitoral gland			
Squamous cell carcinoma	6/117 (5%)	14/250 (6%)	7/100 (7%)
Uterus			
Endometrial stromal polyp	13/117 (11%)	31/250 (12%)	14/100 (14%)
Endometrial stromal sarcoma	5/117 (4%)	4/250 (2%)	0/100 (0%)
Ovary			
Granulosa cell tumor	1/117 (1%)	3/250 (1%)	2/100 (2%)
Brain			
Astrocytoma	4/117 (3%)	4/250 (2%)	2/100 (2%)
Zymbal gland			
Squamous cell carcinoma	3/117 (3%)	4/250 (2%)	3/100 (3%)
Mammary gland			
Adenoma	8/117 (7%)	14/250 (6%)	5/100 (5%)
Fibroadenoma	72/117 (62%)	† 135/250 (54%)	† 52/100 (52%)
Adenocarcinoma	6/117 (5%)	25/250 (10%)	7/100 (7%)

(a) Incidence of neoplasms (other than those already noted) that occurred with an incidence of at least 2% in at least one group.
 † P < 0.05 (decrease) relative to controls (incidental tumor and Fisher exact test)

Nonneoplastic Findings

A plethora of incidental lesions of aging F344 rats was found in all groups. Statistical analyses showed no obvious correlation between the incidence of specific lesion types and the type of exposure. Histopathologic findings are summarized in Appendixes A and B. Nonneoplastic lesions that were observed in more than 2% of the rats in any of the study groups are as follows (alimentary tract nonneoplastic lesions are noted in Table 13):

1. Skin--epidermal inclusion cyst
2. Lung--chronic inflammation
3. Spleen--fibrosis, hemosiderosis, extramedullary hematopoiesis, lymphoid atrophy
4. Lymph nodes (various)--lymphoid or reticulum cell hyperplasia, lymphangiectasis, hemorrhage, pigmentation, chronic inflammation
5. Heart--chronic inflammation
6. Liver--degeneration, necrosis, fatty metamorphosis, toxic hepatitis, granuloma, angiectasis, pigmentation, focal cellular change
7. Bile duct (extrahepatic)--chronic inflammation, mucosal hyperplasia, cysts, fibrosis
8. Pancreas (exocrine)--atrophy, hyperplasia, ectopia; (endocrine)--hyperplasia
9. Kidney--chronic progressive nephropathy, cysts, pigmentation
10. Pituitary gland--cysts, angiectasis, hyperplasia
11. Adrenal gland--fatty metamorphosis, hyperplasia
12. Adrenal medulla--hyperplasia
13. Thyroid gland--follicular cysts, C-cell hyperplasia
14. Parathyroid gland--hyperplasia
15. Testes--seminiferous degeneration, interstitial cell hyperplasia
16. Prostate--abscess, chronic inflammation, glandular hyperplasia
17. Seminal vesicles--cysts
18. Ovary--follicular and parovarian cysts
19. Uterus--hydrometra, endometrial cyst
20. Mammary gland--cystic ducts, glandular hyperplasia, galactocele

21. Mesentery--chronic inflammation
22. Eye--cataract, hemorrhage, inflammation, retinal degeneration
23. Zymbal gland--cystic ducts
24. Bone--osteopetrosis, exostoses, marrow hyperplasia

1,2-Dimethylhydrazine Dihydrochloride Dosed Groups

Two groups of male and female rats were exposed to DMH by gavage at doses of 7.5 mg/kg for males and 15 mg/kg for females, two times per week for a total of five doses. One group served as a positive carcinogen control, and the other received amosite asbestos in feed from weaning throughout life.

Exposure of rats to DMH or amosite + DMH was associated with a dramatically increased incidence of neoplasms of the intestinal tract, Zymbal gland, and liver in male and female rats and kidney in female rats.

Table 18 summarizes the incidence of primary neoplasms in rats exposed to DMH and amosite + DMH. There were no obvious differences in the total number of animals with primary neoplasms. However, there were more animals with malignant neoplasms and fewer with benign tumors in the DMH and amosite + DMH groups than in the untreated controls. It is also noteworthy that survival in the DMH groups was shortened due to the presence of lethal gastrointestinal neoplasms.

Table 19 summarizes the numbers of rats with primary epithelial neoplasms in the gastrointestinal tract by specific site and classification. Intestinal neoplasms, particularly the adenomatous polyps, were often multiple within a given animal.

The incidence of gastrointestinal neoplasia was dramatically increased with DMH exposure. However, the incidence appeared to be essentially similar in groups receiving DMH alone and those receiving amosite + DMH. Furthermore, the number of animals with tumors in either the small intestine or large intestine was

TABLE 18. INCIDENCE OF PRIMARY NEOPLASMS IN RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH)

	Untreated Control	DMH	Amosite + DMH
MALES			
Number of animals examined	117	125	175
Animals with primary tumors	116 (99%)	125 (100%)	173 (99%)
Total primary tumors (a)	402 (3.5)	357 (2.9)	554 (3.2)
Animals with benign tumors	115 (98%)	93 (74%)	150 (86%)
Total benign tumors (a)	277 (2.4)	174 (1.9)	295 (2.0)
Animals with malignant tumors	82 (70%)	110 (88%)	149 (85%)
Total malignant tumors (a)	116 (1.4)	165 (1.5)	231 (1.6)
FEMALES			
Number of animals examined	117	125	175
Animals with primary tumors	113 (97%)	121 (97%)	175 (100%)
Total primary tumors (a)	316 (2.8)	326 (2.7)	477 (2.7)
Animals with benign tumors	99 (85%)	74 (59%)	102 (58%)
Total benign tumors (a)	204 (2.1)	105 (1.4)	172 (1.7)
Animals with malignant tumors	74 (63%)	111 (89%)	164 (94%)
Total malignant tumors (a)	106 (1.4)	192 (1.7)	272 (1.7)

(a) Average number of tumors per animal is in parentheses

also essentially similar in groups receiving DMH alone and those receiving amosite + DMH. There was no difference between groups in time to tumor.

Evaluation of the incidence of the three categories of intestinal neoplasia (carcinoma, adenocarcinoma arising in an adenomatous polyp, and adenomatous polyp) by site reveals an increased incidence of duodenal carcinomas ($P < 0.01$) in the amosite + DMH exposed females compared with that in female rats receiving DMH alone. In the jejunum, however, this incidence is reversed, with more carcinomas ($P < 0.01$) occurring in the female group receiving DMH alone.

In the large intestine, the frequency of adenomatous polyps and carcinomas arising in an adenomatous polyp was greatest in the descending colon. In the cecum of male rats, the incidence of carcinomas was lower in the amosite + DMH-exposed group than in those exposed to DMH alone. This effect was not observed in the female group. The appearance of carcinomas in the ascending colon was somewhat greater in amosite + DMH-exposed males than in males receiving DMH alone. Adenocarcinomas arising in an adenomatous polyp occurred more frequently in the transverse colon of male and female rats receiving amosite + DMH compared with rats receiving DMH alone.

TABLE 19. NUMBER OF PRIMARY EPITHELIAL NEOPLASMS OF THE GASTROINTESTINAL TRACT IN RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS AND 1,2-DIMETHYLHYDRAZINEDIHYDROCHLORIDE (DMH)

Site/Lesion	Untreated Control		DMH		Amosite + DMH	
	Male	Female	Male	Female	Male	Female
Animals examined	117	117	125	125	175	175
Total gastrointestinal (a)	4 (4%)	2 (2%)	91 (73%)	77 (62%)	117 (67%)	114 (65%)
Total stomach	1 (1%)	1 (1%)	0 (0%)	3 (3%)	2 (1%)	1 (1%)
Total small intestine	3 (3%)	0 (0%)	16 (13%)	14 (11%)	18 (10%)	23 (13%)
Duodenum						
Adenomatous polyp					1 (1%)	
Carcinoma			11 (9%)	3 (2%)	14 (8%)	19 (11%)
Jejunum						
Adenomatous polyp			1 (1%)			
Carcinoma	2 (2%)		2 (2%)	11 (9%)	3 (2%)	2 (1%)
Adenocarcinoma in adenomatous polyp						1 (1%)
Ileum						
Adenomatous polyp	1 (1%)					
Carcinoma			2 (1%)			
Adenocarcinoma in adenomatous polyp						1 (1%)
Total large intestine (a)	0 (0%)	1 (1%)	81 (65%)	70 (56%)	109 (62%)	101 (58%)
Cecum						
Adenomatous polyp					2 (1%)	
Carcinoma			16 (13%)	7 (6%)	6 (3%)	6 (3%)
Ascending colon						
Adenomatous polyp			5 (4%)	7 (6%)	5 (3%)	8 (5%)
Carcinoma			10 (8%)	10 (8%)	20 (12%)	14 (8%)
Adenocarcinoma in adenomatous polyp			2 (2%)	4 (3%)	3 (2%)	7 (4%)
Transverse colon						
Adenomatous polyp			9 (7%)	6 (5%)	21 (12%)	22 (13%)
Carcinoma			1 (1%)		2 (1%)	2 (1%)
Adenocarcinoma in adenomatous polyp			8 (6%)	9 (7%)	20 (11%)	20 (11%)
Descending colon						
Adenomatous polyp		1 (1%)	32 (26%)	27 (22%)	41 (23%)	31 (18%)
Carcinoma				1 (1%)	3 (2%)	2 (1%)
Adenocarcinoma in adenomatous polyp			21 (17%)	15 (12%)	26 (15%)	22 (13%)
Colon (specific portion not identified)						
Adenomatous polyp			1 (1%)	1 (1%)		
Carcinoma				4 (3%)	2 (1%)	3 (2%)
Adenocarcinoma in adenomatous polyp			1 (1%)			
Rectum						
Adenomatous polyp						1 (1%)

(a) Number of animals with tumors

III. RESULTS

Kidney Neoplasms: Almost without exception, the renal masses associated with DMH exposure were malignant mesenchymal or mixed malignant tumors. Purely mesenchymal growths were classified according to their morphology (e.g., fibrosarcoma, undifferentiated sarcoma). Those having epithelial elements or epithelial-like elements were classified as mixed malignant tumors. In early stages, these neoplasms appeared as interstitial sclerosing growths near the inner cortex. Collagen formation was accompanied by proliferating, basophilic, primitive-appearing cells. Epithelial elements consisted of glands, ductlike structures, or poorly differentiated solid tubules. The growths were often massive but rarely metastasized.

Table 20 summarizes the incidence of kidney tumors in control and DMH groups. The high incidence of renal neoplasms was confined almost exclusively to exposed female rats receiving either DMH alone or amosite + DMH ($P < 0.01$). The incidence for the two exposed female groups was the same. Renal neoplasms occurred infrequently in male rats.

Zymbal Gland Neoplasms: Squamous cell carcinoma was the most commonly observed neoplasm in Zymbal glands. These neoplasms were composed of proliferating eosinophilic to basophilic squamous epithelial cells which formed thick fingers of tissue, masses of keratin, and nests of sequestered cells. Some had sebaceous features with formation of sebum but nevertheless were classified as squamous cell carcinomas. Infiltration of adjacent tissues was occasionally observed; however, metastases were rare. Other types of tumors present in the Zymbal gland included squamous cell papillomas and keratoacanthoma. These types of neoplasms are a continuum in their progression from benign to malignant, and for this reason, the total number of tumors of this organ is probably the most valid way of comparing exposure effects. Table 21

summarizes the number of control and DMH-exposed rats with Zymbal gland neoplasms.

Approximately one-fourth of all rats receiving DMH alone or amosite + DMH developed Zymbal gland neoplasms ($P < 0.01$), whereas in untreated control animals, the occurrence was low (1%-3%). The incidence appeared essentially similar in the two DMH-exposed groups.

Liver Neoplasms: The classification of hepatocellular proliferative lesions was based on the ILAR Monograph (1980). Table 22 summarizes the number of control and DMH-exposed rats with neoplastic nodules or hepatocellular carcinomas.

A significantly increased incidence of neoplastic nodules and/or hepatocellular carcinomas occurred in groups receiving DMH alone and in groups receiving amosite + DMH. Generally, females had a greater incidence ($P < 0.01$) than males ($P < 0.05$). These neoplasms were first observed in male rats at weeks 101 (DMH) and 69 (amosite + DMH) and in female rats at weeks 60 (DMH) and 59 (amosite + DMH).

Miscellaneous Neoplasms: In several instances, DMH exposure with or without amosite led to statistically significant decreased incidences of certain spontaneous neoplasms when compared with the untreated controls, particularly of the endocrine system (Tables A3b and B3b). These included a reduced number of subcutaneous fibromas and mammary gland tumors; pituitary gland adenomas in females; and adrenal pheochromocytomas, pancreatic acinar cell adenomas, islet cell tumors, and testis interstitial cell tumors in males. No significant differences were observed between the DMH and amosite + DMH groups at any anatomic site other than the kidney (Table 23). Many animals in these two groups died at an early date compared with the controls.

TABLE 20. KIDNEY NEOPLASMS IN RATS IN THE TWO-YEAR FEED STUDIES OF AMOSITE ASBESTOS AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH)

	Untreated Control	DMH	Amosite + DMH
MALE			
	0/117 (0%)	3/125 (2%)	4/173 (2%)
FEMALE			
	1/117 (1%)	** 40/124 (32%)	** 56/175 (32%)

** P<0.01 vs controls (life table and incidental tumor test)

TABLE 21. ZYMBAL GLAND NEOPLASMS IN RATS IN THE TWO-YEAR FEED STUDIES OF AMOSITE ASBESTOS AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH)

	Untreated Control	DMH	Amosite + DMH
Number examined	117	125	175
MALE			
Squamous cell papilloma	0 (0%)	** 7 (6%)	** 17 (10%)
Carcinoma, NOS	1 (1%)	** 23 (18%)	** 35 (20%)
FEMALE			
Squamous cell papilloma	0 (0%)	** 12 (10%)	** 14 (8%)
Carcinoma, NOS	3 (3%)	** 20 (16%)	* 23 (13%)

* P<0.05 vs controls (life table and incidental tumor test)

** P<0.01 vs controls (life table and incidental tumor test)

TABLE 22. LIVER NEOPLASMS IN RATS IN THE TWO-YEAR FEED STUDIES OF AMOSITE ASBESTOS AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH)

	Untreated Control	DMH	Amosite + DMH
Number examined	117	125	175
MALE			
Neoplastic nodule	9 (8%)	** 18 (14%)	** 27 (15%)
Hepatocellular carcinoma	1 (1%)	** 9 (7%)	* 7 (4%)
FEMALE			
Neoplastic nodule	4 (3%)	** 29 (23%)	** 32 (18%)
Hepatocellular carcinoma	1 (1%)	** 10 (8%)	* 8 (5%)

* P<0.05 vs controls (life table and incidental tumor test)

** P<0.01 vs controls (life table and incidental tumor test)

TABLE 23. PRIMARY NEOPLASM INCIDENCE FOR RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH) (a)

Site/Lesion	Male		Female	
	DMH	Amosite + DMH	DMH	Amosite + DMH
Skin				
Keratoacanthoma	0/125 (0%)	5/175 (3%)	0/125 (0%)	0/175 (0%)
Subcutaneous tissue				
Fibroma	3/125 (2%)	6/175 (3%)	0/125 (0%)	0/175 (0%)
Hematopoietic system				
Leukemia	20/125 (16%)	40/175 (23%)	39/125 (31%)	61/175 (35%)
Circulatory system				
Hemangiosarcoma	0/125 (0%)	4/175 (2%)	0/125 (0%)	0/175 (0%)
Kidney				
Tubular cell tumors	1/125 (1%)	0/173(0%)	3/124(2%)	3/175 (2%)
Sarcoma	0/125 (0%)	3/173(2%)	23/124(19%)	19/175 (11%)
Fibrosarcoma	0/125 (0%)	0/173(0%)	4/124(3%)	† 0/175 (0%)
Mixed tumor malignant	0/125 (0%)	1/173(1%)	9/124(7%)	* 35/175 (20%)
Pituitary gland				
Adenoma	6/122 (5%)	12/169 (7%)	16/124 (13%)	19/175 (11%)
Adrenal gland				
Cortical adenoma	0/125 (0%)	0/173(0%)	2/124(2%)	4/175 (2%)
Pheochromocytoma	16/125 (13%)	16/173(9%)	0/124(0%)	3/175 (2%)
Thyroid gland				
Follicular cell adenoma	4/124 (3%)	10/172(6%)	4/123(3%)	6/174 (3%)
Follicular cell carcinoma	3/124 (2%)	3/172(2%)	2/123(2%)	1/174 (1%)
C-cell adenoma	2/124 (2%)	9/172(5%)	4/123(3%)	8/174 (5%)
C-cell carcinoma	7/124 (6%)	10/172(6%)	1/123(1%)	6/174 (3%)
Pancreatic Islets				
Islet cell adenoma	0/125 (0%)	3/173(2%)	0/124(0%)	2/175 (1%)
Islet cell carcinoma	0/125 (0%)	3/173(2%)	0/124(0%)	0/175 (0%)
Mammary gland				
Adenocarcinoma	0/125 (0%)	0/175 (0%)	3/125 (2%)	(b) 1/175 (1%)
Fibroadenoma	1/125 (1%)	5/175 (3%)	13/125 (10%)	18/175 (10%)
Preputial/clitoral gland				
Squamous cell carcinoma	5/125 (4%)	4/175 (2%)	1/125 (1%)	3/175 (2%)
Testis				
Interstitial cell tumor	79/123 (64%)	125/174 (72%)	--	--
Uterus				
Endometrial stromal polyp	--	--	10/124(8%)	19/175 (11%)
Endometrial stromal sarcoma	--	--	4/124(3%)	2/175 (1%)
All sites				
Mesothelioma	4/125 (3%)	6/175 (3%)	0/125 (0%)	0/175 (0%)

(a) Incidence of neoplasms (other than those already noted) that occurred with an incidence of at least 2% in at least one group

(b) Papillary adenocarcinoma

* P < 0.05 (increase) relative to DMH

† P < 0.05 (decrease) relative to DMH

IV. DISCUSSION AND CONCLUSIONS

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Amosite asbestos was administered at a concentration of 1% in the diet to male and female F344/N rats for their lifetime, including exposure of the dams to the study material. Starting at birth, one of three groups of neonate rats from amosite-exposed mothers were given chrysotile asbestos (instead of amosite) by gavage until weaning, at which time they were given the 1% amosite diet. For all intents and purposes, this group of rats should be regarded as being exposed to amosite asbestos for their lifetime. Two groups (control and amosite exposed) of weanling rats were exposed to five biweekly doses of 1,2-dimethylhydrazine dihydrochloride (DMH), a known intestinal carcinogen, to test the promoter or cocarcinogenic effects of DMH and amosite asbestos.

The clinicopathologic results in these studies showed that the ingestion of amosite asbestos did not adversely affect the fertility of the mothers or the litter size of the F₁ animals. However, the average weight at birth of the offspring from mothers exposed to amosite asbestos before and during gestation was slightly less (9%) than that of the offspring of nonexposed mothers. The difference in body weights was more apparent at weaning (15%). The effect on body weight gain became more apparent between weaning and 8 weeks of age (males, 37% less than controls; females, 25%). The amosite asbestos-exposed rats remained smaller throughout their life, although their weight gain paralleled that of the nonexposed rats. The mean body weight of the preweaning (PW) male rats exposed to chrysotile asbestos by gavage and subsequently to amosite asbestos was slightly higher than that of rats exposed to amosite alone. This may be related to the high incidence (approximately 50%) of mortality induced in the neonates by the PW technique, which would allow the remaining pups more milk during lactation. Exposure to DMH caused a small reduction in body weight gain in both male and female rats.

No clinical signs were observed which could be attributed to the ingestion of amosite asbestos. Starting at 9 months of age, the DMH-exposed rats showed signs attributable to DMH-related neoplasia, but no difference was noted between the DMH and amosite + DMH groups.

The ingestion of 1% amosite in the diet for the life of the rats did not adversely affect their survival. In fact, survival of female rats exposed to amosite or of the PW group exposed to chrysotile and amosite asbestos was slightly greater up to week 112 than that of controls. Similarly, the survival of male rats exposed to amosite was slightly greater than that of controls, although the survival of the amosite + PW group was slightly lower.

The most plausible explanation for the increased survival of the amosite-exposed rats is their lower weight throughout the studies. Yu et al. (1982) showed that F344 rats with lower body weight caused by restricted caloric intake lived longer than rats that were allowed to eat an unlimited amount of food.

The survival of rats exposed to DMH was significantly lower than that of untreated controls. It is noteworthy that more male and female rats that received amosite + DMH survived throughout the studies than those that received DMH alone. The reason for this is not known.

The survival of the rats (untreated control and amosite exposed) in these studies compares favorably with that in other NTP studies (Hase-man, 1983). At 112 weeks of age (age at end of a typical 2-year study), the percent of male rats alive in this study was: control, 74%; amosite, 80%; amosite + PW, 62%. The percent of female rats alive at this time was: control, 61%; amosite, 72%; amosite + PW, 69%. Hase-man (1983), in reviewing 25 NTP feed studies, found an average 66% of control males and 73% of control females alive at 112 weeks of age.

The survival of control male rats was greater than that of females at 112 weeks of age. In 2-year studies involving rats, generally more females survive to the end of the study than do males. However, the longer survival of female rats (both untreated control and amosite exposed) was clearly demonstrated after 142 weeks.

The ingestion of amosite asbestos over the lifetime of these rats did not cause a biologically significant increase of neoplasms at any anatomic

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site when compared with the concurrent controls. The gastrointestinal tract was considered a potential target organ based on epidemiologic studies in humans (Cooper et al, 1979) and because the study material was administered in the diet. The overall incidences of intestinal neoplasms in the controls (male 4%, female 2%) and two amosite-exposed groups (male 3% and 3%, female 2% and 3%) were low, and there were no significant differences between exposed and untreated control groups. Based on these observations, it is clear that the maximum tolerated concentration was not exceeded. Possibly, the rats in these studies could have tolerated exposure at a higher concentration, although a dietary concentration of 1% for the entire life of the animal is considered substantial. In addition, nonneoplastic lesions of the gastrointestinal tract were not increased. In summary, amosite asbestos did not cause any adverse effects in the gastrointestinal tract in either male or female F344/N rats.

Rats exposed to DMH showed a high incidence (60%-70%) of neoplasia of the gastrointestinal tract, primarily in the large intestine. This high incidence of intestinal neoplasia was unexpected because an incidence of $15\% \pm 5\%$ would have been predicted in these studies, based on a pilot study using the same dosing regimen of DMH (McConnell et al., 1980). In another NTP study (NTP, 1990a), hamsters exposed to chrysotile asbestos + DMH also failed to develop the predicted incidence of intestinal neoplasms, based on a similar pilot study. Apparently, the neoplastic dose response to DMH is relatively steep, and duplication of low incidences of intestinal neoplasia are difficult to reproduce.

Because of the high background incidence of DMH-induced neoplasia, it is not possible to determine if amosite had a cocarcinogenic or additive effect in these studies. Female rats exposed to amosite + DMH had a higher incidence (11% vs. 2%) of neoplasia of the duodenum than the DMH controls. Conversely, they had a lower incidence (9% vs. 2%) of neoplasms of the jejunum; thus, the total number of animals with neoplasms of the small intestine was similar. The same situation was observed in the large intestine of male rats. The rats exposed to DMH alone had a higher incidence (13% vs. 3%) of

carcinoma of the cecum but a lower incidence (14% vs. 25%) of neoplasms of the transverse colon. Overall, the data suggest that amosite asbestos had neither a cocarcinogenic nor protective effect on the carcinogenic potential of DMH.

The morphologic appearances of the neoplasms induced by DMH were similar to those described previously in rats exposed to hydrazine compounds (Pozhariski, 1975). In addition, the few intestinal neoplasms that occurred in the control and amosite (no DMH) rats were of the same morphologic types as those induced by DMH. The neoplasms observed in the kidney, liver, and Zymbal gland in DMH-exposed rats were consistent with those reported for these types of intestinal carcinogens (Ward, 1975).

A significantly ($P < 0.05$) increased incidence of C-cell carcinomas of the thyroid gland occurred in amosite-exposed male rats. This effect was not observed in the amosite + PW male rats, and the overall incidence of total benign and malignant C-cell neoplasms was similar in control and exposed groups. Therefore, this effect is not considered to be related to amosite exposure.

The incidences of monocytic leukemia (synonyms: mononuclear cell leukemia, Fischer rat leukemia) were increased in amosite (43%) ($P < 0.05$) and amosite + PW (49%) ($P < 0.01$) male rats compared with that in controls (32%). The incidences of monocytic leukemia in male control groups in other studies of the asbestos initiative were 36% in tremolite, 36% in crocidolite, and 42% in short-range chrysotile asbestos. This increased incidence was not observed in exposed female rats. Coleman et al. (1977) reported an incidence of nearly 30% in male F344 rats within the age group of 24-40 months. In 2-year-old F344 rats, Goodman et al. (1979) reported 12% of males and nearly 10% of females had lymphoma or leukemia, a much lower incidence than in the current studies. It is apparent from the current studies and the above-cited studies that the incidence of leukemia increases rapidly after 2 years of age. In view of considerable variation in the leukemia incidence and the fact that the amosite-exposed male rats survived longer, thereby losing statistical significance with life table analysis, it is doubtful that the increase in the incidence of

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leukemia is compound related. More importantly, an increased incidence of neoplasia was not observed in target organs (gastrointestinal tract and mesothelium). Even though it is known that certain types of asbestos are absorbed through the gastrointestinal tract (Cook and Olson, 1979; Sebastien et al., 1980), it is difficult to envision how asbestos given orally could cause an increase in leukemia without causing an increase in neoplasms in the target tissues.

In summary, these effects represent only a modulation of neoplasms that occur in concurrent control groups and are known to occur in historical control rats of this strain. No uncommon or unique neoplasms were observed in any of the amosite-exposed groups. In addition, the biologic importance of the neoplasms in the absence of target organ neoplasia is questionable.

A large variety of nonneoplastic lesions, primarily lesions of aging, were observed in all groups. There was no obvious correlation between exposure and specific lesions. Therefore, amosite at the concentration of 1% in the diet did not appear to cause any overt toxicity. The decrease in initial body weight and body weight gain may or may not be considered a toxic effect, depending on one's viewpoint, particularly since the amosite-exposed rats lived longer.

Studies involving the long-term ingestion of other types of asbestos are few. Donham et al. (1980) reported equivocal tumor results in the intestine of F344 rats that were fed a diet containing 10% chrysotile for their lifetime. Although a significant ($P < 0.05$) increase in the number of neoplasms in exposed animals was not observed, the authors believed that there was a trend toward increased colon lesions in general. They cited evidence of penetration of asbestos into the colonic mucosa and possible cytotoxicity to colonic tissues and suggested a relationship to peritoneal mesothelioma. Another equivocal study is that reported by Gibel et al. (1976), who described increases in malignant neoplasms in the lung, kidney, liver, and reticuloendothelial system but not in intestinal neoplasia in Wistar rats fed asbestos filter material (20 mg/day) for 8-14 months. Cunningham et al. (1977) reported two studies (24 months or 30 months) in which Wistar male rats were admin-

istered 1% chrysotile asbestos in the diet. These authors concluded that trace amounts of ingested asbestos can penetrate the walls of the gastrointestinal tract, but evidence of carcinogenicity was inconclusive. No evidence of carcinogenicity was found by Gross et al. (1974), who fed rats a diet containing 5% chrysotile asbestos for 21 months. Bolton et al. (1982) exposed groups of 22-24 male HAN SPF Wistar-derived rats to amosite, crocidolite, or UICC standard reference chrysotile (similar to intermediate-range chrysotile) asbestos in the diet at a rate of approximately 250 mg/rat per week for 25 months and monitored the rats for the remainder of their lifespan. They concluded that no significant adverse effects occurred as a result of ingestion of any of these forms of asbestos. Previous NTP asbestos studies in rats in which chrysotile (NTP 1985a) or crocidolite (NTP, 1988) was administered orally with and without DMH did not show any indication of a carcinogenic response.

A corollary study to this investigation was conducted in Syrian golden hamsters (NTP, 1985b). The exposure regimen was similar, in that 252 male and 254 female hamsters were exposed to 1% amosite asbestos (same source as in the current studies) in their diet for their natural lifespan. There was no adverse effect on body weight gain or survival, and no amosite-related neoplasms were observed.

In another study, groups of 30 male and 30 female hamsters were exposed via drinking water for their lifetime to amosite asbestos, mine tailings, beach rock, or Lake Superior drinking water (Smith et al., 1980). No adverse effects on body weight or survival were observed for any of the groups. One peritoneal mesothelioma, one pulmonary carcinoma, and two early squamous cell carcinomas of the nonglandular stomach were found in the hamsters exposed to amosite. The authors concluded that the study was "essentially negative." A subsequent study in rats in which similar materials were used also failed to elicit a carcinogenic response (Hilding et al., 1981).

Except for the studies of Donham et al. (1980), Smith et al. (1980), Bolton et al. (1982), and the NTP studies, the other studies were conducted

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with relatively small numbers of animals. Also, some were conducted for an insufficient period of time to study adequately the carcinogenic potential of ingested asbestos.

A long-term study of amosite asbestos was designed to determine the promotor potential of asbestos (Ward et al., 1980). Six-week-old male F344 rats were exposed three times per week for 10 weeks to 1 mg amosite asbestos in saline via gavage. Once per week during this same period, half of the rats received subcutaneous injections of 7.4 mg/kg azoxymethane (AOM), a known intestinal carcinogen in animals which produces effects similar to DMH. The rats were allowed to live out their lifespan or until 94-95 weeks of age, at which time they were killed. The authors reported an intestinal tumor incidence of 66.7% in AOM alone, 77.1% for amosite + AOM, and 32.6% for amosite alone. They concluded that although amosite did not significantly add to the incidence of AOM-induced intestinal neoplasia, amosite alone caused a relatively high incidence of intestinal neoplasia. There was no untreated control group to compare with the exposed groups, however; in addition, these results should be viewed with some suspicion because

the authors also reported a 14% incidence of Zymbal gland tumors in the rats exposed to amosite alone. The historical incidence of Zymbal gland tumors in the NTP Program is about 1% for 2-year studies and 3% for lifetime studies, indicating that this is a relatively rare neoplasm. AOM, however, is known to induce Zymbal gland tumors with a single dose of 5.1 mg/kg in male F344 rats, producing a 14% incidence of tumors in this organ (Ward, 1975); in this study, 5.1 mg/kg AOM also caused a 24% incidence of intestinal neoplasia. A possible explanation for the incidence of Zymbal gland tumors in the amosite groups is that they were inadvertently exposed to AOM. If this occurred, these rats would also be expected to show a high incidence of intestinal neoplasms.

Under the conditions of these feed studies, amosite asbestos was not overtly toxic, did not affect survival, and was not carcinogenic when ingested at a concentration of 1% in the diet by male or female F344/N rats. The cocarcinogenic studies using DMH were considered inadequate because of the high incidence of DMH-induced intestinal neoplasia in both the amosite asbestos-exposed and nonexposed groups.

V. REFERENCES

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1. Berenblum, I., Ed. (1969) *Carcinogenicity Testing: A Report of the Panel on Carcinogenicity of the Cancer Research Commission of UICC, Vol. 2*. Geneva: International Union Against Cancer.
2. Bey, E.; Harrington, J.S. (1971) Cytotoxic effects of some mineral dusts on Syrian hamster peritoneal macrophages. *J. Exp. Med.* 133:1149-1169.
3. Bolton, R.; Davis, J.; Lamb, D. (1982) The pathological effects of prolonged asbestos ingestion in rats. *Environ. Res.* 29:134-150.
4. Boorman, G.A.; Montgomery, C.A., Jr.; Eustis, S.L.; Wolfe, M.J.; McConnell, E.E.; Hardisty, J.F. (1985) Quality assurance in pathology for rodent carcinogenicity studies. Milman, H.; Weisburger, E., Eds.: *Handbook of Carcinogen Testing*. Park Ridge, NJ: Noyes Publications, pp. 345-357.
5. Bureau of Mines (1980) Report No. 8452. U.S. Department of the Interior, Supt. of Documents, No. RI 28.23.
6. Carter, R.E.; Taylor, W.G. (1980) Identification of a particular amphibole asbestos fiber in tissues of persons exposed to a high oral intake of the mineral. *Environ. Res.* 21:85-93.
7. Chamberlain, M.; Tarmy, E.M. (1977) Asbestos and glass fibers in bacterial mutation tests. *Mutat. Res.* 43:159-164.
8. Coleman, G.L.; Barthold, S.W.; Osbaldiston, G.W.; Foster, S.J., Jonas, A.M. (1977) Pathological changes during aging in barrier-reared Fischer 344 male rats. *J. Gerontol.* 32:258-278.
9. Cook, P.M.; Olson, G.F. (1979) Ingested mineral fibers: Elimination in human urine. *Science* 204:195-198.
10. Cooper, R.C.; Murchio, J.C.; Paffenbarger, R.S. (1979) Asbestos in Domestic Water Supplies for Five California Counties. Part II. EHS Pub. No. 79-1. Division of Environmental Health Sciences, School of Public Health, University of California, Berkeley.
11. Cox, D.R. (1972) Regression models and life tables. *J. R. Stat. Soc.* B34:187-220.
12. Craighead, J.E.; Mossman, B.T. (1982) The pathogenesis of asbestos-associated disease. *N. Engl. J. Med.* 306:1446-1455.
13. Cunningham, H.M.; Moodie, C.A.; Lawrence, G.A.; Pontefract, R.D. (1977) Chronic effects of ingested asbestos in rats. *Arch. Environ. Contam. Toxicol.* 6:507-513.
14. Donham, K.J.; Berg, J.W.; Will, L.A.; Leininger, J.R. (1980) The effects of long-term ingestion of asbestos on the colon of F344 rats. *Cancer* 45:1073-1084.
15. Environmental Health Perspectives (EHP) (1974) Proceedings of the Joint NIEHS-EPA Conference on Biological Effects of Ingested Asbestos. 9:113-462.
16. Fiala, E.; Bobotas, G.; Kalukis, C.; Weisburger, J. (1976) Separation of 1,2-dimethylhydrazine metabolites by high pressure liquid chromatography. *J. Chromatog.* 117:181-185.
17. Gart, J.J.; Chu, K.C.; Tarone, R.E. (1979) Statistical issues in interpretation of chronic bioassay tests for carcinogenicity. *J. Natl. Cancer Inst.* 62:957-974.
18. Gibel, W.; Lohs, K.H.; Horn, K.H.; Wildner, G.P.; Hoffman, F. (1976) Investigation into a carcinogenic effect of asbestos filter materials following oral intake in experimental animals. *Arch. Geschwulstforsch.* 46:437-442.
19. Goodman, D.G.; Ward, J.M.; Squire, R.A.; Chu, K.C.; Linhart, M.S. (1979) Neoplastic and nonneoplastic lesions in aging F344 rats. *Toxicol. Appl. Pharmacol.* 48:237-248.
20. Gross, P.; Harley, R.A.; Swinberne, L.M.; Davis, J.M.G.; Green, W.B. (1974) Ingested mineral fibers, do they penetrate tissue or cause cancer? *Arch. Environ. Health* 29:341-347.
21. Harrington, J.M.; Craun, G.F.; Meigs, J.W.; Landrigen, P.J.; Flannery, J.T. (1978) An investigation of the use of asbestos-cement pipe for public water supply and the incidence of gastrointestinal cancer in Connecticut, 1935-1973. *Am. J. Epidemiol.* 107:96-103.

V. REFERENCES

22. Haseman, J.K. (1983) Patterns of tumor incidence in two-year cancer bioassay feeding studies in Fischer 344 rats. *Fundam. Appl. Toxicol.* 3:1-9.
23. Haseman, J.K. (1984) Statistical issues in the design, analysis and interpretation of animal carcinogenicity studies. *Environ. Health Perspect.* 58:385-392.
24. Haseman, J.K.; Huff, J.; Boorman, G.A. (1984) Use of historical control data in carcinogenicity studies in rodents. *Toxicol. Pathol.* 12:126-135.
25. Haseman, J.K.; Huff, J.; Rao, G.N.; Arnold, J.; Boorman, G.A.; McConnell, E.E. (1985) Neoplasms observed in untreated and corn oil gavage control groups of F344/N rats and (C57BL/6N × C3H/HeN)F₁ (B6C3F₁) mice. *J. Natl. Cancer Inst.* 75:975-984.
26. Hilding, A.C.; Hilding, D.A.; Larsen, D.M.; Aufderheide, A.C. (1981) Biological effects of ingested amosite asbestos, taconite tailings, diatomaceous earth and Lake Superior water in rats. *Arch. Environ. Health* 36:298-303.
27. Illinois Institute of Technology Research Institute (IITRI) Special Report and Addendum on Project L6085. Contract No. N01-ES-5-3157. Chicago: Fine Particle Laboratories, IITRI.
28. International Agency for Research on Cancer (IARC) (1977) Asbestos. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man, Vol. 14. Lyon, France: IARC, pp. 1-106.
29. ILAR Monograph (1980) Histologic typing of liver tumors of the rat. Stewart, H.L., Ed. *J. Natl. Cancer Inst.* 64:179-206.
30. Kanarek, M.S.; Conforti, P.M.; Jackson, L.A.; Cooper, R.C.; Murchio, J.C. (1980) Asbestos in drinking water and cancer incidence in the San Francisco Bay area. *Am. J. Epidemiol.* 112:54-72.
31. Kaplan, E.L.; Meier, P. (1958) Nonparametric estimation from incomplete observations. *J. Am. Stat. Assoc.* 53:457-481.
32. Levine, R.J. (1981) Asbestos: An Information Source. DHEW Pub. No. NIH 78-1681. 105 p.
33. Linhart, M.S.; Cooper, J.; Martin, R.L.; Page, N.; Peters, J. (1974) Carcinogenesis Bioassay Data System. *Comput. Biomed. Res.* 7:230-248.
34. Mantel, N.; Haenszel, W. (1959) Statistical aspects of the analysis of data from retrospective studies of disease. *J. Natl. Cancer Inst.* 22:719-748.
35. Maronpot, R.R.; Boorman, G.A. (1982) Interpretation of rodent hepatocellular proliferative alterations and hepatocellular tumors in chemical safety assessment. *Toxicol. Pathol.* 10:71-80.
36. McConnell, E.; Wilson, R.; Moore, J.; Haseman, J. (1980) Dose response of 1,2-dimethylhydrazine and methylazoxymethanol acetate in the F344 rat. *Cancer Lett.* 8:271-278.
37. Millette, J.R. (1979) Exposure to Asbestos from Drinking Water in the United States. EPA Contract No. 600/1-79-150. U.S. Environmental Protection Agency.
38. National Toxicology Program (NTP) (1985a) Toxicology and Carcinogenesis Studies of Chrysotile Asbestos in F344/N Rats. NTP TR 295. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Bethesda, MD. 390 p.
39. National Toxicology Program (NTP) (1985b) Lifetime Carcinogenesis Studies of Amosite Asbestos in Syrian Golden Hamsters. NTP TR 249. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Bethesda, MD. 81 p.
40. National Toxicology Program (NTP) (1988) Lifetime Carcinogenesis Studies of Crocidolite Asbestos in F344/N Rats. NTP TR 280. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Research Triangle Park, NC. 178 p.

V. REFERENCES

41. National Toxicology Program (NTP) (1990a) Lifetime Carcinogenesis Studies of Chrysotile Asbestos in Syrian Golden Hamsters. NTP TR 246. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Research Triangle Park, NC (in preparation).
42. National Toxicology Program (NTP) (1990b) Lifetime Carcinogenesis Studies of Tremolite Asbestos in F344/N Rats. NTP TR 277. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Research Triangle Park, NC. 183 p.
43. Patel-Mandlik, K.J. (1980) Distribution of Orally Administered Chrysotile Asbestos in Newborn Baboon Study. EPA 600/1-80-022. U.S. Environmental Protection Agency, Washington, DC.
44. Peto, R.; Schneiderman, M., Eds. (1981) Quantification of Occupational Cancer. Banbury Report No. 9. Cold Spring Harbor, New York.
45. Pozharisski, K.M. (1975) Morphology and morphogenesis of experimental epithelial tumors of the intestine. J. Natl. Cancer Inst. 54:1115-1135.
46. Rao, C.R. (1958) Some statistical methods for comparison of growth curves. Biometrics 14:1-17.
47. Reiss, B.; Weisburger, J.H.; Williams, G.M. (1979) Asbestos and Gastrointestinal Cancer: Cell Culture Studies. EPA-600/1-79-023. U.S. Environmental Protection Agency, Washington, DC.
48. Sebastien, P.; Masse, R.; Bignon, J. (1980) Recovery of ingested asbestos fibers from the gastrointestinal lymph in rats. Environ. Res. 22:201-216.
49. Selikoff, I.J. (1980) Asbestos-associated disease. Last, J., Ed.: Maxcy-Rosehau's Public Health and Preventive Medicine, 11th ed. Appleton-Century-Croft, pp. 568-589.
50. Selikoff, I.J.; Hammond, E.C., Eds. (1979) Health hazards of asbestos exposure. Ann. N.Y. Acad. Sci. B30:1-814.
51. Smith, W.E.; Hubert, D.D.; Sobel, H.J.; Peters, E.T.; Doerfler, T.E. (1980) Health in experimental animals drinking water with and without amosite and other mineral particles. J. Environ. Pathol. Toxicol. 3:277-300.
52. Stanton, M.F.; Layard, M.; Tegar, A.; Miller, E.; May, M.; Morgan, E.; Smith, A. (1981) Relation of particle dimension to the carcinogenicity in amphibole asbestoses and other fibrous minerals. J. Natl. Cancer Inst. 67:965-975.
53. Storeygard, A.R.; Brown, A.L. (1977) Penetration of the small intestinal mucosa by asbestos fibers. Mayo Clin. Proc. 52:809-812.
54. U.S. Environmental Protection Agency (USEPA) (1980) Ambient Water Quality Criteria for Asbestos. EPA 440/5-80-022. Washington, DC: USEPA, Office of Water Regulations and Standards.
55. Wagner, J.C.; Berry, G.; Skidmore, J.W.; Timbrell, V. (1974) Effects of the inhalation of asbestos in rats. Br. J. Cancer 29:252-269.
56. Ward, J.M. (1975) Dose response to a single injection of azoxymethane in rats. Vet. Pathol. 12:165-177.
57. Ward, J.M.; Frank, A.L.; Wenk, M.; Devor, D.; Tarone, R.E. (1980) Ingested asbestos with frequent spontaneous adrenal tumors. J. Environ. Pathol. Toxicol. 3:301-312.
58. Weisburger, J.H.; Williams, G.M. (1979) Chemical carcinogens. Doull, J.; Klaasen, C., Eds.: Toxicology: The Basic Science of Poisons, 2nd ed. New York: Macmillan Publishing Co., Inc.
59. Yu, B.P.; Masoro, E.J.; Murata, I.; Bertrand, H.A.; Lund, F.T. (1982) Life span study of SPF Fischer 344 rats fed *ad libitum* or restricted diets: Longevity, growth, lean body mass and disease. J. Gerontol. 37:130-141.

APPENDIX A

SUMMARY OF LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS

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TABLE A1a. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (a)

	Untreated Control	DMH	1% Amosite
Animals initially in study	117	125	250
Animals necropsied	117	125	250
Animals examined histopathologically	117	125	249
INTEGUMENTARY SYSTEM			
*Skin	(117)	(125)	(250)
Carcinoma in-situ, NOS			1 (0%)
Squamous cell papilloma	1 (1%)		6 (2%)
Squamous cell carcinoma	1 (1%)		4 (2%)
Basal cell tumor	1 (1%)		1 (0%)
Basal cell carcinoma	3 (3%)		7 (3%)
Trichoepithelioma	1 (1%)		
Keratoacanthoma	4 (3%)		17 (7%)
Fibroma			2 (1%)
Fibrosarcoma	3 (3%)	1 (1%)	4 (2%)
Myxoma			1 (0%)
Osteosarcoma			1 (0%)
Neurofibrosarcoma	1 (1%)		
*Subcut tissue	(117)	(125)	(250)
Sarcoma, NOS	4 (3%)	1 (1%)	2 (1%)
Sarcoma, NOS, invasive			1 (0%)
Fibroma	18 (15%)	3 (2%)	†31 (12%)
Fibrosarcoma	4 (3%)		5 (2%)
Lipoma	2 (2%)		2 (1%)
Liposarcoma	1 (1%)		1 (0%)
Neurofibroma	3 (3%)	1 (1%)	5 (2%)
Neurofibrosarcoma	1 (1%)		
RESPIRATORY SYSTEM			
*Nasal cavity	(117)	(125)	(250)
Fibrosarcoma	1 (1%)		
#Trachea	(117)	(125)	(248)
C-cell carcinoma, invasive			1 (0%)
#Lung/bronchiole	(117)	(125)	(249)
Papillary adenocarcinoma			1 (0%)
#Lung	(117)	(125)	(249)
Carcinoma, NOS, metastatic	1 (1%)		1 (0%)
Squamous cell carcinoma, metasta			1 (0%)
Adenoca in adenomatous polyp, met		1 (1%)	
Alveolar/bronchiolar adenoma	1 (1%)		2 (1%)
Alveolar/bronchiolar carcinoma	1 (1%)	1 (1%)	6 (2%)
C-cell carcinoma, metastatic		1 (1%)	2 (1%)
Mucinous cystadenoca, metastatic		1 (1%)	
Pheochromocytoma, metastatic	2 (2%)		4 (2%)
Sarcoma, NOS, metastatic	3 (3%)		1 (0%)
Liposarcoma, metastatic	1 (1%)		3 (1%)
Osteosarcoma, metastatic	1 (1%)		
Neurofibrosarcoma, metastatic	1 (1%)		
HEMATOPOIETIC SYSTEM			
*Multiple organs	(117)	(125)	(250)
Malign. lymphoma, lymphocytic type			2 (1%)
Malign. lymphoma, histiocytic type	2 (2%)	2 (2%)	1 (0%)
Myelomonocytic leukemia			1 (0%)
Monocytic leukemia	36 (31%)	18 (14%)	103 (41%)
#Bone marrow	(117)	(110)	(248)
Liposarcoma, invasive	2 (2%)		

TABLE A1a. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
HEMATOPOIETIC SYSTEM (Continued)			
#Spleen	(117)	(124)	(249)
Fibrosarcoma			1 (0%)
Mesothelioma, metastatic			1 (0%)
#Mandibular l. node	(117)	(125)	(249)
C-cell carcinoma, metastatic			1 (0%)
Sarcoma, NOS, invasive			1 (0%)
Fibrosarcoma, invasive			1 (0%)
#Cervical lymph node	(117)	(125)	(250)
C-cell carcinoma, metastatic		1 (1%)	
#Mediastinal l. node	(117)	(125)	(249)
Alveolar/bronchiolar carcinoma, invasive	1 (1%)		
#Celiac lymph node	(117)	(125)	(250)
Mucinous cystadenoca, metastatic		2 (2%)	
#Pancreatic lymph node	(117)	(125)	(250)
Mucinous cystadenoca, metastatic		1 (1%)	
#Mesenteric lymph node	(117)	(125)	(250)
Mucinous cystadenoca, metastatic		1 (1%)	
#Liver	(117)	(125)	(249)
Monocytic leukemia	2 (2%)	2 (2%)	3 (1%)
#Ileum	(117)	(125)	(249)
Malig. lymphoma, histiocytic type			1 (0%)
#Thymus	(80)	(83)	(171)
Carcinoma, NOS			1 (1%)
Squamous cell carcinoma	1 (1%)		
CIRCULATORY SYSTEM			
*Subcut tissue	(117)	(125)	(250)
Hemangiosarcoma			1 (0%)
#Spleen	(117)	(124)	(249)
Hemangiosarcoma	1 (1%)		2 (1%)
DIGESTIVE SYSTEM			
*Mouth	(117)	(125)	(250)
Keratoacanthoma		1 (1%)	
*Oral mucous membrane	(117)	(125)	(250)
Squamous cell carcinoma			2 (1%)
Basal cell carcinoma			1 (0%)
*Hard palate	(117)	(125)	(250)
Squamous cell papilloma			1 (0%)
Squamous cell carcinoma			1 (0%)
*Lip	(117)	(125)	(250)
Squamous cell papilloma		1 (1%)	
Basal cell tumor	1 (1%)		
#Salivary gland	(117)	(124)	(245)
Carcinoma, NOS			1 (0%)
Sarcoma, NOS		1 (1%)	2 (1%)
Sarcoma, NOS, invasive	1 (1%)		
Fibrosarcoma	1 (1%)		2 (1%)
Fibrosarcoma, invasive			1 (0%)
#Liver	(117)	(125)	(249)
Neoplastic nodule	9 (8%)	18 (14%)	9 (4%)
Hepatocellular carcinoma	1 (1%)	9 (7%)	3 (1%)
Osteosarcoma	1 (1%)		

**TABLE A1a. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME
FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE
(Continued)**

	Untreated Control	DMH	1% Amosite
DIGESTIVE SYSTEM (Continued)			
#Pancreas	(116)	(125)	(247)
Adenocarcinoma, NOS, metastatic		1 (1%)	
Acinar cell adenoma	9 (8%)		19 (8%)
Acinar cell carcinoma	2 (2%)		2 (1%)
Mixed tumor, benign			2 (1%)
Mesothelioma, metastatic			1 (0%)
Neurofibrosarcoma, metastatic		1 (1%)	
#Pancreatic duct	(116)	(125)	(247)
Carcinoma, NOS	1 (1%)		1 (0%)
#Stomach	(117)	(125)	(249)
Adenocarcinoma, NOS	1 (1%)		
Adenomatous polyp, NOS			1 (0%)
Leiomyosarcoma			1 (0%)
#Gastric mucosa	(117)	(125)	(249)
Carcinoma in-situ, NOS			1 (0%)
#Duodenum	(117)	(125)	(249)
Adenocarcinoma, NOS		2 (2%)	
Mucinous cystadenocarcinoma		6 (5%)	
Signet ring carcinoma		3 (2%)	
Leiomyoma			1 (0%)
Leiomyosarcoma		1 (1%)	
#Jejunum	(117)	(125)	(249)
Adenomatous polyp, NOS		1 (1%)	
Adenoca in adenomatous polyp			1 (0%)
Mucinous cystadenocarcinoma	2 (2%)	2 (2%)	
Leiomyosarcoma		1 (1%)	1 (0%)
#Ileum	(117)	(125)	(249)
Carcinoma, NOS		1 (1%)	
Adenocarcinoma, NOS		1 (1%)	
Adenomatous polyp, NOS	1 (1%)		
#Colon	(117)	(125)	(249)
Adenomatous polyp, NOS		1 (1%)	1 (0%)
Adenoca in adenomatous polyp		1 (1%)	
#Cecum	(117)	(125)	(249)
Adenocarcinoma, NOS		4 (3%)	
Mucinous cystadenocarcinoma		7 (6%)	
Signet ring carcinoma		5 (4%)	
Leiomyoma			1 (0%)
Leiomyosarcoma	1 (1%)		
#Ascending colon	(117)	(125)	(249)
Carcinoma in-situ, NOS		2 (2%)	1 (0%)
Adenocarcinoma, NOS		5 (4%)	
Adenomatous polyp, NOS		5 (4%)	
Adenoca in adenomatous polyp		2 (2%)	
Mucinous cystadenocarcinoma		2 (2%)	
Signet ring carcinoma		1 (1%)	
#Transverse colon	(117)	(125)	(249)
Adenomatous polyp, NOS		9 (7%)	
Adenoca in adenomatous polyp		8 (6%)	
Mucinous cystadenocarcinoma		1 (1%)	
#Descending colon	(117)	(125)	(249)
Adenomatous polyp, NOS		32 (26%)	2 (1%)
Adenoca in adenomatous polyp		21 (17%)	

**TABLE A1a. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME
FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE
(Continued)**

	Untreated Control	DMH	1% Amosite
URINARY SYSTEM			
#Kidney	(117)	(125)	(248)
Transitional cell carcinoma		1 (1%)	
Tubular cell adenoma			2 (1%)
Tubular cell adenocarcinoma		1 (1%)	1 (0%)
Sarcoma, NOS			1 (0%)
Lipoma			1 (0%)
Mixed tumor, malignant			1 (0%)
Neurofibrosarcoma		1 (1%)	
#Kidney/tubule	(117)	(125)	(248)
Carcinoma, NOS			1 (0%)
ENDOCRINE SYSTEM			
#Pituitary	(117)	(122)	(248)
Carcinoma, NOS	2 (2%)		4 (2%)
Adenoma, NOS	24 (21%)	6 (5%)	41 (16%)
#Adrenal	(117)	(125)	(249)
Cortical adenoma			5 (2%)
Pheochromocytoma	39 (33%)	16 (13%)	65 (26%)
Pheochromocytoma, malignant	3 (3%)		5 (2%)
Ganglioneuroma			1 (0%)
#Periadrenal tissue	(117)	(125)	(249)
Tubular cell adenocarcinoma, inv			1 (0%)
#Thyroid	(117)	(124)	(246)
Follicular cell adenoma	4 (3%)	4 (3%)	13 (5%)
Follicular cell carcinoma	7 (6%)	3 (2%)	10 (4%)
C-cell adenoma	16 (14%)	2 (2%)	26 (11%)
C-cell carcinoma	11 (9%)	7 (6%)	50 (20%)
#Parathyroid	(110)	(119)	(234)
Adenoma, NOS	4 (4%)	1 (1%)	1 (0%)
C-cell carcinoma, invasive	1 (1%)		1 (0%)
#Pancreatic islets	(116)	(125)	(247)
Islet cell adenoma	14 (12%)		17 (7%)
Islet cell carcinoma	3 (3%)		5 (2%)
REPRODUCTIVE SYSTEM			
*Mammary gland	(117)	(125)	(250)
Adenoma, NOS	3 (3%)		4 (2%)
Adenocarcinoma, NOS	1 (1%)		1 (0%)
Papillary adenocarcinoma			1 (0%)
Sarcoma, NOS, invasive			1 (0%)
Fibrosarcoma			1 (0%)
Fibroadenoma	17 (15%)	1 (1%)	27 (11%)
*Preputial gland	(117)	(125)	(250)
Carcinoma, NOS	6 (5%)	5 (4%)	9 (4%)
Squamous cell carcinoma			1 (0%)
#Prostate	(117)	(123)	(249)
Squamous cell carcinoma			1 (0%)
Lipoma	1 (1%)		
Liposarcoma, metastatic	1 (1%)		
*Seminal vesicle	(117)	(125)	(250)
Mucinous cystadenocarcinoma	1 (1%)		
#Testis	(117)	(123)	(249)
Interstitial cell tumor	111 (95%)	79 (64%)	240 (96%)

**TABLE A1a. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME
FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE
(Continued)**

	Untreated Control	DMH	1% Amosite
REPRODUCTIVE SYSTEM (Continued)			
*Epididymis	(117)	(125)	(250)
Lipoma			1 (0%)
Mesothelioma, invasive		1 (1%)	
*Scrotum	(117)	(125)	(250)
Keratoacanthoma	1 (1%)		
Mesothelioma, invasive		1 (1%)	1 (0%)
NERVOUS SYSTEM			
#Brain/meninges	(117)	(125)	(250)
Meningioma		1 (1%)	
#Cerebrum	(117)	(125)	(249)
Carcinoma, NOS, invasive	1 (1%)		2 (1%)
Astrocytoma	2 (2%)	1 (1%)	2 (1%)
#Cerebellum	(117)	(125)	(249)
Astrocytoma, invasive	1 (1%)		1 (0%)
*Cauda equina	(117)	(125)	(250)
Liposarcoma, invasive	1 (1%)		
SPECIAL SENSE ORGANS			
*Eye/lacrimal gland	(117)	(125)	(250)
Carcinoma, NOS		1 (1%)	
*Ear	(117)	(125)	(250)
Squamous cell carcinoma		1 (1%)	
*Ear canal	(117)	(125)	(250)
Squamous cell papilloma		1 (1%)	1 (0%)
Squamous cell carcinoma		1 (1%)	
*Zymbal gland	(117)	(125)	(250)
Carcinoma, NOS	1 (1%)	23 (18%)	7 (3%)
Squamous cell papilloma		7 (6%)	2 (1%)
Adenoma, NOS			1 (0%)
Keratoacanthoma		3 (2%)	
MUSCULOSKELETAL SYSTEM			
*Skull	(117)	(125)	(250)
Osteoma	1 (1%)		1 (0%)
*Vertebra	(117)	(125)	(250)
Liposarcoma			1 (0%)
Liposarcoma, invasive	1 (1%)		
*Vertebral column	(117)	(125)	(250)
Liposarcoma	1 (1%)		
*Thoracic vertebra	(117)	(125)	(250)
Osteosarcoma			1 (0%)
*Tibia	(117)	(125)	(250)
Neurofibrosarcoma	1 (1%)		
*Muscle of leg	(117)	(125)	(250)
Rhabdomyosarcoma		1 (1%)	
BODY CAVITIES			
*Mediastinum	(117)	(125)	(250)
Squamous cell carcinoma, metasta	1 (1%)		
Alveolar/bronchiolar carcinoma, invasive	1 (1%)		

TABLE A1a. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
BODY CAVITIES (Continued)			
*Abdominal cavity	(117)	(125)	(250)
Mucinous cystadenocarcinoma, metastatic		2 (2%)	
Sarcoma, NOS		1 (1%)	
Sarcoma, NOS, invasive			1 (0%)
*Abdominal wall	(117)	(125)	(250)
Osteosarcoma, metastatic	1 (1%)		
*Peritoneum	(117)	(125)	(250)
Sarcoma, NOS			1 (0%)
Mesothelioma, invasive			1 (0%)
*Mesentery	(117)	(125)	(250)
Sarcoma, NOS		1 (1%)	
Fibrosarcoma, metastatic	1 (1%)		
Mesothelioma, malignant			2 (1%)
*Tunica vaginalis	(117)	(125)	(250)
Mesothelioma, NOS			1 (0%)
Mesothelioma, malignant	2 (2%)	4 (3%)	7 (3%)
ALL OTHER SYSTEMS			
*Multiple organs	(117)	(125)	(250)
Carcinoma, NOS, invasive	1 (1%)		
Carcinoma, NOS, metastatic		1 (1%)	
Squamous cell carcinoma, invasiv			1 (0%)
Adenocarcinoma, NOS, metastatic		5 (4%)	
Tubular cell adenocarcinoma, met			1 (0%)
C-cell carcinoma, metastatic			1 (0%)
Mucinous cystadenocarcinoma, metastatic		9 (7%)	
Signet ring carcinoma, metastati		7 (6%)	
Sarcoma, NOS, invasive	1 (1%)	1 (1%)	1 (0%)
Fibrosarcoma, invasive			1 (0%)
Mesothelioma, invasive	1 (1%)	3 (2%)	7 (3%)
Mesothelioma, metastatic	1 (1%)	1 (1%)	1 (0%)
Osteosarcoma, metastatic			1 (0%)
Orbital region			
Sarcoma, NOS		1	
Back			
Basal cell carcinoma			1
Shoulder			
Osteosarcoma	1		
Flank			
Rhabdomyosarcoma			1
Sacral region			
Neurofibroma			1
Hip			
Osteosarcoma	1		
Axill			
Fibroma			1
Fibrosarcoma			1
Leg			
Osteosarcoma	1		

TABLE A1a. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	117	125	250
Natural death	15	20	30
Moribund sacrifice	95	92	190
Terminal sacrifice	7	13	29
Accidentally killed, NOS			1
TUMOR SUMMARY			
Total animals with primary tumors**	116	125	249
Total primary tumors	402	357	841
Total animals with benign tumors	115	93	244
Total benign tumors	277	174	547
Total animals with malignant tumors	82	110	201
Total malignant tumors	116	165	284
Total animals with secondary tumors##	20	36	33
Total secondary tumors	27	41	43
Total animals with tumors-- uncertain benign or malignant	9	18	10
Total uncertain tumors	9	18	10

(a) DMH indicates a group receiving five doses of 7.5 mg/kg 1,2-dimethylhydrazine dihydrochloride by gavage in pH 5 acetate buffer.

† Multiple occurrence of morphology in the same tissue; the tissue is counted once only

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically

** Primary tumors: all tumors except secondary tumors

Number of animals examined microscopically at this site

Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE A1b. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (a)

	1% Amosite + PW	1% Amosite + DMH
Animals initially in study	100	175
Animals necropsied	100	175
Animals examined histologically	100	(174)
INTEGUMENTARY SYSTEM		
*Skin	(100)	(175)
Squamous cell papilloma	5 (5%)	1 (1%)
Squamous cell carcinoma	1 (1%)	
Basal cell carcinoma	4 (4%)	1 (1%)
Trichoepithelioma	2 (2%)	
Keratoacanthoma	2 (2%)	5 (3%)
Fibrosarcoma		2 (1%)
*Subcut tissue	(100)	(175)
Squamous cell carcinoma		1 (1%)
Sarcoma, NOS	5 (5%)	1 (1%)
Fibroma	11 (11%)	6 (3%)
Fibrosarcoma	1 (1%)	1 (1%)
Lipoma	1 (1%)	
Osteosarcoma	1 (1%)	
Neurofibroma		1 (1%)
Neurofibrosarcoma	2 (2%)	
RESPIRATORY SYSTEM		
#Lung	(100)	(173)
Carcinoma, NOS, metastatic		1 (1%)
Hepatocellular carcinoma, metast		1 (1%)
Alveolar/bronchiolar adenoma		1 (1%)
Alveolar/bronchiolar carcinoma	4 (4%)	2 (1%)
Interstitial cell tumor, metasta	1 (1%)	
Pheochromocytoma, metastatic		1 (1%)
Fibrosarcoma, metastatic		1 (1%)
Osteosarcoma, metastatic	1 (1%)	
HEMATOPOIETIC SYSTEM		
*Multiple organs	(100)	(175)
Malig. lymphoma, histiocytic type		1 (1%)
Monocytic leukemia	47 (47%)	37 (21%)
#Spleen	(100)	(172)
Adenocarcinoma, NOS, metastatic		1 (1%)
Fibrosarcoma	1 (1%)	
Mesothelioma, metastatic		1 (1%)
#Mandibular l. node	(100)	(173)
Neurofibrosarcoma, metastatic	1 (1%)	
#Cervical lymph node	(100)	(173)
Carcinoma, NOS, metastatic		1 (1%)
#Mediastinal l. node	(100)	(173)
Mesothelioma, metastatic		1 (1%)
#Celiac lymph node	(100)	(173)
Adenocarcinoma, NOS, metastatic		1 (1%)
Mucinous cystadenocarcinoma, metastatic		2 (1%)
#Lumbar lymph node	(100)	(173)
Pheochromocytoma, metastatic		1 (1%)
#Mesenteric lymph node	(100)	(173)
Mucinous cystadenocarcinoma, metastatic		2 (1%)
Signet ring carcinoma, metastati		2 (1%)
#Ileocolic lymph node	(100)	(173)
Mucinous cystadenocarcinoma metastatic		1 (1%)
#Liver	(100)	(173)
Monocytic leukemia	2	3 (2%)

TABLE A1b. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
CIRCULATORY SYSTEM		
*Mediastinum	(100)	(175)
Hemangiosarcoma		1 (1%)
*Subcut tissue	(100)	(175)
Hemangiosarcoma		2 (1%)
#Spleen	(100)	(172)
Hemangiosarcoma	2 (2%)	
Hemangiopericytoma, malignant		1 (1%)
#Liver	(100)	(173)
Hemangioma		1 (1%)
Hemangiosarcoma		1 (1%)
DIGESTIVE SYSTEM		
*Hard palate	(100)	(175)
Squamous cell papilloma	1 (1%)	
#Salivary gland	(100)	(171)
Sarcoma, NOS, invasive	1 (1%)	
Fibrosarcoma, invasive	1 (1%)	
#Liver	(100)	(173)
Neoplastic nodule	5 (5%)	27 (16%)
Hepatocellular carcinoma	3 (3%)	7 (4%)
Alveolar/bronchiolar carcinoma, metasta	1 (1%)	
Sarcoma, NOS		2 (1%)
Lipoma		1 (1%)
#Pancreas	(100)	(173)
Acinar cell adenoma	2 (2%)	5 (3%)
Acinar cell carcinoma	1 (1%)	
*Pharynx	(100)	(175)
Squamous cell papilloma	1 (1%)	
#Esophagus	(100)	(173)
Squamous cell papilloma	1 (1%)	
#Stomach	(100)	(173)
Adenocarcinoma, NOS		1 (1%)
Adenocarcinoma in adenomatous polyp, met		1 (1%)
Mucinous cystadenocarcinoma		1 (1%)
#Duodenum	(100)	(173)
Carcinoma, NOS		1 (1%)
Adenocarcinoma, NOS		9 (5%)
Adenomatous polyp, NOS		1 (1%)
Mucinous cystadenocarcinoma	1 (1%)	4 (2%)
#Jejunum	(100)	(173)
Mucinous cystadenocarcinoma		3 (2%)
Mucinous cystadenocarcinoma, metastatic		1 (1%)
Leiomyosarcoma	2 (2%)	
#Colon	(100)	(173)
Carcinoma in-situ, NOS		1 (1%)
Mucinous cystadenocarcinoma		1 (1%)
#Cecum	(100)	(173)
Adenocarcinoma, NOS		2 (1%)
Adenomatous polyp, NOS	1 (1%)	2 (1%)
Mucinous cystadenocarcinoma		1 (1%)
Signet ring carcinoma		3 (2%)
Leiomyoma	1 (1%)	
#Ascending colon	(100)	(173)
Carcinoma in-situ, NOS		1 (1%)
Adenocarcinoma, NOS		3 (2%)
Adenomatous polyp, NOS		5 (3%)
Adenoca in adenomatous polyp		3 (2%)
Mucinous cystadenocarcinoma		14 (8%)
Signet ring carcinoma		2 (1%)

**TABLE A1b. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME
FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH
(Continued)**

	1% Amosite + PW	1% Amosite + DMH
DIGESTIVE SYSTEM (Continued)		
#Transverse colon	(100)	(173)
Adenocarcinoma, NOS		1 (1%)
Adenomatous polyp, NOS		21 (12%)
Adenocarcinoma in adenomatous polyp		20 (12%)
Mucinous cystadenocarcinoma		1 (1%)
#Descending colon	(100)	(173)
Adenomatous polyp, NOS		41 (24%)
Adenocarcinoma in adenomatous polyp	1 (1%)	26 (15%)
Mucinous cystadenocarcinoma		3 (2%)
URINARY SYSTEM		
#Kidney	(100)	(173)
Alveolar/bronchiolar carcinoma, metasta	1 (1%)	
Tubular cell adenoma	1 (1%)	
Tubular cell adenocarcinoma	1 (1%)	
Sarcoma, NOS		3 (2%)
Mixed tumor, benign	2 (2%)	
Mixed tumor, malignant		1 (1%)
#Urinary bladder	(100)	(172)
Adenomatous polyp, NOS		1 (1%)
ENDOCRINE SYSTEM		
#Pituitary	(99)	(169)
Carcinoma, NOS	2 (2%)	
Adenoma, NOS	19 (19%)	12 (7%)
#Adrenal	(100)	(173)
Cortical adenoma	2 (2%)	
Pheochromocytoma	21 (21%)	16 (9%)
Pheochromocytoma, malignant		2 (1%)
#Thyroid	(100)	(172)
Follicular cell adenoma	8 (8%)	10 (6%)
Follicular cell carcinoma	4 (4%)	3 (2%)
C-cell adenoma	11 (11%)	9 (5%)
C-cell carcinoma	14 (14%)	10 (6%)
#Parathyroid	(99)	(168)
Adenoma, NOS	1 (1%)	1 (1%)
#Pancreatic islets	(100)	(173)
Islet cell adenoma	4 (4%)	3 (2%)
Islet cell carcinoma	4 (4%)	3 (2%)
REPRODUCTIVE SYSTEM		
*Mammary gland	(100)	(175)
Papillary adenoma	1 (1%)	
Fibroadenoma	1 (1%)	5 (3%)
*Preputial gland	(100)	(175)
Carcinoma, NOS		4 (2%)
#Prostate	(100)	(172)
Adenocarcinoma, NOS	1 (1%)	
*Coagulating gland	(100)	(175)
Adenoma, NOS		1 (1%)
#Testis	(100)	(172)
Interstitial cell tumor	92 (92%)	125 (72%)
Interstitial cell tumor, maligna	1 (1%)	
*Epididymis	(100)	(175)
Mesothelioma, invasive		1 (1%)
*Scrotum	(100)	(175)
Mesothelioma, invasive		1 (1%)

**TABLE A1b. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME
FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH
(Continued)**

	1% Amosite + PW	1% Amosite + DMH
NERVOUS SYSTEM		
#Cerebrum	(100)	(171)
Astrocytoma	2 (2%)	
SPECIAL SENSE ORGANS		
*Harderian gland	(100)	(175)
Carcinoma, NOS		1 (1%)
*Ear canal	(100)	(175)
Squamous cell papilloma		1 (1%)
*Zymbal gland	(100)	(175)
Carcinoma, NOS	3 (3%)	35 (20%)
Squamous cell papilloma		17 (10%)
Keratoacanthoma		3 (2%)
MUSCULOSKELETAL SYSTEM		
None		
BODY CAVITIES		
*Abdominal cavity	(100)	(175)
Lipoma	1 (1%)	
*Pleura	(100)	(175)
Alveolar/bronchiolar ca, metasta	1 (1%)	
*Mesentery	(100)	(175)
Adenocarcinoma, NOS, invasive		1 (1%)
Adenocarcinoma in adenomatous polyp, met		2 (1%)
Mesothelioma, metastatic		1 (1%)
*Tunica vaginalis	(100)	(175)
Mesothelioma, NOS		1 (1%)
Mesothelioma, malignant	3 (3%)	5 (3%)
ALL OTHER SYSTEMS		
*Multiple organs	(100)	(175)
Adenocarcinoma, NOS, metastatic		7 (4%)
Alveolar/bronchiolar carcinoma, invasive	1 (1%)	
Alveolar/bronchiolar carcinoma, metasta	1 (1%)	
Mucinous cystadenocarcinoma, metastatic		10 (6%)
Signet ring carcinoma, invasive		1 (1%)
Sarcoma, NOS, invasive	1 (1%)	1 (1%)
Mesothelioma, invasive	3 (3%)	3 (2%)
Mesothelioma, metastatic		1 (1%)
Mesentery of colon		
Mucinous cystadenocarcinoma, metastatic		1

TABLE A1b. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
ANIMAL DISPOSITION SUMMARY		
Animals initially in study	100	175
Natural death	11	22
Moribund sacrifice	83	128
Terminal sacrifice	6	25
TUMOR SUMMARY		
Total animals with primary tumors**	99	173
Total primary tumors	310	554
Total animals with benign tumors	95	150
Total benign tumors	192	295
Total animals with malignant tumors	84	149
Total malignant tumors	113	231
Total animals with secondary tumors##	12	40
Total secondary tumors	14	49
Total animals with tumors-- uncertain benign or malignant	5	28
Total uncertain tumors	5	28

(a) DMH indicates a group receiving five doses of 7.5 mg/kg 1,2-dimethylhydrazine dihydrochloride by gavage in pH 5 acetate buffer; PW indicates a group administered 0.47 mg/g chrysotile asbestos daily by gavage for 3 weeks beginning at birth.

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically

** Primary tumors: all tumors except secondary tumors

Number of animals examined microscopically at this site

Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: CONTROL
(Continued)

ANIMAL NUMBER	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291
WEEKS ON STUDY	11/3	11/0	11/7	11/2	11/0	11/8	11/2	11/2	11/9	11/1	11/2	11/9	11/6	11/7	11/4	11/6	11/3	11/3	11/7	11/2	11/8	11/7	11/0	11/0	11/6
INTEGUMENTARY SYSTEM																									
Skin																									
Squamous cell papilloma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Basal cell tumor																									
Basal cell carcinoma	X																								
Trichoepithelioma																									
Keratoacanthoma																									
Fibrosarcoma																									
Neurofibrosarcoma																									
Subcutaneous tissue																									
Sarcoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma	X	X				X																			
Fibrosarcoma																									
Lipoma																									
Liposarcoma																									
Neurofibroma																									
Neurofibrosarcoma							X																		
RESPIRATORY SYSTEM																									
Lungs and bronchi																									
Carcinoma, NOS, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Pheochromocytoma, metastatic																									
Sarcoma, NOS, metastatic																									
Liposarcoma, metastatic																									
Osteosarcoma, metastatic																									
Neurofibrosarcoma, metastatic																									
Trachea																									
Nasal cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Fibrosarcoma																									
HEMATOPOIETIC SYSTEM																									
Bone marrow																									
Liposarcoma, invasive	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen																									
Hemangiosarcoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes																									
Alveolar/bronchiolar carcinoma, invasive	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	-	-	+	-	-	+	-	+	+	+	-	+	-	+	+	-	+	+	-	+
Squamous cell carcinoma																									
CIRCULATORY SYSTEM																									
Heart																									
	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Oral cavity																									
Basal cell tumor	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS, invasive																									
Fibrosarcoma																									
Liver																									
Neoplastic nodule	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																									
Osteosarcoma																									
Monocytic leukemia																									
Bile duct																									
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas																									
Carcinoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Acinar cell carcinoma	X																								X
Esophagus																									
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS	X																								
Small intestine																									
Adenomatous polyp, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma																									
Large intestine																									
Leiomyosarcoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: CONTROL
(Continued)

ANIMAL NUMBER	217	218	219	220	221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240	241	
WEEKS ON STUDY	140	118	119	111	113	112	111	111	110	110	111	111	111	111	111	111	111	111	111	111	111	111	111	111	111	111
ENDOCRINE SYSTEM																										
Pituitary																										
Carcinoma, NOS																										
Adenoma, NOS																										
Adrenal																										
Pheochromocytoma																										
Pheochromocytoma, malignant																										
Thyroid																										
Follicular cell adenoma																										
Follicular cell carcinoma																										
C-cell adenoma																										
C-cell carcinoma																										
Parathyroid																										
Adenoma, NOS																										
C cell carcinoma, invasive																										
Pancreatic islets																										
Islet cell adenoma																										
Islet cell carcinoma																										
REPRODUCTIVE SYSTEM																										
Mammary gland																										
Adenoma, NOS																										
Adenocarcinoma, NOS																										
Fibroadenoma																										
Testis																										
Interstitial cell tumor																										
Prostate																										
Lipoma																										
Liposarcoma, metastatic																										
Seminal vesicle																										
Mucinous cystadenocarcinoma																										
Preputial/choral gland																										
Carcinoma, NOS																										
NERVOUS SYSTEM																										
Brain																										
Carcinoma, NOS, invasive																										
Astrocytoma																										
Astrocytoma, invasive																										
Spinal cord																										
Liposarcoma, invasive																										
SPECIAL SENSE ORGANS																										
Zymbal gland																										
Carcinoma, NOS																										
MUSCULOSKELETAL SYSTEM																										
Bone																										
Liposarcoma																										
Liposarcoma, invasive																										
Osteoma																										
Neurofibrosarcoma																										
BODY CAVITIES																										
Mediastinum																										
Squamous cell carcinoma, metastatic																										
Alveolar/bronchiolar carcinoma, invasive																										
Peritoneum																										
Osteosarcoma, metastatic																										
Tunica vaginalis																										
Mesothelioma, malignant																										
Mesentery																										
Fibrosarcoma, metastatic																										
ALL OTHER SYSTEMS																										
Multiple organs, NOS																										
Carcinoma, NOS, invasive																										
Sarcoma, NOS, invasive																										
Mesothelioma, invasive																										
Mesothelioma, metastatic																										
Malignant lymphoma, histiocytic type																										
Monocytic leukemia																										
Shoulder, NOS																										
Osteosarcoma																										
Hip, NOS																										
Osteosarcoma																										
Leg, NOS																										
Osteosarcoma																										
Scrotum, NOS																										
Keratoacanthoma																										

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	451	452	453	454	455	456	457	458	459	460	461	462	463	464	465	466	467	468	469	470	471	472	473	474	475	
WEEKS ON STUDY	689	877	079	171	064	066	165	167	068	069	167	167	066	167	167	065	067	067	067	068	167	167	067	167	067	167
INTEGUMENTARY SYSTEM																										
Skin	N	+	+	+	+	+	N	+	+	N	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	
Fibrosarcoma																										
Subcutaneous tissue	N	+	+	+	+	+	N	+	+	N	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS																										
Fibroma																										
Neurofibroma				X																			X			
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma in adenomatous polyp, metastatic																										
Alveolar/bronchiolar carcinoma																								X		
C cell carcinoma, metastatic																										
Mucinous cystadenocarcinoma, metastatic									X																	
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	-	+	+	-	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
C cell carcinoma, metastatic																										
Mucinous cystadenocarcinoma, metastatic									X																	
Thymus	+	-	+	+	+	-	+	+	-	+	-	+	+	+	-	-	+	+	+	+	+	+	+	-	-	
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
DIGESTIVE SYSTEM																										
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Squamous cell papilloma																										
Keratoacanthoma																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Neoplastic nodule														X												
Hepatocellular carcinoma																						X				
Monocytic leukemia																						X				
Bile duct																										
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma, NOS, metastatic																										
Neurofibrosarcoma, metastatic																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																										
Adenocarcinoma, NOS																										
Adenomatous polyp, NOS																										
Mucinous cystadenocarcinoma				X																						
Signet ring carcinoma																										
Leiomyosarcoma																										
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma in situ, NOS																										
Adenocarcinoma, NOS																										
Adenomatous polyp, NOS				X	X																					
Adenocarcinoma in adenomatous polyp	X																									
Mucinous cystadenocarcinoma																										
Signet ring carcinoma							X	X		X															X	
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Transitional cell carcinoma																										
Tubular cell adenocarcinoma																										
Neurofibrosarcoma																										
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	4676	4776	4777	4778	4779	4880	4881	4882	4883	4884	4885	4886	4887	4888	4889	4990	4991	4992	4993	4994	4995	4996	4997	4998	4999	5000	
WEEKS ON STUDY	080	085	081	077	077	066	066	011	066	011	077	088	066	088	000	011	011	000	011	000	000	000	011	000	011	000	011
INTEGUMENTARY SYSTEM																											
Skin	+	N	+	+	N	N	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Fibrosarcoma																											
Subcutaneous tissue	+	N	+	+	N	N	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS																											
Fibroma																											
Neurofibroma																											
RESPIRATORY SYSTEM																											
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma in adenomatous polyp, metastatic																											
Alveolar/bronchiolar carcinoma																											
C-cell carcinoma, metastatic																											
Mucinous cystadenocarcinoma, metastatic																											
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMATOPOIETIC SYSTEM																											
Bone marrow	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
C cell carcinoma, metastatic																											
Mucinous cystadenocarcinoma, metastatic																											
Thymus	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	
CIRCULATORY SYSTEM																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
DIGESTIVE SYSTEM																											
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Squamous cell papilloma																											
Keratoacanthoma																											
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Neoplastic nodule																											
Hepatocellular carcinoma																											
Monocytic leukemia																											
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma, NOS, metastatic																											
Neurofibrosarcoma, metastatic																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																											
Adenocarcinoma, NOS																											
Adenomatous polyp, NOS																											
Mucinous cystadenocarcinoma																											
Signet ring carcinoma																											
Leiomyosarcoma																											
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma in situ, NOS																											
Adenocarcinoma, NOS																											
Adenomatous polyp, NOS																											
Adenocarcinoma in adenomatous polyp																											
Mucinous cystadenocarcinoma																											
Signet ring carcinoma																											
URINARY SYSTEM																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Transitional cell carcinoma																											
Tubular cell adenocarcinoma																											
Neurofibrosarcoma																											
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	

@ Multiple occurrence of morphology

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525
WEEKS ON STUDY	87	117	166	166	169	177	177	177	177	177	177	177	177	177	177	177	177	177	177	177	177	177	177	177	177
INTEGUMENTARY SYSTEM																									
Skin	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	N	+	+	+	+
Fibrosarcoma																									
Subcutaneous tissue	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	N	+	+	+	+
Sarcoma, NOS																									
Fibroma																									
Neurofibroma																									X
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma in adenomatous polyp, metastatic																									
Alveolar/bronchiolar carcinoma																									
C cell carcinoma, metastatic																									
Mucinous cystadenocarcinoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C cell carcinoma, metastatic																									
Mucinous cystadenocarcinoma, metastatic																									
Thymus	+	-	+	-	+	-	+	+	+	+	-	+	+	-	-	+	-	+	+	+	-	-	-	+	-
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Oral cavity																									
Squamous cell papilloma																									
Keratoacanthoma																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma																									
Monocytic leukemia																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic																									
Neurofibrosarcoma, metastatic																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenocarcinoma, NOS																									
Adenomatous polyp, NOS																									
Mucinous cystadenocarcinoma																									
Signet ring carcinoma																									
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma in situ, NOS																									
Adenocarcinoma, NOS																									
Adenomatous polyp, NOS																									
Adenocarcinoma in adenomatous polyp	X		X		X		X		X		X		X		X		X		X		X		X		
Mucinous cystadenocarcinoma																									
Signet ring carcinoma																									
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Transitional cell carcinoma																									
Tubular cell adenocarcinoma																									
Neurofibrosarcoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

@ Multiple occurrence of morphology

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65
WEEKS ON STUDY	069	087	079	071	064	065	061	067	068	069	066	067	067	066	067	067	065	067	067	060	061	060	068	067	067
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS												X	X					X	X						
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma			X						X				X	X	X										X
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																									
C-cell adenoma																									
C-cell carcinoma																									
Parathyroid																									
Adenoma, NOS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+
Fibroadenoma												X													
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor		X	X	X	X		X			X	X	X		X	X	X		X		X	X	X	X	X	X
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS												X													
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, invasive																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma																									
Meningioma																									
SPECIAL SENSE ORGANS																									
Lacrimal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
Ear	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Zymbal gland	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS						X		X		X	X	X											X		X
Squamous cell papilloma																									
Keratoacanthoma																									
MUSCULOSKELETAL SYSTEM																									
Muscle	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Rhabdomyosarcoma																									
BODY CAVITIES																									
Pertoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mucinous cystadenocarcinoma, metastatic																									
Sarcoma, NOS																									
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, malignant																								X	+
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Sarcoma, NOS																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS, metastatic																									
Adenocarcinoma, NOS, metastatic			X	X												X								X	
Mucinous cystadenocarcinoma, metastatic						X	X																		
Signet ring carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Mesothelioma, invasive																									X
Mesothelioma, metastatic																									
Malignant lymphoma, histiocytic type																									
Monocytic leukemia					X											X						X			
Orbital region																									
Sarcoma, NOS																									
Scrotum, NOS																									
Mesothelioma, invasive																									

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70
WEEKS ON STUDY	80	85	91	97	100	106	112	118	124	130	136	142	148	154	160	166	172	178	184	190	196	202	208	214	220
ENDOCRINE SYSTEM																									
Pituitary Adenoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal Pheochromocytoma	X	+	X	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid Follicular cell adenoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma																									
C-cell adenoma																									
C-cell carcinoma																									
Parathyroid Adenoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland Fibroadenoma	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N
Testis Interstitial cell tumor	X	+	X	+	+	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial/choral gland Carcinoma, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Epididymis Mesothelioma, invasive	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
NERVOUS SYSTEM																									
Brain Astrocytoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Meningioma																									
SPECIAL SENSE ORGANS																									
Lacrimal gland Carcinoma, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Ear Squamous cell papilloma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Zymbal gland Carcinoma, NOS	X	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Keratoacanthoma																									
MUSCULOSKELETAL SYSTEM																									
Muscle Rhabdomyosarcoma	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
BODY CAVITIES																									
Peritoneum Mucinous cystadenocarcinoma, metastatic	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Sarcoma, NOS																									
Tunica vaginalis Mesothelioma, malignant	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery Sarcoma, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS, metastatic																									
Adenocarcinoma, NOS, metastatic																									
Mucinous cystadenocarcinoma, metastatic																									
Signet ring carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Mesothelioma, invasive																									
Mesothelioma, metastatic																									
Malignant lymphoma, histiocytic type																									
Monocytic leukemia																									
Orbital region Sarcoma, NOS																									
Scrotum, NOS																									
Mesothelioma, invasive																									

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525
WEEKS ON STUDY	87	117	161	166	199	196	199	251	127	147	144	175	150	183	193	183	194	186	199	199	188	199	198	192	192
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma																							X		
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																X		X							
C-cell adenoma																									
C-cell carcinoma					X																	X			
Parathyroid	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
REPRODUCTIVE SYSTEM																									
Mammary gland	N	+	+	+	+	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																									
Testis	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor	X	X		X	X	X		X		X	X				X	X	X	X		X	X	X	X	X	X
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, invasive																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma																							X		
Meningioma																						X			
SPECIAL SENSE ORGANS																									
Lacrimal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
Ear	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Zymbal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																						X			
Squamous cell papilloma																								X	
Keratoacanthoma											X														
MUSCULOSKELETAL SYSTEM																									
Muscle	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Rhabdomyosarcoma																									
BODY CAVITIES																									
Pertoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mucinous cystadenocarcinoma, metastatic																									
Sarcoma, NOS																							X		
Tunica vaginalis	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, malignant			X																						
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Sarcoma, NOS																							X		
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS, metastatic																									
Adenocarcinoma, NOS, metastatic													X												
Mucinous cystadenocarcinoma, metastatic																									
Signet ring carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Mesothelioma, invasive			X																				X		
Mesothelioma, metastatic			X																						
Malignant lymphoma, histiocytic type																									
Monocytic leukemia																									
Orbital region																									
Sarcoma, NOS																									
Scrotum, NOS																									
Mesothelioma, invasive																									

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: 1% AMOSITE

ANIMAL NUMBER	676	677	678	679	680	681	682	683	684	685	686	687	688	689	690	691	692	693	694	695	696	697	698	699	700	
WEEKS ON STUDY	116	117	118	119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140	
INTEGUMENTARY SYSTEM																										
Skin																										
Carcinoma in situ, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell papilloma																										
Squamous cell carcinoma																		X								
Basal cell tumor																										
Basal cell carcinoma																			X							
Keratoacanthoma	X																									
Fibroma	X												X					X			X					
Fibrosarcoma													X													
Myxoma																										
Osteosarcoma																										
Subcutaneous tissue																										
Sarcoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS, invasive																										
Fibroma																										
Fibrosarcoma	X				X								X								X				X	
Lipoma																										
Liposarcoma																										
Hemangiosarcoma																										
Neurofibroma																										
RESPIRATORY SYSTEM																										
Lungs and bronchi																										
Carcinoma, NOS, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell carcinoma, metastatic																										
Alveolar/bronchiolar adenoma																										
Alveolar/bronchiolar carcinoma																										
Papillary adenocarcinoma																										
C cell carcinoma, metastatic																										
Pheochromocytoma, metastatic																										
Sarcoma, NOS, metastatic																										
Liposarcoma, metastatic																										
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
C-cell carcinoma, invasive																										
HEMATOPOIETIC SYSTEM																										
Bone marrow																										
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Fibrosarcoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Mesothelioma, metastatic																										
Hemangiosarcoma																										
Lymph nodes																										
C-cell carcinoma, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS, invasive																										
Fibrosarcoma, invasive																										
Thymus	-	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	-	-	+	+	-	+	+	-	+	
Carcinoma, NOS																										
CIRCULATORY SYSTEM																										
Heart																										
	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	

**TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7		
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5		
WEEKS ON STUDY	13	13	13	13	13	13	13	13	13	13	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1		
	7	4	0	7	8	1	7	8	6	7	1	6	1	3	7	1	9	1	0	9	8	0	1	9	5		
INTEGUMENTARY SYSTEM																											
Skin																											
Carcinoma in-situ, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Squamous cell papilloma																											
Squamous cell carcinoma																											
Basal cell tumor																											
Basal cell carcinoma																											
Keratoacanthoma																											
Fibroma																											
Fibrosarcoma																									X		
Myxoma																											
Osteosarcoma																											
Subcutaneous tissue																											
Sarcoma, NOS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Sarcoma, NOS, invasive								X																			
Fibroma														X													
Fibrosarcoma												X				X	X							X			
Lipoma												X															
Liposarcoma																											
Hemangiosarcoma																											
Neurofibroma																											
RESPIRATORY SYSTEM																											
Lungs and bronchi																											
Carcinoma, NOS, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Squamous cell carcinoma, metastatic																							X	+	+		
Alveolar/bronchiolar adenoma																											
Alveolar/bronchiolar carcinoma								X																			
Papillary adenocarcinoma																											
C-cell carcinoma, metastatic																											
Pheochromocytoma, metastatic																											
Sarcoma, NOS, metastatic									X																		
Liposarcoma, metastatic																											
Trachea																											
C-cell carcinoma, invasive	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
HEMATOPOIETIC SYSTEM																											
Bone marrow																											
	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Spleen																											
	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Fibrosarcoma																											
Mesothelioma, metastatic																											
Hemangiosarcoma																									X		
Lymph nodes																											
C cell carcinoma, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Sarcoma, NOS, invasive																											
Fibrosarcoma, invasive																											
Thymus																											
Carcinoma, NOS	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	-	+	+	+	-	-		
CIRCULATORY SYSTEM																											
Heart																											
	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		

**TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	7 6	7 7	7 8	7 9	7 0	7 1	7 2	7 3	7 4	7 5	7 6	7 7	7 8	7 9	7 0	7 1	7 2	7 3	7 4	7 5	7 6	7 7	7 8	7 9	8 0		
WEEKS ON STUDY	1 0	1 4	1 1	1 4	1 7	1 9	0 9	0 9	1 8	1 6	0 2	1 9	1 3	1 1	1 1	1 1	1 4	1 2	1 2	1 4	1 0	1 3	1 4	1 3	1 3	1 2	
INTEGUMENTARY SYSTEM																											
Skin																											
Carcinoma in-situ, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell papilloma	X																										
Squamous cell carcinoma																											
Basal cell tumor																											
Basal cell carcinoma																											
Keratoacanthoma																											
Fibroma																											
Fibrosarcoma																											
Myxoma																											
Osteosarcoma																											
Subcutaneous tissue																											
Sarcoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS, invasive																											
Fibroma																											
Fibrosarcoma																											
Lipoma																											
Liposarcoma																											
Hemangiosarcoma																											
Neurofibroma																											
RESPIRATORY SYSTEM																											
Lungs and bronchi																											
Carcinoma, NOS, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell carcinoma, metastatic																											
Alveolar/bronchiolar adenoma																											
Alveolar/bronchiolar carcinoma																											
Papillary adenocarcinoma																											
C-cell carcinoma, metastatic																											
Pheochromocytoma, metastatic																											
Sarcoma, NOS, metastatic																											
Liposarcoma, metastatic																											
Trachea																											
C-cell carcinoma, invasive	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMATOPOIETIC SYSTEM																											
Bone marrow																											
	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Spleen																											
Fibrosarcoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Mesothelioma, metastatic																											
Hemangiosarcoma																											
Lymph nodes																											
C-cell carcinoma, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS, invasive																											
Fibrosarcoma, invasive																											
Thymus																											
Carcinoma, NOS	-	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
CIRCULATORY SYSTEM																											
Heart																											
	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	

**TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	801	802	803	804	805	806	807	808	809	810	811	812	813	814	815	816	817	818	819	820	821	822	823	824	825	
WEEKS ON STUDY	096	117	119	119	112	112	112	080	134	110	114	110	083	111	111	111	111	111	111	111	111	111	111	111	111	070
INTEGUMENTARY SYSTEM																										
Skin																										
Carcinoma in situ, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																										
Squamous cell carcinoma																										
Basal cell tumor																										
Basal cell carcinoma																										
Keratoacanthoma																										
Fibroma																										
Fibrosarcoma																										
Myxoma																										
Osteosarcoma																										
Subcutaneous tissue																										
Sarcoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS, invasive																										
Fibroma																										
Fibrosarcoma																										
Lipoma																										
Liposarcoma																										
Hemangiosarcoma																										
Neurofibroma																										
RESPIRATORY SYSTEM																										
Lungs and bronchi																										
Carcinoma, NOS, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																										
Alveolar/bronchiolar adenoma																										
Alveolar/bronchiolar carcinoma																										
Papillary adenocarcinoma																										
C cell carcinoma, metastatic																										
Pheochromocytoma, metastatic																										
Sarcoma, NOS, metastatic																										
Liposarcoma, metastatic																										
Trachea	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C cell carcinoma, invasive																										
HEMATOPOIETIC SYSTEM																										
Bone marrow																										
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																										
Mesothelioma, metastatic																										
Hemangiosarcoma																										
Lymph nodes																										
C-cell carcinoma, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS, invasive																										
Fibrosarcoma, invasive																										
Thymus	-	+	+	+	-	+	+	-	-	-	-	+	-	-	-	+	+	+	+	+	+	-	-	+	+	
Carcinoma, NOS																										
CIRCULATORY SYSTEM																										
Heart																										
	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)

ANIMAL NUMBER	8 2 6	8 2 7	8 2 8	8 2 9	8 3 0	8 3 1	8 3 2	8 3 3	8 3 4	8 3 5	8 3 6	8 3 7	8 3 8	8 3 9	8 4 0	8 4 1	8 4 2	8 4 3	8 4 4	8 4 5	8 4 6	8 4 7	8 4 8	8 4 9	8 5 0		
WEEKS ON STUDY	11 2 7	11 1 5	11 2 2	11 3 9	11 3 1	11 3 4	11 3 3	11 3 9	11 2 2	11 4 0	11 3 6	11 5 5	11 1 3	11 4 0	11 4 4	11 3 3	11 1 1	11 4 3	11 8 8	11 0 2	11 0 9	11 0 0	11 4 4	11 4 1	11 4 4	11 2 8	
INTEGUMENTARY SYSTEM																											
Skin																											
Carcinoma in situ, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																											
Squamous cell carcinoma	X																										
Basal cell tumor																											
Basal cell carcinoma																											
Keratoacanthoma																											
Fibroma																											
Fibrosarcoma																											
Myxoma																											
Osteosarcoma																											
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																											
Sarcoma, NOS, invasive																											
Fibroma																											
Fibrosarcoma																											
Lipoma																											
Liposarcoma																											
Hemangiosarcoma																											
Neurofibroma																											
RESPIRATORY SYSTEM																											
Lungs and bronchi																											
Carcinoma, NOS, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																											
Alveolar/bronchiolar adenoma																											
Alveolar/bronchiolar carcinoma																											
Papillary adenocarcinoma																											
C cell carcinoma, metastatic																											
Pheochromocytoma, metastatic																											
Sarcoma, NOS, metastatic																											
Liposarcoma, metastatic																											
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell carcinoma, invasive																											
HEMATOPOIETIC SYSTEM																											
Bone marrow																											
Fibrosarcoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, metastatic																											
Hemangiosarcoma																											
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell carcinoma, metastatic																											
Sarcoma, NOS, invasive																											
Fibrosarcoma, invasive																											
Thymus	-	-	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																											
CIRCULATORY SYSTEM																											
Heart																											
Carcinoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

**TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	876	877	878	879	880	881	882	883	884	885	886	887	888	889	890	891	892	893	894	895	896	897	898	899	900		
WEEKS ON STUDY	10	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11		
INTEGUMENTARY SYSTEM																											
Skin																											
Carcinoma in-situ, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell papilloma																											
Squamous cell carcinoma																									X		
Basal cell tumor																											
Basal cell carcinoma																											
Keratoacanthoma																											
Fibroma																											
Fibrosarcoma																											
Myxoma																											
Osteosarcoma																											
Subcutaneous tissue																											
Sarcoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS, invasive																											
Fibroma																											
Fibrosarcoma																											
Lipoma																											
Liposarcoma																											
Hemangiosarcoma																											
Neurofibroma																											
RESPIRATORY SYSTEM																											
Lungs and bronchi																											
Carcinoma, NOS, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell carcinoma, metastatic																											
Alveolar/bronchiolar adenoma																											
Alveolar/bronchiolar carcinoma																											
Papillary adenocarcinoma																											
C-cell carcinoma, metastatic																											
Phoehromocytoma, metastatic																											
Sarcoma, NOS, metastatic																											
Liposarcoma, metastatic																											
Trachea																											
C-cell carcinoma, invasive	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMATOPOIETIC SYSTEM																											
Bone marrow																											
	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Spleen																											
Fibrosarcoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Mesothelioma, metastatic																											
Hemangiosarcoma																											
Lymph nodes																											
C-cell carcinoma, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS, invasive																											
Fibrosarcoma, invasive																											
Thymus																											
Carcinoma, NOS	+	+	+	+	+	+	-	-	+	-	+	+	-	-	+	-	+	-	+	+	+	+	+	+	-	+	
CIRCULATORY SYSTEM																											
Heart																											
	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	

@ Multiple occurrence of morphology

**TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	676	677	678	679	680	681	682	683	684	685	686	687	688	689	690	691	692	693	694	695	696	697	698	699	700		
WEEKS ON STUDY	11	12	11	11	11	11	11	11	11	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
	7	1	1	5	4	1	1	2	1	8	2	4	4	3	3	4	3	4	2	2	2	1	3	3	3	2	
DIGESTIVE SYSTEM																											
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Squamous cell papilloma																											
Squamous cell carcinoma						X																					
Basal cell carcinoma																											
Salivary gland	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																											
Sarcoma, NOS																											
Fibrosarcoma																											
Fibrosarcoma, invasive																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Neoplastic nodule																											
Hepatocellular carcinoma																											
Monocytic leukemia																											
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																											
Acinar cell adenoma																											
Acinar cell carcinoma						X										X	X										
Mixed tumor, benign																											
Mesothelioma, metastatic																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma in-situ, NOS																											
Adenomatous polyp, NOS																											
Leiomyosarcoma																											
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma in adenomatous polyp																											
Leiomyoma																											
Leiomyosarcoma																											
Malignant lymphoma, histiocytic type																											
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma in-situ, NOS																											
Adenomatous polyp, NOS																											
Leiomyoma																										X	
URINARY SYSTEM																											
Kidney	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																											
Tubular cell adenoma																											
Tubular cell adenocarcinoma																											
Sarcoma, NOS																											
Lipoma																											
Mixed tumor, malignant																											
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ENDOCRINE SYSTEM																											
Pituitary	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																											
Adenoma, NOS		X				X									X	X	X				X	X	X				
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Tubular cell adenocarcinoma, invasive																											
Cortical adenoma																											
Pheochromocytoma	X		X	X	X				X	X	X	X									X						
Pheochromocytoma, malignant																											
Ganglioneuroma																											
Thyroid	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Follicular cell adenoma																											
Follicular cell carcinoma		X																			X	X					
C-cell adenoma																											
C-cell carcinoma	X																X										
Parathyroid	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenoma, NOS																											
C-cell carcinoma, invasive																											
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Islet cell adenoma																											
Islet cell carcinoma																											

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)

ANIMAL NUMBER	7101	7102	7103	7104	7105	7106	7107	7108	7109	7110	7111	7112	7113	7114	7115	7116	7117	7118	7119	7120	7121	7122	7123	7124	7125
WEEKS ON STUDY	37	34	20	33	08	31	37	18	38	8	11	01	98	71	33	37	11	24	24	44	33	22	24	34	30
DIGESTIVE SYSTEM																									
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell carcinoma																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Sarcoma, NOS																									
Fibrosarcoma																									
Fibrosarcoma, invasive																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma																									
Monocytic leukemia																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Acinar cell adenoma																									
Acinar cell carcinoma																									
Mixed tumor, benign																									
Mesothelioma, metastatic																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma in-situ, NOS																									
Adenomatous polyp, NOS																									
Leiomyosarcoma																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma in adenomatous polyp																									
Leiomyoma																									
Leiomyosarcoma																									
Malignant lymphoma, histiocytic type																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma in-situ, NOS																									
Adenomatous polyp, NOS																									
Leiomyoma																									
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Tubular cell adenoma																									
Tubular cell adenocarcinoma																									
Sarcoma, NOS																									
Lipoma																									
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS																									
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenocarcinoma, invasive																									
Cortical adenoma																									
Pheochromocytoma																									
Pheochromocytoma, malignant																									
Ganglioneuroma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																									
C-cell adenoma																									
C-cell carcinoma																									
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
C-cell carcinoma, invasive																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
Islet cell carcinoma																									

**TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	00		
WEEKS ON STUDY	10	11	11	11	11	11	09	09	09	08	06	02	01	03	01	01	01	02	02	04	07	07	04	03	03	03	
DIGESTIVE SYSTEM																											
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Squamous cell papilloma																											
Squamous cell carcinoma																											
Basal cell carcinoma																											
Salivary gland																											
Carcinoma, NOS																											
Sarcoma, NOS																											
Fibrosarcoma																											
Fibrosarcoma, invasive																											
Liver																											
Neoplastic nodule																											
Hepatocellular carcinoma																											
Monocytic leukemia																											
Bile duct																											
Gallbladder & common bile duct																											
Pancreas																											
Carcinoma, NOS																											
Acinar cell adenoma																											
Acinar cell carcinoma																											
Mixed tumor, benign																											
Mesothelioma, metastatic																											
Esophagus																											
Stomach																											
Carcinoma in-situ, NOS																											
Adenomatous polyp, NOS																											
Leiomyosarcoma																											
Small intestine																											
Adenocarcinoma in adenomatous polyp																											
Leiomyoma																											
Leiomyosarcoma																											
Malignant lymphoma, histiocytic type																											
Large intestine																											
Carcinoma in-situ, NOS																											
Adenomatous polyp, NOS																											
Leiomyoma																											
URINARY SYSTEM																											
Kidney																											
Carcinoma, NOS																											
Tubular cell adenoma																											
Tubular cell adenocarcinoma																											
Sarcoma, NOS																											
Lipoma																											
Mixed tumor, malignant																											
Urinary bladder																											
ENDOCRINE SYSTEM																											
Pituitary																											
Carcinoma, NOS																											
Adenoma, NOS																											
Adrenal																											
Tubular cell adenocarcinoma, invasive																											
Cortical adenoma																											
Pheochromocytoma																											
Pheochromocytoma, malignant																											
Ganglioneuroma																											
Thyroid																											
Follicular cell adenoma																											
Follicular cell carcinoma																											
C-cell adenoma																											
C-cell carcinoma																											
Parathyroid																											
Adenoma, NOS																											
C-cell carcinoma, invasive																											
Pancreatic islets																											
Islet cell adenoma																											
Islet cell carcinoma																											

**TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	8051	8052	8053	8054	8055	8056	8057	8058	8059	8060	8061	8062	8063	8064	8065	8066	8067	8068	8069	8070	8071	8072	8073	8074	8075		
WEEKS ON STUDY	14	20	20	24	20	11	11	11	11	11	20	20	20	20	20	20	20	20	20	20	20	20	20	20	27		
DIGESTIVE SYSTEM																											
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Squamous cell papilloma																											
Squamous cell carcinoma																											
Basal cell carcinoma																											
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																											
Sarcoma, NOS																											
Fibrosarcoma																											
Fibrosarcoma, invasive																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Neoplastic nodule																											
Hepatocellular carcinoma																											
Monocytic leukemia																											
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																											
Acinar cell adenoma																											
Acinar cell carcinoma																											
Mixed tumor, benign																											
Mesothelioma, metastatic																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma in-situ, NOS																											
Adenomatous polyp, NOS																											
Leiomyosarcoma																											
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma in adenomatous polyp																											
Leiomyoma																											
Leiomyosarcoma																											
Malignant lymphoma, histiocytic type																											
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma in-situ, NOS																											
Adenomatous polyp, NOS																											
Leiomyoma																											
URINARY SYSTEM																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																											
Tubular cell adenoma																											
Tubular cell adenocarcinoma																											
Sarcoma, NOS																											
Lipoma																											
Mixed tumor, malignant																											
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ENDOCRINE SYSTEM																											
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																											
Adenoma, NOS																											
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Tubular cell adenocarcinoma, invasive																											
Cortical adenoma																											
Pheochromocytoma																											
Pheochromocytoma, malignant																											
Ganglioneuroma																											
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Follicular cell adenoma																											
Follicular cell carcinoma																											
C-cell adenoma																											
C-cell carcinoma																											
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenoma, NOS																											
C-cell carcinoma, invasive																											
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Islet cell adenoma																											
Islet cell carcinoma																											

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)

ANIMAL NUMBER	878	877	876	875	874	873	872	871	870	869	868	867	866	865	864	863	862	861	860	859	858	857	856	855	854	853	852	851	850
WEEKS ON STUDY	10	11	18	05	11	13	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
DIGESTIVE SYSTEM																													
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Squamous cell papilloma																													
Squamous cell carcinoma																													
Basal cell carcinoma																													
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																													
Sarcoma, NOS																													
Fibrosarcoma					X																								
Fibrosarcoma, invasive																													
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																													
Hepatocellular carcinoma																										X			
Monocytic leukemia																													
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																													
Acinar cell adenoma																													
Acinar cell carcinoma					X								X															X	X
Mixed tumor, benign																													
Mesothelioma, metastatic																													
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma in-situ, NOS																													
Adenomatous polyp, NOS																													
Leiomyosarcoma																													
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma in adenomatous polyp																													
Leiomyoma																													
Leiomyosarcoma																													
Malignant lymphoma, histiocytic type																													
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma in-situ, NOS																													
Adenomatous polyp, NOS																													
Leiomyoma																													
URINARY SYSTEM																													
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																													
Tubular cell adenoma																													
Tubular cell adenocarcinoma																													
Sarcoma, NOS																													
Lipoma																													
Mixed tumor, malignant																													
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																													
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																													
Adenoma, NOS																													
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenocarcinoma, invasive																													
Cortical adenoma																												X	
Pheochromocytoma				X	X	X	X						X				X	X	X										X
Pheochromocytoma, malignant																													
Ganglioneuroma																													
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma	X	X																											
Follicular cell carcinoma																													
C-cell adenoma																													
C-cell carcinoma			X																										
Parathyroid	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																													
C-cell carcinoma, invasive																													
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																													
Islet cell carcinoma																												X	

**TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	7 0 1	7 0 2	7 0 3	7 0 4	7 0 5	7 0 6	7 0 7	7 0 8	7 0 9	7 1 0	7 1 1	7 1 2	7 1 3	7 1 4	7 1 5	7 1 6	7 1 7	7 1 8	7 1 9	7 2 0	7 2 1	7 2 2	7 2 3	7 2 4	7 2 5
WEEKS ON STUDY	1 3 7	1 3 4	1 2 0	1 3 7	1 0 8	1 3 1	1 3 7	1 8 8	1 6 6	1 7 7	0 9 1	0 7 6	1 3 7	1 4 1	1 2 9	1 4 1	1 4 0	1 3 9	1 2 8	1 2 0	1 2 2	1 2 2	1 2 3	1 4 4	1 3 0
REPRODUCTIVE SYSTEM																									
Mammary gland																									
Adenoma, NOS																									
Adenocarcinoma, NOS																									
Papillary adenocarcinoma																									
Sarcoma, NOS, invasive																									
Fibrosarcoma																									
Fibroadenoma																									
Testis																									
Interstitial cell tumor																									
Prostate																									
Squamous cell carcinoma																									
Preputial/clitoral gland																									
Carcinoma, NOS																									
Squamous cell carcinoma																									
Epididymis																									
Lipoma																									
NERVOUS SYSTEM																									
Brain																									
Carcinoma, NOS, invasive																									
Astrocytoma																									
Astrocytoma, invasive																									
SPECIAL SENSE ORGANS																									
Ear																									
Squamous cell papilloma																									
Zymbal gland																									
Carcinoma, NOS																									
Squamous cell papilloma																									
Adenoma, NOS																									
MUSCULOSKELETAL SYSTEM																									
Bone																									
Liposarcoma																									
Osteoma																									
Osteosarcoma																									
BODY CAVITIES																									
Peritoneum																									
Sarcoma, NOS																									
Sarcoma, NOS, invasive																									
Mesothelioma, invasive																									
Tunica vaginalis																									
Mesothelioma, NOS																									
Mesothelioma, malignant																									
Mesentery																									
Mesothelioma, malignant																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS																									
Squamous cell carcinoma, invasive																									
Tubular cell adenocarcinoma, metastatic																									
C-cell carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Fibrosarcoma, invasive																									
Mesothelioma, invasive																									
Mesothelioma, metastatic																									
Osteosarcoma, metastatic																									
Malignant lymphoma, lymphocytic type																									
Malignant lymphoma, histiocytic type																									
Myelomonocytic leukemia																									
Monocytic leukemia																									
Back, NOS																									
Basal cell carcinoma																									
Flank, NOS																									
Rhabdomyosarcoma																									
Sacral region																									
Neurofibroma																									
Axilla, NOS																									
Fibroma																									
Fibrosarcoma																									
Scrotum, NOS																									
Mesothelioma, invasive																									

**TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	7 2 6	7 2 7	7 2 8	7 2 9	7 3 0	7 3 1	7 3 2	7 3 3	7 3 4	7 3 5	7 3 6	7 3 7	7 3 8	7 3 9	7 4 0	7 4 1	7 4 2	7 4 3	7 4 4	7 4 5	7 4 6	7 4 7	7 4 8	7 4 9	7 5 0	
WEEKS ON STUDY	1 2 7	1 1 3																								
REPRODUCTIVE SYSTEM																										
Mammary gland																										
Adenoma, NOS																										
Adenocarcinoma, NOS																										
Papillary adenocarcinoma																										
Sarcoma, NOS, invasive																										
Fibrosarcoma																										
Fibroadenoma																										
Testis																										
Interstitial cell tumor																										
Prostate																										
Squamous cell carcinoma																										
Preputial/clitoral gland																										
Carcinoma, NOS																										
Squamous cell carcinoma																										
Epididymis																										
Lipoma																										
NERVOUS SYSTEM																										
Brain																										
Carcinoma, NOS, invasive																										
Astrocytoma																										
Astrocytoma, invasive																										
SPECIAL SENSE ORGANS																										
Ear																										
Squamous cell papilloma																										
Zymbal gland																										
Carcinoma, NOS																										
Squamous cell papilloma																										
Adenoma, NOS																										
MUSCULOSKELETAL SYSTEM																										
Bone																										
Liposarcoma																										
Osteoma																										
Osteosarcoma																										
BODY CAVITIES																										
Peritoneum																										
Sarcoma, NOS																										
Sarcoma, NOS, invasive																										
Mesothelioma, invasive																										
Tunica vaginalis																										
Mesothelioma, NOS																										
Mesothelioma, malignant																										
Mesentery																										
Mesothelioma, malignant																										
ALL OTHER SYSTEMS																										
Multiple organs, NOS																										
Squamous cell carcinoma, invasive																										
Tubular cell adenocarcinoma, metastatic																										
C-cell carcinoma, metastatic																										
Sarcoma, NOS, invasive																										
Fibrosarcoma, invasive																										
Mesothelioma, invasive																										
Mesothelioma, metastatic																										
Osteosarcoma, metastatic																										
Malignant lymphoma, lymphocytic type																										
Malignant lymphoma, histiocytic type																										
Myelomonocytic leukemia																										
Monocytic leukemia																										
Back, NOS																										
Basal cell carcinoma																										
Flank, NOS																										
Rhabdomyosarcoma																										
Sacral region																										
Neurofibroma																										
Axilla, NOS																										
Fibroma																										
Fibrosarcoma																										
Scrotum, NOS																										
Mesothelioma, invasive																										

**TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	8 5 1	8 5 2	8 5 3	8 5 4	8 5 5	8 5 6	8 5 7	8 5 8	8 5 9	8 6 0	8 6 1	8 6 2	8 6 3	8 6 4	8 6 5	8 6 6	8 6 7	8 6 8	8 6 9	8 7 0	8 7 1	8 7 2	8 7 3	8 7 4	8 7 5		
WEEKS ON STUDY	1 4 1	1 2 6	1 0 8	1 2 4	1 0 8	1 4 1	1 1 6	1 4 1	1 1 0	1 2 6	1 3 6	1 2 6	1 2 8	1 4 1	1 4 1	1 2 4	1 2 1	1 3 1	1 3 1	1 2 0	1 3 8	1 4 1	1 3 1	1 3 8	1 4 5		
REPRODUCTIVE SYSTEM																											
Mammary gland																											
Adenoma, NOS																											
Adenocarcinoma, NOS																											
Papillary adenocarcinoma																											
Sarcoma, NOS, invasive																											
Fibrosarcoma																											
Fibroadenoma																											
Testis																											
Interstitial cell tumor																											
Prostate																											
Squamous cell carcinoma																											
Preputial/clitoral gland																											
Carcinoma, NOS																											
Squamous cell carcinoma																											
Epididymis																											
Lipoma																											
NERVOUS SYSTEM																											
Brain																											
Carcinoma, NOS, invasive																											
Astrocytoma																											
Astrocytoma, invasive																											
SPECIAL SENSE ORGANS																											
Ear																											
Squamous cell papilloma																											
Zymbal gland																											
Carcinoma, NOS																											
Squamous cell papilloma																											
Adenoma, NOS																											
MUSCULOSKELETAL SYSTEM																											
Bone																											
Liposarcoma																											
Osteoma																											
Osteosarcoma																											
BODY CAVITIES																											
Peritoneum																											
Sarcoma, NOS																											
Sarcoma, NOS, invasive																											
Mesothelioma, invasive																											
Tunica vaginalis																											
Mesothelioma, NOS																											
Mesothelioma, malignant																											
Mesentery																											
Mesothelioma, malignant																											
ALL OTHER SYSTEMS																											
Multiple organs, NOS																											
Squamous cell carcinoma, invasive																											
Tubular cell adenocarcinoma, metastatic																											
C-cell carcinoma, metastatic																											
Sarcoma, NOS, invasive																											
Fibrosarcoma, invasive																											
Mesothelioma, invasive																											
Mesothelioma, metastatic																											
Osteosarcoma, metastatic																											
Malignant lymphoma, lymphocytic type																											
Malignant lymphoma, histiocytic type																											
Mysiomonocytic leukemia																											
Monocytic leukemia																											
Back, NOS																											
Basal cell carcinoma																											
Flank, NOS																											
Rhabdomyosarcoma																											
Sacral region																											
Neurofibroma																											
Fibroma																											
Fibrosarcoma																											
Scrotum, NOS																											
Mesothelioma, invasive																											

**TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	86	87	88	89	90	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10		
WEEKS ON STUDY	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144		
REPRODUCTIVE SYSTEM																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenoma, NOS																											
Adenocarcinoma, NOS																											
Papillary adenocarcinoma																											
Sarcoma, NOS, invasive																											
Fibrosarcoma																											
Fibroadenoma																											
Testis	X	+	+	+	+	X	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Interstitial cell tumor	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell carcinoma																											
Preputial/clitoral gland																											
Carcinoma, NOS																											
Squamous cell carcinoma																											
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Lipoma																											
NERVOUS SYSTEM																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS, invasive																											
Astrocytoma																											
Astrocytoma, invasive																											
SPECIAL SENSE ORGANS																											
Ear	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell papilloma																											
Zymbal gland																											
Carcinoma, NOS																											
Squamous cell papilloma																											
Adenoma, NOS																											
MUSCULOSKELETAL SYSTEM																											
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Liposarcoma																											
Osteoma																											
Osteosarcoma																											
BODY CAVITIES																											
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Sarcoma, NOS																											
Sarcoma, NOS, invasive																											
Mesothelioma, invasive																											
Tunica vaginalis																											
Mesothelioma, NOS																											
Mesothelioma, malignant																											
Mesentery																											
Mesothelioma, malignant																											
ALL OTHER SYSTEMS																											
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Squamous cell carcinoma, invasive																											
Tubular cell adenocarcinoma, metastatic																											
C-cell carcinoma, metastatic																											
Sarcoma, NOS, invasive																											
Fibrosarcoma, invasive																											
Mesothelioma, invasive																											
Mesothelioma, metastatic																											
Osteosarcoma, metastatic																											
Malignant lymphoma, lymphocytic type																											
Malignant lymphoma, histiocytic type																											
Myelomonocytic leukemia																											
Monocytic leukemia	X							X																			
Back, NOS																											
Basal cell carcinoma																											
Flank, NOS																											
Rhabdomyosarcoma																											
Sacral region																											
Neurofibroma																											
Axilla, NOS																											
Fibroma																											
Fibrosarcoma																											
Scrotum, NOS																											
Mesothelioma, invasive																											

**TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	9 0 1	9 0 2	9 0 3	9 0 4	9 0 5	9 0 6	9 0 7	9 0 8	9 0 9	9 1 0	9 1 1	9 1 2	9 1 3	9 1 4	9 1 5	9 1 6	9 1 7	9 1 8	9 1 9	9 2 0	9 2 1	9 2 2	9 2 3	9 2 4	9 2 5	TOTAL TISSUES TUMORS
WEEKS ON STUDY	1 6	1 1	1 0	1 0	1 2	1 1	1 9	1 1	1 6	1 0	1 2	1 1	1 6	1 7	1 2	1 1	1 4	1 2	1 3	1 9	1 5	1 1	1 0	1 2	1 1	1 2
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*250
Adenoma, NOS																					X					4
Adenocarcinoma, NOS																										1
Papillary adenocarcinoma																										1
Sarcoma, NOS, invasive																										1
Fibrosarcoma																										1
Fibroadenoma			X																							27
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Interstitial cell tumor	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	240
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Squamous cell carcinoma																										1
Preputial/citoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*250
Carcinoma, NOS																										9
Squamous cell carcinoma																										1
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*250
Lipoma																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Carcinoma, NOS, invasive																										2
Astrocytoma																										2
Astrocytoma, invasive																										1
SPECIAL SENSE ORGANS																										
Ear	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*250
Squamous cell papilloma																										1
Zymbal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*250
Carcinoma, NOS																										7
Squamous cell papilloma																										2
Adenoma, NOS																										1
MUSCULOSKELETAL SYSTEM																										
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*250
Liposarcoma																										1
Osteoma																										1
Osteosarcoma																										1
BODY CAVITIES																										
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*250
Sarcoma, NOS																										1
Sarcoma, NOS, invasive																										1
Mesothelioma, invasive																										1
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*250
Mesothelioma, NOS																										1
Mesothelioma, malignant																										7
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*250
Mesothelioma, malignant																										2
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*250
Squamous cell carcinoma, invasive																										1
Tubular cell adenocarcinoma, metastatic																										1
C-cell carcinoma, metastatic																										1
Sarcoma, NOS, invasive																										1
Fibrosarcoma, invasive																										1
Mesothelioma, invasive																										7
Mesothelioma, metastatic																										1
Osteosarcoma, metastatic																										1
Malignant lymphoma, lymphocytic type																										2
Malignant lymphoma, histiocytic type																										1
Myelomonocytic leukemia																										1
Monocytic leukemia																										103
Back, NOS																										1
Basal cell carcinoma																										1
Flank, NOS																										1
Rhabdomyosarcoma																										1
Sacral region																										1
Neurofibroma																										1
Axilla, NOS																										1
Fibroma																										1
Fibrosarcoma																										1
Scrotum, NOS																										1
Mesothelioma, invasive																										1

* Animals necropsied

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	
WEEKS ON STUDY	6	7	7	7	8	8	8	8	8	8	8	8	8	8	9	9	9	9	9	9	9	9	9	9	0
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell papilloma																									
Basal cell carcinoma																									
Keratoacanthoma																									
Fibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell carcinoma																									
Sarcoma, NOS																									
Fibroma																									
Fibrosarcoma																									
Hemangiosarcoma																									
Neurofibroma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS, metastatic																									
Hepatocellular carcinoma, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Pheochromocytoma, metastatic																									
Fibrosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma, NOS, metastatic																									
Mesothelioma, metastatic																									
Hemangiopericytoma, malignant																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS, metastatic																									
Adenocarcinoma, NOS, metastatic																									
Mucinous cystadenocarcinoma, metastatic																									
Signet ring carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Mesothelioma, metastatic																									
Thymus	+	+	-	-	-	+	+	+	+	+	+	+	+	+	-	+	-	-	+	-	-	+	+	+	
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Neoplastic nodule																									
Hepatocellular carcinoma																									
Sarcoma, NOS																									
Lipoma																									
Hemangioma																									
Hemangiosarcoma																									
Monocytic leukemia																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Acinar cell adenoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma, NOS																									
Adenocarcinoma in adenomatous polyp, metastatic																									
Mucinous cystadenocarcinoma																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																									
Adenocarcinoma, NOS																									
Adenomatous polyp, NOS																									
Mucinous cystadenocarcinoma																									
Mucinous cystadenocarcinoma, metastatic																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma in-situ, NOS																									
Adenocarcinoma, NOS																									
Adenomatous polyp, NOS																									
Adenocarcinoma in adenomatous polyp																									
Mucinous cystadenocarcinoma																									
Mucinous cystadenocarcinoma, metastatic																									
Signet ring carcinoma																									
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS																									
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenomatous polyp, NOS																									

@ Multiple occurrence of morphology

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275		
WEEKS ON STUDY	89	103	080	073	097	120	070	074	073	089	083	097	080	088	100	073	079	080	112	084	074	059	071	077	077		
ENDOCRINE SYSTEM																											
Pituitary	+	+	+	+	X	+	+	+	+	+	+	X	+	+	+	+	X	+	+	+	+	+	+	+	+		
Adenoma, NOS																											
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Pheochromocytoma	X																	X	X								
Pheochromocytoma, malignant																											
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Follicular cell adenoma					X							X	X														
Follicular cell carcinoma																											
C-cell adenoma															X												
C-cell carcinoma																					X						
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+		
Adenoma, NOS																											
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Islet cell adenoma																											
Islet cell carcinoma	X																										
REPRODUCTIVE SYSTEM																											
Mammary gland	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Fibroadenoma																											
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Interstitial cell tumor	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Coagulating gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
Adenoma, NOS																											
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
Carcinoma, NOS																											
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
Mesothelioma, invasive																											
NERVOUS SYSTEM																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
SPECIAL SENSE ORGANS																											
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
Carcinoma, NOS																											
Ear	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Squamous cell papilloma																											
Zymbal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Carcinoma, NOS					X		X			X							X		X	X		X		X	X		
Squamous cell papilloma																											
Keratoacanthoma																							X	X	X		
BODY CAVITIES																											
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
Hemangiosarcoma																											
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+		
Mesothelioma, NOS																											
Mesothelioma, malignant	X																										
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
Adenocarcinoma, NOS, invasive																											
Adenocarcinoma in adenomatous polyp, metastatic																											
Mesothelioma, metastatic																											
ALL OTHER SYSTEMS																											
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
Adenocarcinoma, NOS, metastatic																											
Mucinous cystadenocarcinoma, metastatic					X																						
Signet ring carcinoma, invasive																											
Sarcoma, NOS, invasive																											
Mesothelioma, invasive																											
Mesothelioma, metastatic	X																										
Malignant lymphoma, histiocytic type																											
Monocytic leukemia						X						X	X						X	X		X					
Scrotum, NOS																											
Mesothelioma, invasive																											

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	3 3																								
	0 0 0 0 0 0 0 0 0 0 1 1 1 1 1 1 1 1 1 1 2 2 2 2 2																								
WEEKS ON STUDY	1 0 1 1 0 0 0 0 0 0 0 0 0 0 0 1 1 1 1 0 0 0 1 0 0 0 0																								
	3 0 0 1 3 2 4 6 9 9 9 7 8 7 5 2 2 2 9 8 9 2 7 7 8 2 4 2 4																								
ENDOCRINE SYSTEM																									
Pituitary	+																								
Adenoma, NOS	+																								
Adrenal	+																								
Pheochromocytoma	+																								
Pheochromocytoma, malignant	+																								
Thyroid	+																								
Follicular cell adenoma	+																								
Follicular cell carcinoma	+																								
C-cell adenoma	X																								
C-cell carcinoma	+																								
Parathyroid	+																								
Adenoma, NOS	+																								
Pancreatic islets	+																								
Islet cell adenoma	+																								
Islet cell carcinoma	X																								
REPRODUCTIVE SYSTEM																									
Mammary gland	+																								
Fibroadenoma	+																								
Testis	+																								
Interstitial cell tumor	+																								
Prostate	+																								
Coagulating gland	+																								
Adenoma, NOS	+																								
Preputial/clitoral gland	+																								
Carcinoma, NOS	+																								
Epididymis	+																								
Mesothelioma, invasive	+																								
NERVOUS SYSTEM																									
Brain	+																								
SPECIAL SENSE ORGANS																									
Harderian gland	N																								
Carcinoma, NOS	N																								
Ear	+																								
Squamous cell papilloma	+																								
Zymbal gland	+																								
Carcinoma, NOS	+																								
Squamous cell papilloma	+																								
Keratoacanthoma	+																								
BODY CAVITIES																									
Mediastinum	N																								
Hemangiosarcoma	N																								
Tunica vaginalis	+																								
Mesothelioma, NOS	+																								
Mesothelioma, malignant	+																								
Mesentery	N																								
Adenocarcinoma, NOS, invasive	N																								
Adenocarcinoma in adenomatous polyp, metastatic	X																								
Mesothelioma, metastatic	N																								
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N																								
Adenocarcinoma, NOS, metastatic	N																								
Mucinous cystadenocarcinoma, metastatic	X																								
Signet ring carcinoma, invasive	N																								
Sarcoma, NOS, invasive	N																								
Mesothelioma, invasive	N																								
Mesothelioma, metastatic	N																								
Malignant lymphoma, histiocytic type	N																								
Monocytic leukemia	X																								
Scrotum, NOS	X																								
Mesothelioma, invasive	X																								

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	WEEKS ON STUDY																				TOTAL TISSUES TUMORS					
	3/26	3/27	3/28	3/29	3/30	3/31	3/32	3/33	3/34	3/35	3/36	3/37	3/38	3/39	3/40	3/41	3/42	3/43	3/44	3/45		3/46	3/47	3/48	3/49	3/50
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS								X																		
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma																										
Pheochromocytoma, malignant																										
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																										
Follicular cell carcinoma																										
C-cell adenoma																										
C-cell carcinoma																										
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																										
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																										
Islet cell carcinoma																										
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																										
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor	X			X	X			X	X				X	X	X	X	X	X	X	X	X	X	X	X	X	X
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Coagulating gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																										
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																										
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, invasive																										
NERVOUS SYSTEM																										
Brain	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																										
Ear	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																										
Zymbal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																										
Squamous cell papilloma																										
Keratoacanthoma	X		X					X																		X
BODY CAVITIES																										
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Hemangiosarcoma																										
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, NOS																										
Mesothelioma, malignant																										
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenocarcinoma, NOS, invasive																										
Adenocarcinoma in adenomatous polyp, meta																										
Mesothelioma, metastatic																										
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenocarcinoma, NOS, metastatic																										
Mucinous cystadenocarcinoma, meta																										
Signet ring carcinoma, invasive																										
Sarcoma, NOS, invasive																										
Mesothelioma, invasive																										
Mesothelioma, metastatic																										
Malignant lymphoma, histiocytic type																										
Monocytic leukemia																										
Scrotum, NOS																										
Mesothelioma, invasive																										

* Animals necropsied

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: 1% AMOSITE AND PREWEANING GAVAGE

ANIMAL NUMBER	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80							
WEEKS ON STUDY	12	11	22	33	00	22	88	22	22	88	00	99	99	88	44	11	11	00	33	33	11	11	22	33	44	00	11	11	00	44	55	00
INTEGUMENTARY SYSTEM																																
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Squamous cell papilloma																																
Squamous cell carcinoma																																
Basal cell carcinoma																																
Trichoepithelioma																																
Keratoacanthoma																																
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Sarcoma, NOS																																
Fibroma	X	X																														
Fibrosarcoma																																
Lipoma																																
Osteosarcoma																																
Neurofibrosarcoma																																
RESPIRATORY SYSTEM																																
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Alveolar/bronchiolar carcinoma																																
Interstitial cell tumor, metastatic																																
Osteosarcoma, metastatic																																
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
HEMATOPOIETIC SYSTEM																																
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Fibrosarcoma																																
Hemangiosarcoma																																
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Neurofibrosarcoma, metastatic																																
Thymus	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	-	+	-	-	+	-	+	+	+	+	+	+	+			
CIRCULATORY SYSTEM																																
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
DIGESTIVE SYSTEM																																
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
Squamous cell papilloma																																
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Sarcoma, NOS, invasive																																
Fibrosarcoma, invasive																																
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Neoplastic nodule																																
Hepatocellular carcinoma																																
Alveolar/bronchiolar carcinoma, metastatic																																
Monocytic leukemia																																
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Acinar cell adenoma																																
Acinar cell carcinoma																																
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Squamous cell papilloma																																
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Mucinous cystadenocarcinoma																																
Leiomyosarcoma																																
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Adenomatous polyp, NOS																																
Adenocarcinoma in adenomatous polyp																																
Leiomyoma																																
URINARY SYSTEM																																
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Alveolar/bronchiolar carcinoma, metastatic																																
Tubular cell adenoma																																
Tubular cell adenocarcinoma																																
Mixed tumor, benign																																
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE AND PREWEANING GAVAGE (Continued)

ANIMAL NUMBER	5 2 6	5 2 7	5 2 8	5 2 9	5 3 0	5 3 1	5 3 2	5 3 3	5 3 4	5 3 5	5 3 6	5 3 7	5 3 8	5 3 9	5 4 0	5 4 1	5 4 2	5 4 3	5 4 4	5 4 5	5 4 6	5 4 7	5 4 8	5 4 9	5 5 0		
WEEKS ON STUDY	1 2	1 6	1 0	1 4	1 2	1 7	0 2	1 8	1 2	0 7	1 4	0 6	0 8	0 9	1 8	1 4	1 0	1 3	1 7	1 7	1 9	1 1	1 3	1 4	1 0	1 4	
ENDOCRINE SYSTEM																											
Pituitary	+																										
Carcinoma, NOS	+																										
Adenoma, NOS	X			X	X					X											X	X					
Adrenal	+																										
Cortical adenoma	+																										
Pheochromocytoma	+																										
Thyroid	+																										
Follicular cell adenoma	+																										
Follicular cell carcinoma	+																										
C-cell adenoma	+																										
C-cell carcinoma		X				X				X											X	X					
Parathyroid	+																										
Adenoma, NOS	+																										
Pancreatic islets	+																										
Islet cell adenoma	+																										
Islet cell carcinoma					X																						
REPRODUCTIVE SYSTEM																											
Mammary gland	+																										
Papillary adenoma	+																										
Fibroadenoma	+																										
Testis	+																										
Interstitial cell tumor	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Interstitial cell tumor, malignant	+																										
Prostate	+																										
Adenocarcinoma, NOS	+																										
NERVOUS SYSTEM																											
Brain	+																										
Astrocytoma	+																										
SPECIAL SENSE ORGANS																											
Zymbal gland	+																										
Carcinoma, NOS	+																										
BODY CAVITIES																											
Pleura	N																										
Alveolar/bronchiolar carcinoma, metastatic	N																										
Peritoneum	N																										
Lipoma	N																										
Tunica vaginalis	+																										
Mesothelioma, malignant	+																										
ALL OTHER SYSTEMS																											
Multiple organs, NOS	N																										
Alveolar/bronchiolar carcinoma, invasive	N																										
Alveolar/bronchiolar carcinoma, metastatic	N																										
Sarcoma, NOS, invasive	N																										
Mesothelioma, invasive	N																										
Monocytic leukemia	X	X	X	X	X			X	X	X				X	X						X	X			X	X	

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1% AMOSITE AND PREWEANING GAVAGE (Continued)

ANIMAL NUMBER	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	6		
	7	7	7	7	8	8	8	8	8	8	8	8	8	8	8	9	9	9	9	9	9	9	9	9	9	0	
WEEKS ON STUDY	1	1	1	1	1	0	1	1	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	0		
	3	1	2	1	2	9	1	0	0	4	1	9	7	0	2	0	3	4	2	0	3	0	2	1	8		
	5	5	5	5	1	7	7	7	6	1	0	6	0	7	9	7	2	1	8	4	4	7	5	0	7		
ENDOCRINE SYSTEM																											
Pituitary																											
Carcinoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Adenoma, NOS			X			X		X	X					X		X											
Adrenal																											
Cortical adenoma	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Pheochromocytoma				X					X	X					X		X					X					
Thyroid																											
Follicular cell adenoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			
Follicular cell carcinoma																			X								
C-cell adenoma																	X										
C-cell carcinoma								X	X									X				X					
Parathyroid																											
Adenoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			
Pancreatic islets																											
Islet cell adenoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			
Islet cell carcinoma					X				X																		
REPRODUCTIVE SYSTEM																											
Mammary gland																											
Papillary adenoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			
Fibroadenoma																	X										
Testis																											
Interstitial cell tumor	X	X		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X			
Interstitial cell tumor, malignant																											
Prostate																											
Adenocarcinoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			
NERVOUS SYSTEM																											
Brain																											
Astrocytoma					+																						
SPECIAL SENSE ORGANS																											
Zymbal gland																											
Carcinoma, NOS																	X										
BODY CAVITIES																											
Pleura																											
Alveolar/bronchiolar carcinoma, metastatic	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N			
Peritoneum																											
Lipoma	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N			
Tunica vaginalis																											
Mesothelioma, malignant	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				
ALL OTHER SYSTEMS																											
Multiple organs, NOS																											
Alveolar/bronchiolar carcinoma, invasive	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N				
Alveolar/bronchiolar carcinoma, metastatic									X																		
Sarcoma, NOS, invasive																											
Mesothelioma, invasive			X																X								
Monocytic leukemia	X			X	X		X		X			X							X	X	X	X					

TABLE A3a. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Skin: Squamous Cell Papilloma				
Overall Rates (a)	1/117 (1%)	6/250 (2%)	5/100 (5%)	
Adjusted Rates (b)	2.0%	7.8%	18.1%	
Terminal Rates (c)	0/8 (0%)	2/41 (5%)	0/8 (0%)	
Week of First Observation	124	110	101	
Life Table Test (d)		P=0.476	P=0.045	P=0.024
Incidental Tumor Test (d)		P=0.285	P=0.050	P=0.082
Fisher Exact Test (d)		P=0.289	P=0.074	P=0.177
Skin: Squamous Cell Papilloma or Carcinoma				
Overall Rates (a)	2/117 (2%)	10/250 (4%)	6/100 (6%)	
Adjusted Rates (b)	9.5%	11.5%	26.3%	
Terminal Rates (c)	0/8 (0%)	2/41 (5%)	0/8 (0%)	
Week of First Observation	124	80	101	
Life Table Test (d)		P=0.435	P=0.049	P=0.039
Incidental Tumor Test (d)		P=0.263	P=0.054	P=0.142
Fisher Exact Test (d)		P=0.206	P=0.095	P=0.291
Skin: Keratoacanthoma				
Overall Rates (a)	4/117 (3%)	17/250 (7%)	2/100 (2%)	
Adjusted Rates (b)	13.7%	30.9%	6.9%	
Terminal Rates (c)	0/8 (0%)	10/41 (24%)	0/8 (0%)	
Week of First Observation	125	117	122	
Life Table Test (d)		P=0.590	P=0.540N	P=0.358N
Incidental Tumor Test (d)		P=0.290	P=0.518N	P=0.232N
Fisher Exact Test (d)		P=0.144	P=0.418N	P=0.055N
Skin: Basal Cell Carcinoma				
Overall Rates (a)	3/117 (3%)	7/250 (3%)	4/100 (4%)	
Adjusted Rates (b)	20.7%	9.5%	39.1%	
Terminal Rates (c)	1/8 (13%)	3/41 (7%)	3/8 (38%)	
Week of First Observation	123	104	123	
Life Table Tests (d)		P=0.424N	P=0.408	P=0.122
Incidental Tumor Tests (d)		P=0.616	P=0.301	P=0.276
Fisher Exact Test (d)		P=0.599	P=0.414	P=0.388
Skin: Basal Cell Tumor or Carcinoma				
Overall Rates (a)	4/117 (3%)	8/250 (3%)	4/100 (4%)	
Adjusted Rates (b)	21.7%	10.0%	39.1%	
Terminal Rates (c)	1/8 (13%)	3/41 (7%)	3/8 (38%)	
Week of First Observation	117	104	123	
Life Table Tests (d)		P=0.325N	P=0.537	P=0.176
Incidental Tumor Tests (d)		P=0.592N	P=0.436	P=0.370
Fisher Exact Test (d)		P=0.567N	P=0.549	P=0.464
Skin: Trichoepithelioma, Basal Cell Tumor, or Basal Cell Carcinoma				
Overall Rates (a)	5/117 (4%)	8/250 (3%)	6/100 (6%)	
Adjusted Rates (b)	23.1%	10.0%	43.7%	
Terminal Rates (c)	1/8 (13%)	3/41 (7%)	3/8 (38%)	
Week of First Observation	117	104	123	
Life Table Tests (d)		P=0.178N	P=0.331	P=0.020
Incidental Tumor Tests (d)		P=0.441N	P=0.274	P=0.104
Fisher Exact Test (d)		P=0.402N	P=0.393	P=0.180
Subcutaneous Tissue: Fibroma				
Overall Rates (a)	18/117 (15%)	33/250 (13%)	11/100 (11%)	
Adjusted Rates (b)	29.6%	34.2%	30.6%	
Terminal Rates (c)	0/8 (0%)	7/41 (17%)	1/8 (13%)	
Week of First Observation	95	96	82	
Life Table Tests (d)		P=0.056N	P=0.400N	P=0.210
Incidental Tumor Tests (d)		P=0.389N	P=0.247N	P=0.469N
Fisher Exact Test (d)		P=0.340N	P=0.229N	P=0.358N

TABLE A3a. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Subcutaneous Tissue: Neurofibroma				
Overall Rates (a)	3/117 (3%)	5/250 (2%)	0/100 (0%)	
Adjusted Rates (b)	16.9%	10.5%	0.0%	
Terminal Rates (c)	1/8 (13%)	4/41 (10%)	0/8 (0%)	
Week of First Observation	127	128		
Life Table Tests (d)		P=0.189N	P=0.187N	P=0.347N
Incidental Tumor Tests (d)		P=0.342N	P=0.209N	P=0.322N
Fisher Exact Test (d)		P=0.497N	P=0.155N	P=0.184N
Subcutaneous Tissue: Fibroma or Neurofibroma				
Overall Rates (a)	21/117 (18%)	36/250 (14%)	11/100 (11%)	
Adjusted Rates (b)	41.5%	40.0%	30.6%	
Terminal Rates (c)	1/8 (13%)	10/41 (24%)	1/8 (13%)	
Week of First Observation	95	96	82	
Life Table Tests (d)		P=0.017N	P=0.244N	P=0.273
Incidental Tumor Tests (d)		P=0.230N	P=0.133N	P=0.393N
Fisher Exact Test (d)		P=0.234N	P=0.106N	P=0.255N
Subcutaneous Tissue: Sarcoma				
Overall Rates (a)	4/117 (3%)	2/250 (1%)	5/100 (5%)	
Adjusted Rates (b)	7.1%	1.0%	5.9%	
Terminal Rates (c)	0/8 (0%)	0/41 (0%)	0/8 (0%)	
Week of First Observation	90	108	80	
Life Table Tests (d)		P=0.053N	P=0.343	P=0.010
Incidental Tumor Tests (d)		P=0.136N	P=0.568	P=0.111
Fisher Exact Test (d)		P=0.085N	P=0.403	P=0.022
Subcutaneous Tissue: Fibrosarcoma				
Overall Rates (a)	7/117 (6%)	9/250 (4%)	1/100 (1%)	
Adjusted Rates (b)	40.9%	7.7%	2.7%	
Terminal Rates (c)	3/8 (38%)	1/41 (2%)	0/8 (0%)	
Week of First Observation	72	80	124	
Life Table Tests (d)	P=0.030N	P=0.073N	P=0.059N	P=0.333N
Incidental Tumor Tests (d)	P=0.028N	P=0.192N	P=0.050N	P=0.138N
Fisher Exact Test (d)		P=0.218N	P=0.053N	P=0.169N
Subcutaneous Tissue: Fibroma or Fibrosarcoma				
Overall Rates (a)	25/117 (21%)	41/250 (16%)	12/100 (12%)	
Adjusted Rates (b)	58.4%	37.7%	32.5%	
Terminal Rates (c)	3/8 (38%)	7/41 (17%)	1/8 (13%)	
Week of First Observation	72	80	82	
Life Table Tests (d)	P=0.061N	P=0.010N	P=0.132N	P=0.338
Incidental Tumor Tests (d)	P=0.050N	P=0.176N	P=0.053N	P=0.240N
Fisher Exact Test (d)		P=0.157N	P=0.049N	P=0.193N
Subcutaneous Tissue: Neurofibroma or Neurofibrosarcoma				
Overall Rates (a)	5/117 (4%)	5/250 (2%)	2/100 (2%)	
Adjusted Rates (b)	18.8%	10.5%	2.3%	
Terminal Rates (c)	1/8 (13%)	4/41 (10%)	0/8 (0%)	
Week of First Observation	78	128	70	
Life Table Tests (d)		P=0.032N	P=0.341N	P=0.446
Incidental Tumor Tests (d)		P=0.094N	P=0.218N	P=0.595
Fisher Exact Test (d)		P=0.181N	P=0.292N	P=0.642
Subcutaneous Tissue: Sarcoma, Fibrosarcoma, or Neurofibrosarcoma				
Overall Rates (a)	13/117 (11%)	11/250 (4%)	8/100 (8%)	
Adjusted Rates (b)	46.3%	8.6%	10.6%	
Terminal Rates (c)	3/8 (38%)	1/41 (2%)	0/8 (0%)	
Week of First Observation	72	80	70	
Life Table Tests (d)	P=0.210N	P=0.002N	P=0.359N	P=0.045
Incidental Tumor Tests (d)	P=0.098N	P=0.017N	P=0.134N	P=0.367
Fisher Exact Test (d)		P=0.016N	P=0.295N	P=0.140

TABLE A3a. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Subcutaneous Tissue: Fibroma, Neurofibroma, Sarcoma, Fibrosarcoma, or Neurofibrosarcoma				
Overall Rates (a)	33/117 (28%)	46/250 (18%)	19/100 (19%)	
Adjusted Rates (b)	70.9%	43.8%	38.0%	
Terminal Rates (c)	4/8 (50%)	10/41 (24%)	1/8 (13%)	
Week of First Observation	72	80	70	
Life Table Tests (d)		P<0.001N	P=0.209N	P=0.046
Incidental Tumor Tests (d)		P=0.025N	P=0.045N	P=0.549
Fisher Exact Test (d)		P=0.024N	P=0.077N	P=0.503
Integumentary System or Salivary Gland: Sarcoma, Fibrosarcoma, or Neurofibrosarcoma				
Overall Rates (a)	14/117 (12%)	15/250 (6%)	8/100 (8%)	
Adjusted Rates (b)	47.4%	13.2%	10.6%	
Terminal Rates (c)	4/8 (50%)	2/41 (5%)	0/8 (0%)	
Week of First Observation	72	80	70	
Life Table Tests (d)	P=0.174N	P=0.005N	P=0.298N	P=0.103
Incidental Tumor Tests (d)	P=0.084N	P=0.037N	P=0.099N	P=0.509
Fisher Exact Test (d)		P=0.041N	P=0.231N	P=0.320
Integumentary System or Salivary Gland: Fibroma, Neurofibroma, Sarcoma, Fibrosarcoma, or Neurofibrosarcoma				
Overall Rates (a)	34/117 (29%)	48/250 (19%)	19/100 (19%)	
Adjusted Rates (b)	71.5%	44.8%	38.0%	
Terminal Rates (c)	4/8 (50%)	10/41 (24%)	1/8 (13%)	
Week of First Observation	72	80	70	
Life Table Tests (d)	P=0.067N	P<0.001N	P=0.180N	P=0.058
Incidental Tumor Tests (d)	P=0.035N	P=0.025N	P=0.034N	P=0.530N
Fisher Exact Test (d)		P=0.025N	P=0.059N	P=0.548N
Lung: Alveolar/Bronchiolar Carcinoma				
Overall Rates (e)	1/117 (1%)	6/249 (2%)	4/100 (4%)	
Adjusted Rates (b)	2.2%	9.8%	16.3%	
Terminal Rates (c)	0/8 (0%)	2/41 (5%)	0/8 (0%)	
Week of First Observation	127	131	126	
Life Table Test (d)		P=0.514	P=0.071	P=0.044
Incidental Tumor Test (d)		P=0.409	P=0.083	P=0.099
Fisher Exact Test (d)		P=0.287	P=0.140	P=0.313
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma				
Overall Rates (e)	2/117 (2%)	8/249 (3%)	4/100 (4%)	
Adjusted Rates (b)	3.8%	11.1%	16.3%	
Terminal Rates (c)	0/8 (0%)	2/41 (5%)	0/8 (0%)	
Week of First Observation	122	117	126	
Life Table Test (d)		P=0.568	P=0.163	P=0.108
Incidental Tumor Test (d)		P=0.413	P=0.187	P=0.219
Fisher Exact Test (d)		P=0.329	P=0.271	P=0.466
Hematopoietic System: Leukemia				
Overall Rates (a)	38/117 (32%)	107/250 (43%)	49/100 (49%)	
Adjusted Rates (b)	71.1%	75.8%	89.7%	
Terminal Rates (c)	2/8 (25%)	19/41 (46%)	5/8 (63%)	
Week of First Observation	87	80	87	
Life Table Test (d)		P=0.351N	P=0.004	P<0.001
Incidental Tumor Test (d)		P=0.030	P=0.003	P=0.107
Fisher Exact Test (d)		P=0.038	P=0.010	P=0.175

TABLE A3a. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Liver: Neoplastic Nodule				
Overall Rates (e)	9/117 (8%)	9/250 (4%)	5/100 (5%)	
Adjusted Rates (b)	28.9%	10.4%	16.4%	
Terminal Rates (c)	1/8 (13%)	2/41 (5%)	0/8 (0%)	
Week of First Observation	108	101	122	
Life Table Test (d)		P=0.009N	P=0.458N	P=0.087
Incidental Tumor Test (d)		P=0.058N	P=0.417N	P=0.305
Fisher Exact Test (d)		P=0.079N	P=0.301N	P=0.368
Liver: Hepatocellular Carcinoma				
Overall Rates (e)	1/117 (1%)	3/250 (1%)	3/100 (3%)	
Adjusted Rates (b)	1.8%	5.1%	22.2%	
Terminal Rates (c)	0/8 (0%)	1/41 (2%)	1/8 (13%)	
Week of First Observation	123	136	95	
Life Table Test (d)		P=0.663N	P=0.218	P=0.045
Incidental Tumor Test (d)		P=0.652	P=0.226	P=0.114
Fisher Exact Test (d)		P=0.619	P=0.254	P=0.228
Liver: Neoplastic Nodule or Hepatocellular Carcinoma				
Overall Rates (e)	9/117 (8%)	12/250 (5%)	8/100 (8%)	
Adjusted Rates (b)	28.9%	15.1%	34.9%	
Terminal Rates (c)	1/8 (13%)	3/41 (7%)	1/8 (13%)	
Week of First Observation	108	101	95	
Life Table Test (d)		P=0.027N	P=0.403	P=0.009
Incidental Tumor Test (d)		P=0.136N	P=0.436	P=0.088
Fisher Exact Test (d)		P=0.190N	P=0.565	P=0.180
Pancreas: Acinar Cell Adenoma				
Overall Rates (e)	9/116 (8%)	19/248 (8%)	2/100 (2%)	
Adjusted Rates (b)	24.5%	27.2%	19.8%	
Terminal Rates (c)	1/8 (13%)	7/41 (17%)	1/8 (13%)	
Week of First Observation	115	123	136	
Life Table Tests (d)		P=0.144N	P=0.098N	P=0.301N
Incidental Tumor Tests (d)		P=0.442N	P=0.092N	P=0.181N
Fisher Exact Test (d)		P=0.562N	P=0.051N	P=0.032N
Pancreas: Acinar Cell Adenoma or Carcinoma				
Overall Rates (e)	11/116 (9%)	20/248 (8%)	3/100 (3%)	
Adjusted Rates (b)	37.5%	28.2%	22.0%	
Terminal Rates (c)	2/8 (25%)	7/41 (17%)	1/8 (13%)	
Week of First Observation	115	123	124	
Life Table Tests (d)		P=0.050N	P=0.091N	P=0.461N
Incidental Tumor Tests (d)		P=0.252N	P=0.094N	P=0.276N
Fisher Exact Test (d)		P=0.394N	P=0.047N	P=0.063N
Small Intestine: Adenomatous Polyp, Adenocarcinoma in Adenomatous Polyp, or Mucinous Cystadenocarcinoma				
Overall Rates (a)	3/117 (3%)	1/250 (0%)	1/100 (1%)	
Adjusted Rates (b)	12.9%	0.5%	1.2%	
Terminal Rates (c)	0/8 (0%)	0/41 (0%)	0/8 (0%)	
Week of First Observation	100	108	101	
Life Table Tests (d)		P=0.045N	P=0.446N	
Incidental Tumor Tests (d)		P=0.094N	P=0.358N	
Fisher Exact Test (d)		P=0.097N	P=0.372N	

TABLE A3a. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Large Intestine: Adenomatous Polyp or Adenocarcinoma in Adenomatous Polyp				
Overall Rates (a)	0/117 (0%)	3/250 (1%)	2/100 (2%)	
Adjusted Rates (b)	0.0%	2.7%	13.4%	
Terminal Rates (c)	0/8 (0%)	0/41 (0%)	1/8 (13%)	
Week of First Observation		110	82	
Life Table Tests (d)		P=0.369	P=0.221	P=0.282
Incidental Tumor Tests (d)		P=0.306	P=0.258	P=0.461
Fisher Exact Test (d)		P=0.315	P=0.211	P=0.443
Pituitary Gland: Adenoma				
Overall Rates (e)	24/117 (21%)	41/248 (17%)	19/99 (19%)	
Adjusted Rates (b)	54.2%	42.9%	51.7%	
Terminal Rates (c)	1/8 (13%)	10/41 (24%)	1/8 (13%)	
Week of First Observation	96	58	86	
Life Table Test (d)		P=0.008N	P=0.414	P=0.007
Incidental Tumor Test (d)		P=0.129N	P=0.567	P=0.155
Fisher Exact Test (d)		P=0.216N	P=0.473N	P=0.328
Pituitary Gland: Carcinoma				
Overall Rates (e)	2/117 (2%)	4/248 (2%)	2/99 (2%)	
Adjusted Rates (b)	2.4%	4.0%	2.4%	
Terminal Rates (c)	0/8 (0%)	1/41 (2%)	0/8 (0%)	
Week of First Observation	114	110	88	
Life Table Test (d)		P=0.551N	P=0.584	P=0.456
Incidental Tumor Test (d)		P=0.586	P=0.671	P=0.627N
Fisher Exact Test (d)		P=0.625N	P=0.624	P=0.549
Pituitary Gland: Adenoma or Carcinoma				
Overall Rates (e)	26/117 (22%)	45/248 (18%)	21/99 (21%)	
Adjusted Rates (b)	55.3%	45.6%	52.9%	
Terminal Rates (c)	1/8 (13%)	11/41 (27%)	1/8 (13%)	
Week of First Observation	96	58	86	
Life Table Test (d)		P=0.008N	P=0.384	P=0.006
Incidental Tumor Test (d)		P=0.155N	P=0.556	P=0.177
Fisher Exact Test (d)		P=0.218N	P=0.496N	P=0.303
Adrenal Cortex: Cortical Adenoma				
Overall Rates (e)	0/117 (0%)	5/250 (2%)	2/100 (2%)	
Adjusted Rates (b)	0.0%	6.4%	3.7%	
Terminal Rates (c)	0/8 (0%)	0/41 (0%)	0/8 (0%)	
Week of First Observation		131	114	
Life Table Tests (d)		P=0.264	P=0.176	P=0.370
Incidental Tumor Tests (d)		P=0.215	P=0.187	P=0.523
Fisher Exact Test (d)		P=0.145	P=0.211	P=0.642
Adrenal Medulla: Pheochromocytoma				
Overall Rates (e)	39/117 (33%)	65/250 (26%)	21/100 (21%)	
Adjusted Rates (b)	84.1%	60.9%	73.3%	
Terminal Rates (c)	4/8 (50%)	14/41 (34%)	4/8 (50%)	
Week of First Observation	78	101	87	
Life Table Test (d)		P<0.001N	P=0.166N	P=0.057
Incidental Tumor Test (d)		P=0.021N	P=0.090N	P=0.479
Fisher Exact Test (d)		P=0.093N	P=0.030N	P=0.200N
Adrenal Medulla: Malignant Pheochromocytoma				
Overall Rates (e)	3/117 (3%)	5/250 (2%)	0/100 (0%)	
Adjusted Rates (b)	5.4%	2.6%	0.0%	
Terminal Rates (c)	0/8 (0%)	0/41 (0%)	0/8 (0%)	
Week of First Observation	117	89		
Life Table Test (d)		P=0.427N	P=0.198N	P=0.240N
Incidental Tumor Test (d)		P=0.610N	P=0.182N	P=0.106N
Fisher Exact Test (d)		P=0.497N	P=0.155N	P=0.184N

TABLE A3a. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Adrenal Medulla: Pheochromocytoma or Malignant Pheochromocytoma				
Overall Rates (e)	39/117 (33%)	68/249 (27%)	21/100 (21%)	
Adjusted Rates (b)	84.1%	61.4%	73.3%	
Terminal Rates (c)	4/8 (50%)	14/41 (34%)	4/8 (50%)	
Week of First Observation	78	89	87	
Life Table Test (d)		P<0.001N	P=0.166N	P=0.092
Incidental Tumor Test (d)		P=0.045N	P=0.090N	P=0.498N
Fisher Exact Test (d)		P=0.145N	P=0.030N	P=0.138N
Thyroid Gland: Follicular Cell Adenoma				
Overall Rates (e)	4/117 (3%)	13/246 (5%)	8/100 (8%)	
Adjusted Rates (b)	22.9%	16.6%	34.5%	
Terminal Rates (c)	1/8 (13%)	3/41 (7%)	2/8 (25%)	
Week of First Observation	128	120	107	
Life Table Test (d)		P=0.526N	P=0.076	P=0.015
Incidental Tumor Test (d)		P=0.453	P=0.076	P=0.115
Fisher Exact Test (d)		P=0.310	P=0.120	P=0.234
Thyroid Gland: Follicular Cell Carcinoma				
Overall Rates (e)	7/117 (6%)	10/246 (4%)	4/100 (4%)	
Adjusted Rates (b)	19.1%	16.2%	29.0%	
Terminal Rates (c)	0/8 (0%)	5/41 (12%)	2/8 (25%)	
Week of First Observation	98	96	119	
Life Table Test (d)		P=0.061N	P=0.475N	P=0.243
Incidental Tumor Test (d)		P=0.235N	P=0.475N	P=0.434
Fisher Exact Test (d)		P=0.287N	P=0.365N	P=0.621N
Thyroid Gland: Follicular Cell Adenoma or Carcinoma				
Overall Rates (e)	11/117 (9%)	23/246 (9%)	11/100 (11%)	
Adjusted Rates (b)	37.7%	30.9%	57.9%	
Terminal Rates (c)	1/8 (13%)	8/41 (20%)	4/8 (50%)	
Week of First Observation	98	96	107	
Life Table Test (d)		P=0.099N	P=0.292	P=0.019
Incidental Tumor Test (d)		P=0.402N	P=0.287	P=0.154
Fisher Exact Test (d)		P=0.563N	P=0.434	P=0.386
Thyroid Gland: C-Cell Adenoma				
Overall Rates (e)	16/117 (14%)	26/246 (11%)	11/100 (11%)	
Adjusted Rates (b)	53.6%	26.5%	34.1%	
Terminal Rates (c)	2/8 (25%)	3/41 (7%)	0/8 (0%)	
Week of First Observation	109	106	86	
Life Table Test (d)		P=0.020N	P=0.575N	P=0.048
Incidental Tumor Test (d)		P=0.162N	P=0.471N	P=0.366
Fisher Exact Test (d)		P=0.243N	P=0.350N	P=0.521
Thyroid Gland: C-Cell Carcinoma				
Overall Rates (e)	11/117 (9%)	50/246 (20%)	14/100 (14%)	
Adjusted Rates (b)	27.6%	48.7%	31.5%	
Terminal Rates (c)	0/8 (0%)	9/41 (22%)	0/8 (0%)	
Week of First Observation	95	65	106	
Life Table Test (d)		P=0.194	P=0.089	P=0.277
Incidental Tumor Test (d)		P=0.015	P=0.140	P=0.266N
Fisher Exact Test (d)		P=0.006	P=0.199	P=0.110N
Thyroid Gland: C-Cell Adenoma or Carcinoma				
Overall Rates (e)	27/117 (23%)	75/246 (30%)	25/100 (25%)	
Adjusted Rates (b)	66.5%	63.2%	54.9%	
Terminal Rates (c)	2/8 (25%)	12/41 (29%)	0/8 (0%)	
Week of First Observation	95	65	86	
Life Table Test (d)		P=0.265N	P=0.175	P=0.044
Incidental Tumor Test (d)		P=0.189	P=0.275	P=0.474N
Fisher Exact Test (d)		P=0.089	P=0.431	P=0.187N

TABLE A3a. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Parathyroid Gland: Adenoma				
Overall Rates (e)	4/110 (4%)	1/234 (<1%)	1/99 (1%)	
Adjusted Rates (b)	10.6%	0.7%	2.5%	
Terminal Rates (c)	0/8 (0%)	0/39 (0%)	0/8 (0%)	
Week of First Observation	114	126	123	
Life Table Test (d)		P=0.011N	P=0.320N	
Incidental Tumor Test (d)		P=0.039N	P=0.285N	
Fisher Exact Test (d)		P=0.038N	P=0.219N	
Pancreatic Islets: Islet Cell Adenoma				
Overall Rates (e)	14/116 (12%)	17/247 (7%)	4/100 (4%)	
Adjusted Rates (b)	33.8%	17.4%	10.4%	
Terminal Rates (c)	0/8 (0%)	3/41 (7%)	0/8 (0%)	
Week of First Observation	101	103	103	
Life Table Test (d)		P=0.007N	P=0.092N	P=0.580N
Incidental Tumor Test (d)		P=0.075N	P=0.057N	P=0.252N
Fisher Exact Test (d)		P=0.076N	P=0.027N	P=0.225N
Pancreatic Islets: Islet Cell Carcinoma				
Overall Rates (e)	3/116 (3%)	5/247 (2%)	4/100 (4%)	
Adjusted Rates (b)	20.0%	8.3%	28.5%	
Terminal Rates (c)	1/8 (13%)	2/41 (5%)	2/8 (25%)	
Week of First Observation	131	117	121	
Life Table Test (d)		P=0.220N	P=0.373	P=0.046
Incidental Tumor Test (d)		P=0.390N	P=0.301	P=0.123
Fisher Exact Test (d)		P=0.498N	P=0.418	P=0.242
Pancreatic Islets: Islet Cell Adenoma or Carcinoma				
Overall Rates (e)	17/116 (15%)	22/247 (9%)	8/100 (8%)	
Adjusted Rates (b)	47.0%	24.6%	36.0%	
Terminal Rates (c)	1/8 (13%)	5/41 (12%)	2/8 (25%)	
Week of First Observation	101	103	103	
Life Table Test (d)		P=0.003N	P=0.224N	P=0.202
Incidental Tumor Test (d)		P=0.052N	P=0.191N	P=0.566
Fisher Exact Test (d)		P=0.073N	P=0.094N	P=0.486N
Mammary Gland: Adenoma				
Overall Rates (a)	3/117 (3%)	4/250 (2%)	0/100 (0%)	
Adjusted Rates (b)	17.2%	5.3%	0.0%	
Terminal Rates (c)	0/8 (0%)	1/41 (2%)	0/8 (0%)	
Week of First Observation	133	126		
Life Table Test (d)		P=0.169N	P=0.203N	
Incidental Tumor Test (d)		P=0.302N	P=0.209N	
Fisher Exact Test (d)		P=0.396N	P=0.155N	
Mammary Gland: Fibroadenoma				
Overall Rates (a)	17/117 (15%)	27/250 (11%)	1/100 (1%)	
Adjusted Rates (b)	65.2%	38.4%	4.3%	
Terminal Rates (c)	4/8 (50%)	10/41 (24%)	0/8 (0%)	
Week of First Observation	107	117	129	
Life Table Test (d)		P=0.004N	P=0.002N	P=0.053N
Incidental Tumor Test (d)		P=0.078N	P=0.001N	P=0.016N
Fisher Exact Test (d)		P=0.196N	P<0.001N	P=0.001N
Testis: Interstitial Cell Tumor				
Overall Rates (e)	111/117 (95%)	240/249 (96%)	92/100 (92%)	
Adjusted Rates (b)	100.0%	100.0%	98.9%	
Terminal Rates (c)	8/8 (100%)	41/41 (100%)	7/8 (88%)	
Week of First Observation	78	80	80	
Life Table Test (d)		P<0.001N	P=0.180	P<0.001
Incidental Tumor Test (d)		P=0.284	P=0.552N	P=0.363N
Fisher Exact Test (d)		P=0.336	P=0.280N	P=0.078N

TABLE A3a. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Testis: Interstitial Cell Tumor or Interstitial Cell Tumor, Malignant				
Overall Rates (e)	111/117 (95%)	240/249 (96%)	93/100 (93%)	
Adjusted Rates (b)	100.0%	100.0%	100.0%	
Terminal Rates (c)	8/8 (100%)	41/41 (100%)	8/8 (100%)	
Week of First Observation	78	80	80	
Life Table Test (d)		P<0.001N	P=0.160	P<0.001
Incidental Tumor Test (d)		P=0.284	P=0.546	P=0.554N
Fisher Exact Test (d)		P=0.336	P=0.383N	P=0.140N
Preputial Gland: Carcinoma				
Overall Rates (e)	6/117 (5%)	9/250 (4%)	0/100 (0%)	
Adjusted Rates (b)	9.2%	9.7%	0.0%	
Terminal Rates (c)	0/8 (0%)	1/41 (2%)	0/8 (0%)	
Week of First Observation	90	106		
Life Table Tests (d)		P=0.166N	P=0.049N	P=0.163N
Incidental Tumor Tests (d)		P=0.368N	P=0.024N	P=0.079N
Fisher Exact Test (d)		P=0.333N	P=0.023N	P=0.046N
Preputial Gland: Carcinoma or Squamous Cell Papilloma				
Overall Rates (e)	6/117 (5%)	10/250 (4%)	0/100 (0%)	
Adjusted Rates (b)	9.2%	10.4%	0.0%	
Terminal Rates (c)	0/8 (0%)	1/41 (2%)	0/8 (0%)	
Week of First Observation	90	106		
Life Table Tests (d)		P=0.211N	P=0.049N	P=0.142N
Incidental Tumor Tests (d)		P=0.425N	P=0.024N	P=0.068N
Fisher Exact Test (d)		P=0.402N	P=0.023N	P=0.033N
Zymbal Gland: Carcinoma				
Overall Rates (e)	1/117 (1%)	7/250 (3%)	3/100 (3%)	
Adjusted Rates (b)	0.9%	4.6%	4.8%	
Terminal Rates (c)	0/8 (0%)	0/41 (0%)	0/8 (0%)	
Week of First Observation	94	113	80	
Life Table Tests (d)		P=0.290	P=0.232	P=0.387
Incidental Tumor Tests (d)		P=0.153	P=0.371	P=0.569N
Fisher Exact Test (d)		P=0.217	P=0.254	P=0.581
Zymbal Gland: Carcinoma or Squamous Cell Papilloma				
Overall Rates (e)	1/117 (1%)	9/250 (4%)	3/100 (3%)	
Adjusted Rates (b)	0.9%	5.8%	4.8%	
Terminal Rates (c)	0/8 (0%)	0/41 (0%)	0/8 (0%)	
Week of First Observation	94	108	80	
Life Table Tests (d)		P=0.190	P=0.232	P=0.505
Incidental Tumor Tests (d)		P=0.087	P=0.371	P=0.410N
Fisher Exact Test (d)		P=0.119	P=0.254	P=0.536N
All Sites: Malignant Mesothelioma				
Overall Rates (a)	2/117 (2%)	9/250 (4%)	3/100 (3%)	
Adjusted Rates (b)	2.2%	7.9%	8.3%	
Terminal Rates (c)	0/8 (0%)	1/41 (2%)	0/8 (0%)	
Week of First Observation	95	108	98	
Life Table Test (d)		P=0.395	P=0.373	P=0.489
Incidental Tumor Test (d)		P=0.207	P=0.443	P=0.494N
Fisher Exact Test (d)		P=0.263	P=0.426	P=0.536N
All Sites: Mesothelioma or Malignant Mesothelioma				
Overall Rates (a)	2/117 (2%)	10/250 (4%)	3/100 (3%)	
Adjusted Rates (b)	2.2%	8.4%	8.3%	
Terminal Rates (c)	0/8 (0%)	1/41 (2%)	0/8 (0%)	
Week of First Observation	95	108	98	
Life Table Test (d)		P=0.328	P=0.373	P=0.550
Incidental Tumor Test (d)		P=0.152	P=0.443	P=0.410N
Fisher Exact Test (d)		P=0.206	P=0.426	P=0.464N

TABLE A3a. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
All Sites: Benign Tumors				
Overall Rates (a)	115/117 (98%)	244/250 (98%)	95/100 (95%)	
Adjusted Rates (b)	100.0%	100.0%	99.0%	
Terminal Rates (c)	8/8 (100%)	41/41 (100%)	7/8 (88%)	
Week of First Observation	78	58	80	
Life Table Test (d)		P<0.001N	P=0.182	P<0.001
Incidental Tumor Test (d)		P=0.500N	P=0.413N	P=0.495N
Fisher Exact Test (d)		P=0.503N	P=0.163N	P=0.177N
All Sites: Malignant Tumors				
Overall Rates (a)	82/117 (70%)	201/250 (80%)	84/100 (84%)	
Adjusted Rates (b)	94.5%	96.0%	100.0%	
Terminal Rates (c)	5/8 (63%)	34/41 (83%)	8/8 (100%)	
Week of First Observation	72	58	70	
Life Table Test (d)		P=0.054N	P=0.015	P<0.001
Incidental Tumor Test (d)		P=0.025	P=0.018	P=0.254
Fisher Exact Test (d)		P=0.021	P=0.012	P=0.267
All Sites: All Tumors				
Overall Rates (a)	116/117 (99%)	249/250 (100%)	99/100 (99%)	
Adjusted Rates (b)	100.0%	100.0%	100.0%	
Terminal Rates (c)	8/8 (100%)	41/41 (100%)	8/8 (100%)	
Week of First Observation	72	58	70	
Life Table Test (d)		P<0.001N	P=0.125	P<0.001
Incidental Tumor Test (d)		P=0.606	P=0.603	P=0.651N
Fisher Exact Test (d)		P=0.537	P=0.710N	P=0.490N

(a) Number of tumor-bearing animals/number of animals examined grossly at the site

(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality

(c) Observed tumor incidence in animals killed at the end of the study

(d) Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in a dosed group than in controls is indicated by (N). The comparison of the 1% amosite and the 1% amosite + PW groups is presented in the last column for sites with an incidence of at least 2% in at least one of the groups.

(e) Number of tumor-bearing animals/number of animals examined microscopically at the site

TABLE A3b. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. 1% Amosite + DMH
Skin: Basal Cell Carcinoma				
Overall Rates (a)	3/117 (3%)	0/125 (0%)	1/175 (1%)	
Adjusted Rates (b)	3.8%	0.0%	2.6%	
Terminal Rates (c)	3/79 (4%)	0/15 (0%)	0/29 (0%)	
Week of First Observation	117		108	
Life Table Tests (d)		P=0.514N	P=0.676N	
Incidental Tumor Tests (d)		P=0.522N	P=0.518N	
Fisher Exact Test (d)		P=0.112N	P=0.178N	
Skin: Basal Cell Tumor or Carcinoma				
Overall Rates (a)	4/117 (3%)	0/125 (0%)	1/175 (1%)	
Adjusted Rates (b)	5.1%	0.0%	2.6%	
Terminal Rates (c)	4/79 (5%)	0/15 (0%)	0/29 (0%)	
Week of First Observation	117		108	
Life Table Tests (d)		P=0.424N	P=0.555N	
Incidental Tumor Tests (d)		P=0.432N	P=0.409N	
Fisher Exact Test (d)		P=0.053N	P=0.086N	
Skin: Trichoepithelioma, Basal Cell Tumor, or Basal Cell Carcinoma				
Overall Rates (a)	5/117 (4%)	0/125 (0%)	1/175 (1%)	
Adjusted Rates (b)	6.3%	0.0%	2.6%	
Terminal Rates (c)	5/79 (6%)	0/15 (0%)	0/29 (0%)	
Week of First Observation	117		108	
Life Table Tests (d)		P=0.355N	P=0.451N	
Incidental Tumor Tests (d)		P=0.364N	P=0.323N	
Fisher Exact Test (d)		P=0.025N	P=0.040N	
Skin: Keratoacanthoma				
Overall Rates (a)	4/117 (3%)	0/125 (0%)	5/175 (3%)	
Adjusted Rates (b)	5.1%	0.0%	8.8%	
Terminal Rates (c)	4/79 (5%)	0/15 (0%)	1/29 (3%)	
Week of First Observation	117		72	
Life Table Tests (d)		P=0.424N	P=0.140	P=0.118
Incidental Tumor Tests (d)		P=0.432N	P=0.426	P=0.084
Fisher Exact Test (d)		P=0.053N	P=0.520N	P=0.066
Subcutaneous Tissue: Fibroma				
Overall Rates (e)	18/117 (15%)	3/125 (2%)	6/175 (3%)	
Adjusted Rates (b)	20.1%	12.5%	18.6%	
Terminal Rates (c)	11/79 (14%)	1/15 (7%)	4/29 (14%)	
Week of First Observation	95	71	110	
Life Table Tests (d)		P=0.403N	P=0.443N	P=0.607
Incidental Tumor Tests (d)		P=0.061N	P=0.138N	P=0.549
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.440
Subcutaneous Tissue: Neurofibroma				
Overall Rates (e)	3/117 (3%)	1/125 (1%)	1/175 (1%)	
Adjusted Rates (b)	3.8%	3.7%	0.7%	
Terminal Rates (c)	3/79 (4%)	0/15 (0%)	0/29 (0%)	
Week of First Observation	117	103	71	
Life Table Tests (d)		P=0.602	P=0.566N	
Incidental Tumor Tests (d)		P=0.719N	P=0.371N	
Fisher Exact Test (d)		P=0.286N	P=0.178N	
Skin: Fibroma or Neurofibroma				
Overall Rates (a)	21/117 (18%)	4/125 (3%)	7/175 (4%)	
Adjusted Rates (b)	23.7%	15.7%	19.2%	
Terminal Rates (c)	14/79 (18%)	1/15 (7%)	4/29 (13%)	
Week of First Observation	95	71	71	
Life Table Tests (d)		P=0.476N	P=0.386N	P=0.587N
Incidental Tumor Tests (d)		P=0.073N	P=0.083N	P=0.587
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.486

TABLE A3b. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. 1% Amosite + DMH
Subcutaneous Tissue: Fibrosarcoma				
Overall Rates (e)	7/117 (6%)	1/125 (1%)	3/175 (2%)	
Adjusted Rates (b)	7.8%	6.7%	6.0%	
Terminal Rates (c)	4/79 (5%)	1/15 (7%)	1/29 (3%)	
Week of First Observation	72	117	49	
Life Table Tests (d)		P=0.460N	P=0.514N	
Incidental Tumor Tests (d)		P=0.105N	P=0.086N	
Fisher Exact Test (d)		P=0.027N	P=0.052N	
Subcutaneous Tissue: Fibroma or Fibrosarcoma				
Overall Rates (e)	25/117 (21%)	4/125 (3%)	9/175 (5%)	
Adjusted Rates (b)	27.0%	18.7%	23.9%	
Terminal Rates (c)	15/79 (19%)	2/15 (13%)	5/29 (16%)	
Week of First Observation	72	71	49	
Life Table Tests (d)		P=0.303N	P=0.382N	P=0.489
Incidental Tumor Tests (d)		P=0.011N	P=0.027N	P=0.381
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.304
Subcutaneous Tissue: Neurofibroma or Neurofibrosarcoma				
Overall Rates (e)	5/117 (4%)	1/125 (1%)	1/175 (1%)	
Adjusted Rates (b)	5.9%	3.7%	0.7%	
Terminal Rates (c)	4/79 (5%)	0/15 (0%)	0/29 (0%)	
Week of First Observation	78	103	71	
Life Table Tests (d)		P=0.620N	P=0.294N	
Incidental Tumor Tests (d)		P=0.242N	P=0.054N	
Fisher Exact Test (d)		P=0.092N	P=0.040N	
Subcutaneous Tissue: Sarcoma, Fibrosarcoma, or Neurofibrosarcoma				
Overall Rates (e)	13/117 (11%)	2/125 (2%)	4/175 (2%)	
Adjusted Rates (b)	14.2%	8.4%	8.3%	
Terminal Rates (c)	8/79 (10%)	1/15 (7%)	1/29 (3%)	
Week of First Observation	72	84	49	
Life Table Tests (d)		P=0.322N	P=0.256N	P=0.612
Incidental Tumor Tests (d)		P=0.007N	P=0.007N	P=0.499
Fisher Exact Test (d)		P=0.002N	P=0.002N	P=0.510
Subcutaneous Tissue: Fibroma, Neurofibroma, Sarcoma, Fibrosarcoma, or Neurofibrosarcoma				
Overall Rates (e)	33/117 (28%)	6/125 (5%)	11/175 (6%)	
Adjusted Rates (b)	35.0%	23.2%	26.3%	
Terminal Rates (c)	22/79 (28%)	2/15 (13%)	5/29 (16%)	
Week of First Observation	72	71	49	
Life Table Tests (d)		P=0.307N	P=0.227N	P=0.602
Incidental Tumor Tests (d)		P=0.001N	P=0.002N	P=0.467
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.389
Integumentary System or Salivary Gland: Fibrosarcoma				
Overall Rates (a)	8/117 (7%)	1/125 (1%)	3/175 (2%)	
Adjusted Rates (b)	9.0%	6.7%	6.0%	
Terminal Rates (c)	5/79 (6%)	1/15 (7%)	1/29 (3%)	
Week of First Observation	72	117	49	
Life Table Tests (d)		P=0.408N	P=0.442N	
Incidental Tumor Tests (d)		P=0.091N	P=0.067N	
Fisher Exact Test (d)		P=0.014N	P=0.027N	

TABLE A3b. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. 1% Amosite + DMH
Integumentary System or Salivary Glands: Sarcoma, Fibrosarcoma, or Neurofibrosarcoma				
Overall Rates (a)	14/117 (12%)	3/125 (2%)	4/175 (2%)	
Adjusted Rates (b)	15.4%	10.8%	8.3%	
Terminal Rates (c)	9/79 (11%)	1/15 (7%)	1/29 (3%)	
Week of First Observation	72	84	49	
Life Table Tests (d)		P=0.469N	P=0.217N	P=0.511N
Incidental Tumor Tests (d)		P=0.019N	P=0.006N	P=0.629N
Fisher Exact Test (d)		P=0.003N	P<0.001N	P=0.618N
Integumentary System or Salivary Gland: Fibroma, Neurofibroma, Sarcoma, Fibrosarcoma, or Neurofibrosarcoma				
Overall Rates (a)	34/117 (29%)	7/125 (6%)	11/175 (6%)	
Adjusted Rates (b)	36.1%	25.2%	26.3%	
Terminal Rates (c)	23/79 (29%)	2/15 (13%)	5/29 (16%)	
Week of First Observation	72	71	49	
Life Table Tests (d)		P=0.402N	P=0.200N	P=0.474N
Incidental Tumor Tests (d)		P=0.003N	P=0.002N	P=0.585
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.505
Hematopoietic System: Leukemia				
Overall Rates (e)	38/117 (32%)	20/125 (16%)	40/175 (23%)	
Adjusted Rates (b)	42.4%	60.0%	72.8%	
Terminal Rates (c)	29/79 (37%)	5/15 (33%)	17/29 (59%)	
Week of First Observation	87	72	73	
Life Table Test (d)		P<0.001	P<0.001	P=0.423
Incidental Tumor Test (d)		P=0.509N	P=0.024	P=0.210
Fisher Exact Test (d)		P=0.002N	P=0.046N	P=0.093
Circulatory System: Hemangiosarcoma				
Overall Rates (e)	1/117 (1%)	0/125 (0%)	4/175 (2%)	
Adjusted Rates (b)	1.3%	0.0%	6.4%	
Terminal Rates (c)	1/79 (1%)	0/15 (0%)	1/29 (3%)	
Week of First Observation	132		70	
Life Table Test (d)		P=0.824N	P=0.075	P=0.170
Incidental Tumor Test (d)		P=0.829N	P=0.316	P=0.135
Fisher Exact Test (d)		P=0.483N	P=0.334	P=0.114
Circulatory System: Hemangioma or Hemangiosarcoma				
Overall Rates (e)	1/117 (1%)	0/125 (0%)	5/175 (3%)	
Adjusted Rates (b)	1.3%	0.0%	7.7%	
Terminal Rates (c)	1/79 (1%)	0/15 (0%)	1/29 (3%)	
Week of First Observation	132		70	
Life Table Test (d)		P=0.824N	P=0.035	P=0.117
Incidental Tumor Test (d)		P=0.829N	P=0.218	P=0.085
Fisher Exact Test (d)		P=0.483N	P=0.230	P=0.066
Liver: Neoplastic Nodule				
Overall Rates (a)	9/117 (8%)	18/125 (14%)	27/175 (15%)	
Adjusted Rates (b)	11.1%	63.2%	54.2%	
Terminal Rates (c)	8/79 (10%)	7/15 (47%)	13/29 (41%)	
Week of First Observation	108	75	69	
Life Table Tests (d)		P<0.001	P<0.001	P=0.285
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.435
Fisher Exact Test (d)		P=0.072	P=0.035	P=0.470

TABLE A3b. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. 1% Amosite + DMH
Liver: Hepatocellular Carcinoma				
Overall Rates (a)	1/117 (1%)	9/125 (7%)	7/175 (4%)	
Adjusted Rates (b)	1.3%	33.9%	15.7%	
Terminal Rates (c)	1/79 (1%)	2/15 (13%)	2/29 (9%)	
Week of First Observation	117	68	78	
Life Table Tests (d)		P<0.001	P=0.001	P=0.065N
Incidental Tumor Tests (d)		P=0.005	P=0.019	P=0.113N
Fisher Exact Test (d)		P=0.013	P=0.102	P=0.169N
Liver: Neoplastic Nodule or Hepatocellular Carcinoma				
Overall Rates (a)	9/117 (8%)	24/125 (19%)	31/175 (18%)	
Adjusted Rates (b)	11.1%	70.5%	59.0%	
Terminal Rates (c)	8/79 (10%)	7/15 (47%)	13/29 (45%)	
Week of First Observation	108	68	69	
Life Table Tests (d)		P<0.001	P<0.001	P=0.103N
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.215N
Fisher Exact Test (d)		P=0.007	P=0.010	P=0.428N
Small Intestine: Adenocarcinoma				
Overall Rates (e)	0/117 (0%)	3/125 (2%)	9/175 (5%)	
Adjusted Rates (b)	0.0%	9.0%	15.0%	
Terminal Rates (c)	0/79 (0%)	1/15 (7%)	2/29 (6%)	
Week of First Observation		49	57	
Life Table Tests (d)		P=0.028	P<0.001	P=0.293
Incidental Tumor Tests (d)		P=0.175	P=0.024	P=0.171
Fisher Exact Test (d)		P=0.136	P=0.009	P=0.186
Small Intestine: Mucinous Cystadenocarcinoma				
Overall Rates (e)	2/117 (2%)	8/125 (6%)	7/175 (4%)	
Adjusted Rates (b)	2.2%	16.6%	9.0%	
Terminal Rates (c)	1/79 (1%)	1/15 (7%)	1/29 (3%)	
Week of First Observation	100	45	60	
Life Table Tests (d)		P=0.002	P=0.032	P=0.155N
Incidental Tumor Tests (d)		P=0.268	P=0.449	P=0.310N
Fisher Exact Test (d)		P=0.063	P=0.227	P=0.249N
Small Intestine: Adenocarcinoma or Mucinous Cystadenocarcinoma				
Overall Rates (e)	2/117 (2%)	11/125 (9%)	16/175 (9%)	
Adjusted Rates (b)	2.2%	24.5%	22.9%	
Terminal Rates (c)	1/79 (1%)	2/15 (13%)	3/29 (9%)	
Week of First Observation	100	45	57	
Life Table Tests (d)		P<0.001	P<0.001	P=0.422N
Incidental Tumor Tests (d)		P=0.086	P=0.033	P=0.474
Fisher Exact Test (d)		P=0.013	P=0.007	P=0.544
Small Intestine: Adenomatous Polyp, Adenocarcinoma, or Mucinous Cystadenocarcinoma				
Overall Rates (e)	3/117 (3%)	12/125 (10%)	17/175 (10%)	
Adjusted Rates (b)	3.5%	25.4%	23.4%	
Terminal Rates (c)	2/79 (2%)	2/15 (13%)	3/29 (9%)	
Week of First Observation	100	45	57	
Life Table Tests (d)		P<0.001	P<0.001	P=0.380N
Incidental Tumor Tests (d)		P=0.114	P=0.053	P=0.503
Fisher Exact Test (d)		P=0.021	P=0.013	P=0.569

TABLE A3b. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. 1% Amosite + DMH
Small Intestine: Signet Ring Carcinoma				
Overall Rates (e)	0/117 (0%)	3/125 (2%)	0/175 (0%)	
Adjusted Rates (b)	0.0%	5.4%	0.0%	
Terminal Rates (c)	0/79 (0%)	0/15 (0%)	0/29 (0%)	
Week of First Observation		75		
Life Table Tests (d)		P=0.031	(f)	P=0.052N
Incidental Tumor Tests (d)		P=0.285	(f)	P=0.070N
Fisher Exact Test (d)		P=0.136	(f)	P=0.071N
Large Intestine: Signet Ring Carcinoma				
Overall Rates (e)	0/117 (0%)	6/125 (5%)	5/175 (3%)	
Adjusted Rates (b)	0.0%	9.1%	8.3%	
Terminal Rates (c)	0/79 (0%)	0/15 (0%)	1/29 (3%)	
Week of First Observation		31	74	
Life Table Tests (d)		P=0.003	P=0.011	P=0.182N
Incidental Tumor Tests (d)		P=0.267	P=0.168	P=0.337N
Fisher Exact Test (d)		P=0.018	P=0.076	P=0.281N
Large Intestine: Adenomatous Polyp				
Overall Rates (e)	0/117 (0%)	43/125 (34%)	61/175 (35%)	
Adjusted Rates (b)	0.0%	69.0%	60.7%	
Terminal Rates (c)	0/79 (0%)	6/15 (40%)	8/29 (28%)	
Week of First Observation		66	57	
Life Table Tests (d)		P<0.001	P<0.001	P=0.158
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.440
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.517
Large Intestine: Adenocarcinoma				
Overall Rates (e)	0/117 (0%)	9/125 (7%)	6/175 (3%)	
Adjusted Rates (b)	0.0%	9.8%	5.6%	
Terminal Rates (c)	0/79 (0%)	0/15 (0%)	0/29 (0%)	
Week of First Observation		44	39	
Life Table Tests (d)		P<0.001	P=0.019	P=0.064N
Incidental Tumor Tests (d)		P=0.490	P=0.481	P=0.143N
Fisher Exact Test (d)		P=0.002	P=0.045	P=0.114N
Large Intestine: Mucinous Cystadenocarcinoma				
Overall Rates (a)	0/117 (0%)	10/125 (8%)	18/175 (10%)	
Adjusted Rates (b)	0.0%	8.5%	17.6%	
Terminal Rates (c)	0/79 (0%)	0/15 (0%)	1/29 (3%)	
Week of First Observation		41	49	
Life Table Tests (d)		P=0.002	P<0.001	P=0.458
Incidental Tumor Tests (d)		P=0.693	P=0.058	P=0.139
Fisher Exact Test (d)		P=0.001	P<0.001	P=0.322
Large Intestine: Adenocarcinoma in Adenomatous Polyp				
Overall Rates (a)	0/117 (0%)	30/125 (24%)	45/175 (26%)	
Adjusted Rates (b)	0.0%	51.8%	50.9%	
Terminal Rates (c)	0/79 (0%)	2/15 (13%)	6/29 (21%)	
Week of First Observation		40	51	
Life Table Tests (d)		P<0.001	P<0.001	P=0.315N
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.454
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.421

TABLE A3b. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. 1% Amosite + DMH
Large Intestine: Adenocarcinoma, Mucinous Cystadenocarcinoma, or Adenocarcinoma in Adenomatous Polyp				
Overall Rates (a)	0/117 (0%)	44/125 (35%)	65/175 (37%)	
Adjusted Rates (b)	0.0%	58.3%	60.5%	
Terminal Rates (c)	0/79 (0%)	2/15 (13%)	7/29 (24%)	
Week of First Observation		40	39	
Life Table Tests (d)		P<0.001	P<0.001	P=0.272N
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.313
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.412
Large Intestine: Adenomatous Polyp, Adenocarcinoma, Mucinous Cystadenocarcinoma, or Adenocarcinoma in Adenomatous Polyp				
Overall Rates (a)	0/117 (0%)	77/125 (62%)	106/175 (61%)	
Adjusted Rates (b)	0.0%	86.0%	81.1%	
Terminal Rates (c)	0/79 (0%)	8/15 (53%)	13/29 (45%)	
Week of First Observation		40	39	
Life Table Tests (d)		P<0.001	P<0.001	P=0.071N
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.476N
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.477N
Pancreas: Acinar Cell Adenoma				
Overall Rates (e)	9/116 (8%)	0/125 (0%)	5/175 (3%)	
Adjusted Rates (b)	11.2%	0.0%	14.5%	
Terminal Rates (c)	8/79 (10%)	0/15 (0%)	3/29 (10%)	
Week of First Observation	115		103	
Life Table Tests (d)		P=0.188N	P=0.344	P=0.121
Incidental Tumor Tests (d)		P=0.195N	P=0.513	P=0.104
Fisher Exact Test (d)		P=0.001N	P=0.055N	P=0.066
Pancreas: Acinar Cell Adenoma or Carcinoma				
Overall Rates (e)	11/117 (9%)	0/125 (0%)	5/175 (3%)	
Adjusted Rates (b)	13.7%	0.0%	14.5%	
Terminal Rates (c)	10/79 (13%)	0/15 (0%)	3/29 (10%)	
Week of First Observation	115		103	
Life Table Tests (d)		P=0.139N	P=0.474	P=0.121
Incidental Tumor Tests (d)		P=0.145N	P=0.599N	P=0.104
Fisher Exact Test (d)		P<0.001N	P=0.017N	P=0.066
Pituitary Gland: Adenoma				
Overall Rates (e)	24/117 (21%)	6/122 (5%)	12/169 (7%)	
Adjusted Rates (b)	27.7%	26.2%	24.5%	
Terminal Rates (c)	18/79 (23%)	3/14 (21%)	4/28 (14%)	
Week of First Observation	96	66	79	
Life Table Test (d)		P=0.483	P=0.376	P=0.525
Incidental Tumor Test (d)		P=0.258N	P=0.203N	P=0.421
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.307
Pituitary Gland: Adenoma or Carcinoma				
Overall Rates (e)	26/117 (22%)	6/122 (5%)	12/169 (7%)	
Adjusted Rates (b)	29.8%	26.2%	24.5%	
Terminal Rates (c)	19/79 (24%)	3/14 (21%)	4/28 (14%)	
Week of First Observation	96	66	79	
Life Table Test (d)		P=0.545	P=0.457	P=0.525
Incidental Tumor Test (d)		P=0.214N	P=0.152N	P=0.421
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.307

TABLE A3b. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. 1% Amosite + DMH
Adrenal Medulla: Pheochromocytoma				
Overall Rates (e)	39/117 (33%)	16/125 (13%)	16/175 (9%)	
Adjusted Rates (b)	45.4%	62.2%	37.0%	
Terminal Rates (c)	33/79 (42%)	8/15 (53%)	8/29 (28%)	
Week of First Observation	78	76	73	
Life Table Tests (d)		P=0.012	P=0.565N	P=0.041N
Incidental Tumor Tests (d)		P=0.344	P=0.102N	P=0.074N
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.205N
Adrenal Medulla: Malignant Pheochromocytoma				
Overall Rates (e)	3/117 (3%)	0/125 (0%)	2/175 (1%)	
Adjusted Rates (b)	3.8%	0.0%	5.7%	
Terminal Rates (c)	3/79 (4%)	0/15 (0%)	0/29 (0%)	
Week of First Observation	117		110	
Life Table Tests (d)		P=0.514N	P=0.447	
Incidental Tumor Tests (d)		P=0.522N	P=0.591	
Fisher Exact Test (d)		P=0.112N	P=0.322N	
Adrenal Medulla: Pheochromocytoma or Malignant Pheochromocytoma				
Overall Rates (e)	39/117 (33%)	16/125 (13%)	17/175 (10%)	
Adjusted Rates (b)	45.4%	62.2%	39.0%	
Terminal Rates (c)	33/79 (42%)	8/15 (53%)	8/29 (28%)	
Week of First Observation	78	76	73	
Life Table Tests (d)		P=0.012	P=0.473	P=0.058N
Incidental Tumor Tests (d)		P=0.344	P=0.160N	P=0.097N
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.255N
Thyroid Gland: Follicular Cell Adenoma				
Overall Rates (e)	4/117 (3%)	4/124 (3%)	10/174 (6%)	
Adjusted Rates (b)	5.1%	14.5%	21.1%	
Terminal Rates (c)	4/79 (5%)	1/15 (7%)	4/29 (14%)	
Week of First Observation	117	80	74	
Life Table Tests (d)		P=0.044	P=0.002	P=0.385
Incidental Tumor Tests (d)		P=0.277	P=0.047	P=0.304
Fisher Exact Test (d)		P=0.606N	P=0.261	P=0.234
Thyroid Gland: Follicular Cell Carcinoma				
Overall Rates (e)	7/117 (6%)	3/124 (2%)	3/174 (2%)	
Adjusted Rates (b)	8.5%	20.0%	9.0%	
Terminal Rates (c)	6/79 (8%)	3/15 (20%)	2/29 (7%)	
Week of First Observation	98	117	106	
Life Table Tests (d)		P=0.239	P=0.595	P=0.343N
Incidental Tumor Tests (d)		P=0.324	P=0.512N	P=0.355N
Fisher Exact Test (d)		P=0.144N	P=0.053N	P=0.489N
Thyroid Gland: Follicular Cell Adenoma or Carcinoma				
Overall Rates (e)	11/117 (9%)	6/124 (5%)	13/174 (7%)	
Adjusted Rates (b)	13.5%	26.7%	29.1%	
Terminal Rates (c)	10/79 (13%)	3/15 (20%)	6/29 (21%)	
Week of First Observation	98	80	74	
Life Table Tests (d)		P=0.060	P=0.009	P=0.455
Incidental Tumor Tests (d)		P=0.292	P=0.149	P=0.371
Fisher Exact Test (d)		P=0.129N	P=0.352N	P=0.256
Thyroid Gland: C-Cell Adenoma				
Overall Rates (e)	16/117 (14%)	2/124 (2%)	9/174 (5%)	
Adjusted Rates (b)	19.3%	9.3%	26.0%	
Terminal Rates (c)	13/79 (16%)	0/15 (0%)	7/29 (24%)	
Week of First Observation	109	108	80	
Life Table Tests (d)		P=0.380N	P=0.243	P=0.188
Incidental Tumor Tests (d)		P=0.108N	P=0.512	P=0.162
Fisher Exact Test (d)		P<0.001N	P=0.011N	P=0.095

TABLE A3b. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. 1% Amosite + DMH
Thyroid Gland: C-Cell Carcinoma				
Overall Rates (e)	11/117 (9%)	7/124 (6%)	10/174 (6%)	
Adjusted Rates (b)	13.1%	29.5%	24.7%	
Terminal Rates (c)	9/79 (11%)	2/15 (13%)	5/29 (14%)	
Week of First Observation	95	68	98	
Life Table Tests (d)		P=0.029	P=0.046	P=0.387N
Incidental Tumor Tests (d)		P=0.382	P=0.278	P=0.481N
Fisher Exact Test (d)		P=0.194N	P=0.171N	P=0.590
Thyroid Gland: C-Cell Adenoma or Carcinoma				
Overall Rates (e)	27/117 (23%)	8/124 (6%)	19/174 (11%)	
Adjusted Rates (b)	31.7%	32.7%	47.2%	
Terminal Rates (c)	22/79 (28%)	2/15 (13%)	11/29 (38%)	
Week of First Observation	95	68	80	
Life Table Tests (d)		P=0.271	P=0.025	P=0.343
Incidental Tumor Tests (d)		P=0.244N	P=0.272	P=0.253
Fisher Exact Test (d)		P<0.001N	P=0.005N	P=0.131
Parathyroid: Adenoma				
Overall Rates (e)	4/110 (4%)	1/119 (1%)	1/170 (1%)	
Adjusted Rates (b)	5.1%	1.0%	3.8%	
Terminal Rates (c)	3/79 (4%)	0/15 (0%)	1/29 (3%)	
Week of First Observation	114	67	117	
Life Table Tests (d)		P=0.671N	P=0.589N	
Incidental Tumor Tests (d)		P=0.462N	P=0.589N	
Fisher Exact Test (d)		P=0.161N	P=0.080N	
Pancreatic Islets: Islet Cell Adenoma				
Overall Rates (e)	14/116 (12%)	0/125 (0%)	3/175 (2%)	
Adjusted Rates (b)	17.0%	0.0%	6.8%	
Terminal Rates (c)	12/79 (15%)	0/15 (0%)	1/29 (3%)	
Week of First Observation	101		99	
Life Table Tests (d)		P=0.085N	P=0.228N	
Incidental Tumor Tests (d)		P=0.056N	P=0.101N	
Fisher Exact Test (d)		P<0.001N	P<0.001N	
Pancreatic Islets: Islet Cell Carcinoma				
Overall Rates (e)	3/116 (3%)	0/125 (0%)	3/175 (2%)	
Adjusted Rates (b)	3.8%	0.0%	7.4%	
Terminal Rates (c)	3/79 (3%)	0/15 (0%)	1/29 (3%)	
Week of First Observation	117		103	
Life Table Tests (d)		P=0.514N	P=0.243	
Incidental Tumor Tests (d)		P=0.522N	P=0.464	
Fisher Exact Test (d)		P=0.110N	P=0.453N	
Pancreatic Islets: Islet Cell Adenoma or Carcinoma				
Overall Rates (e)	17/116 (15%)	0/125 (0%)	6/175 (3%)	
Adjusted Rates (b)	20.7%	0.0%	13.8%	
Terminal Rates (c)	15/79 (19%)	0/15 (0%)	2/29 (7%)	
Week of First Observation	101		99	
Life Table Tests (d)		P=0.054N	P=0.488N	P=0.083
Incidental Tumor Tests (d)		P=0.036N	P=0.207N	P=0.059
Fisher Exact Test (d)		P<0.001	P<0.001N	P=0.038
Mammary Gland: Adenoma				
Overall Rates (a)	3/117 (3%)	0/125 (0%)	0/175 (0%)	
Adjusted Rates (b)	3.8%	0.0%	0.0%	
Terminal Rates (c)	3/79 (4%)	0/15 (0%)	0/29 (0%)	
Week of First Observation	133			
Life Table Tests (d)		P=0.514N	P=0.344N	
Incidental Tumor Test (d)		P=0.522N	P=0.344N	
Fisher Exact Test (d)		P=0.112N	P=0.063N	

TABLE A3b. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. 1% Amosite + DMH
Mammary Gland: Fibroadenoma				
Overall Rates (a)	17/117 (15%)	1/125 (1%)	5/175 (3%)	
Adjusted Rates (b)	20.8%	6.7%	16.1%	
Terminal Rates (c)	15/79 (19%)	1/15 (7%)	4/29 (14%)	
Week of First Observation	107	117	108	
Life Table Test (d)		P=0.166N	P=0.406N	P=0.305
Incidental Tumor Test (d)		P=0.120N	P=0.270N	P=0.302
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.206
Preputial Gland: Carcinoma				
Overall Rates (e)	6/117 (5%)	5/125 (4%)	4/175 (2%)	
Adjusted Rates (b)	6.7%	22.5%	8.2%	
Terminal Rates (c)	3/79 (4%)	3/15 (20%)	1/29 (3%)	
Week of First Observation	90	67	97	
Life Table Test (d)		P=0.051	P=0.411	P=0.182N
Incidental Tumor Test (d)		P=0.399	P=0.364N	P=0.221N
Fisher Exact Test (d)		P=0.454N	P=0.163N	P=0.296N
Testis: Interstitial Cell Tumor				
Overall Rates (e)	111/117 (95%)	79/123 (64%)	125/174 (72%)	
Adjusted Rates (b)	98.2%	100.0%	100.0%	
Terminal Rates (c)	77/79 (97%)	15/15 (100%)	29/29 (100%)	
Week of First Observation	78	66	70	
Life Table Tests (d)		P<0.001	P<0.001	P=0.182N
Incidental Tumor Tests (d)		P=0.547	P=0.456	P=0.473
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.103
Zymbal Gland: Keratoacanthoma				
Overall Rates (e)	0/117 (0%)	3/125 (2%)	3/175 (2%)	
Adjusted Rates (b)	0.0%	3.1%	2.3%	
Terminal Rates (c)	0/79 (0%)	0/15 (0%)	0/29 (4%)	
Week of First Observation		66	67	
Life Table Tests (d)		P=0.093	P=0.145	P=0.422N
Incidental Tumor Tests (d)		P=0.768	P=0.844	P=0.489N
Fisher Exact Test (d)		P=0.136	P=0.214	P=0.140
Zymbal Gland: Squamous Cell Papilloma				
Overall Rates (e)	0/117 (0%)	7/125 (6%)	17/175 (10%)	
Adjusted Rates (b)	0.0%	25.3%	29.6%	
Terminal Rates (c)	0/79 (0%)	2/15 (13%)	4/29 (14%)	
Week of First Observation		67	59	
Life Table Tests (d)		P<0.001	P<0.001	P=0.324
Incidental Tumor Tests (d)		P=0.006	P<0.001	P=0.185
Fisher Exact Test (d)		P=0.009	P<0.001	P=0.140
Zymbal Gland: Carcinoma				
Overall Rates (e)	1/117 (1%)	23/125 (18%)	35/175 (20%)	
Adjusted Rates (b)	0.9%	56.7%	42.0%	
Terminal Rates (c)	0/79 (0%)	6/15 (40%)	5/29 (17%)	
Week of First Observation	94	46	57	
Life Table Tests (d)		P<0.001	P<0.001	P=0.340N
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.439
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.424
Zymbal Gland: Carcinoma or Squamous Cell Papilloma				
Overall Rates (e)	1/117 (1%)	30/125 (24%)	52/175 (30%)	
Adjusted Rates (b)	0.9%	71.0%	60.6%	
Terminal Rates (c)	0/79 (0%)	8/15 (53%)	9/29 (31%)	
Week of First Observation	94	46	57	
Life Table Tests (d)		P<0.001	P<0.001	P=0.508N
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.207
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.168

TABLE A3b. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYL HYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. 1% Amosite + DMH
All Sites: Mesothelioma				
Overall Rates (a)	2/117 (2%)	4/125 (3%)	6/175 (3%)	
Adjusted Rates (b)	2.2%	15.9%	6.9%	
Terminal Rates (c)	1/79 (1%)	1/15 (7%)	0/29 (0%)	
Week of First Observation	95	93	72	
Life Table Test (d)		P=0.013	P=0.059	P=0.526N
Incidental Tumor Test (d)		P=0.206	P=0.588	P=0.612
Fisher Exact Test (d)		P=0.374	P=0.311	P=0.592
All Sites: Benign Tumors				
Overall Rates (a)	115/117 (98%)	93/125 (74%)	150/175 (86%)	
Adjusted Rates (b)	100.0%	100.0%	100.0%	
Terminal Rates (c)	79/79 (100%)	15/15 (100%)	29/29 (100%)	
Week of First Observation	78	66	49	
Life Table Test (d)		P<0.001	P<0.001	P=0.237N
Incidental Tumor Test (d)		P=0.637	P=0.490	P=0.088
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.011
All Sites: Malignant Tumors				
Overall Rates (a)	82/117 (70%)	110/125 (88%)	149/175 (85%)	
Adjusted Rates (b)	76.8%	99.0%	97.8%	
Terminal Rates (c)	55/79 (70%)	14/15 (93%)	26/29 (90%)	
Week of First Observation	72	31	39	
Life Table Test (d)		P<0.001	P<0.001	P=0.018N
Incidental Tumor Test (d)		P=0.008	P=0.004	P=0.330N
Fisher Exact Test (d)		P<0.001	P=0.002	P=0.297N
All Sites: All Tumors				
Overall Rates (a)	116/117 (99%)	125/125 (100%)	173/175 (99%)	
Adjusted Rates (b)	100.0%	100.0%	100.0%	
Terminal Rates (c)	79/79 (100%)	15/15 (100%)	29/29 (100%)	
Week of First Observation	72	31	39	
Life Table Test (d)		P<0.001	P<0.001	P=0.021N
Incidental Tumor Test (d)		P=0.038	P=0.156	P=0.321N
Fisher Exact Test (d)		P=0.483	P=0.648N	P=0.339N

(a) Number of tumor-bearing animals/number of animals examined grossly at the site

(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality

(c) Observed tumor incidence in animals killed at the end of the study

(d) Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in a dosed group than in controls is indicated by (N). The P values for the comparison of the DMH group with the 1% amosite + DMH group are presented in the last column for those sites where there was an incidence of at least 2% in at least one group.

(e) Number of tumor-bearing animals/number of animals examined microscopically at the site

TABLE A3c. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH)

	1% Amosite	1% Amosite + DMH
Skin: Squamous Cell Papilloma		
Overall Rates (a)	6/250 (2%)	1/175 (1%)
Adjusted Rates (b)	3.1%	3.4%
Terminal Rates (c)	5/188 (3%)	1/29 (3%)
Week of First Observation	110	117
Life Table Tests (d)		P=0.693
Incidental Tumor Tests (d)		P=0.548N
Fisher Exact Test (d)		P=0.142N
Skin: Squamous Cell Papilloma or Carcinoma		
Overall Rates (a)	10/250 (4%)	1/175 (1%)
Adjusted Rates (b)	5.1%	3.4%
Terminal Rates (c)	8/188 (4%)	1/29 (3%)
Week of First Observation	80	117
Life Table Tests (d)		P=0.449N
Incidental Tumor Tests (d)		P=0.156N
Fisher Exact Test (d)		P=0.024N
Skin: Basal Cell Carcinoma		
Overall Rates (a)	7/250 (3%)	1/175 (1%)
Adjusted Rates (b)	3.6%	2.6%
Terminal Rates (c)	6/188 (3%)	0/29 (0%)
Week of First Observation	104	108
Life Table Tests (d)		P=0.650N
Incidental Tumor Tests (d)		P=0.346N
Fisher Exact Test (d)		P=0.092N
Skin: Basal Cell Tumor or Carcinoma		
Overall Rates (a)	8/250 (3%)	1/175 (1%)
Adjusted Rates (b)	4.2%	2.6%
Terminal Rates (c)	7/188 (4%)	0/29 (0%)
Week of First Observation	104	108
Life Table Tests (d)		P=0.593N
Incidental Tumor Tests (d)		P=0.309N
Fisher Exact Test (d)		P=0.060N
Skin: Keratoacanthoma		
Overall Rates (a)	17/250 (7%)	5/175 (3%)
Adjusted Rates (b)	9.0%	8.8%
Terminal Rates (c)	17/188 (9%)	1/29 (3%)
Week of First Observation	117	72
Life Table Tests (d)		P=0.254
Incidental Tumor Tests (d)		P=0.609N
Fisher Exact Test (d)		P=0.054N
Subcutaneous Tissue: Fibroma		
Overall Rates (a)	33/250 (13%)	6/175 (3%)
Adjusted Rates (b)	17.2%	18.6%
Terminal Rates (c)	31/188(16%)	4/29 (14%)
Week of First Observation	96	110
Life Table Tests (d)		P=0.471
Incidental Tumor Tests (d)		P=0.398N
Fisher Exact Test (d)		P<0.001N
Subcutaneous Tissue: Neurofibroma		
Overall Rates (a)	5/250 (2%)	1/175 (1%)
Adjusted Rates (b)	2.7%	0.7%
Terminal Rates (c)	5/188 (3%)	0/29 (0%)
Week of First Observation	117	71
Life Table Tests (d)		P=0.701N
Incidental Tumor Tests (d)		P=0.459N
Fisher Exact Test (d)		P=0.214N

**TABLE A3c. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY
OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)**

	1% Amosite	1% Amosite + DMH
Subcutaneous Tissue: Fibroma or Neurofibroma		
Overall Rates (a)	36/250 (14%)	7/175 (4%)
Adjusted Rates (b)	18.8%	19.2%
Terminal Rates (c)	34/188 (18%)	4/29 (14%)
Week of First Observation	96	71
Life Table Tests (d)		P=0.428
Incidental Tumor Tests (d)		P=0.348N
Fisher Exact Test (d)		P<0.001N
Subcutaneous Tissue: Fibrosarcoma		
Overall Rates (a)	9/250 (4%)	3/175 (2%)
Adjusted Rates (b)	4.4%	6.0%
Terminal Rates (c)	5/188 (3%)	1/29 (3%)
Week of First Observation	80	49
Life Table Tests (d)		P=0.392
Incidental Tumor Tests (d)		P=0.238N
Fisher Exact Test (d)		P=0.198N
Subcutaneous Tissue: Fibroma or Fibrosarcoma		
Overall Rates (a)	41/250 (16%)	9/175 (5%)
Adjusted Rates (b)	20.8%	23.9%
Terminal Rates (c)	35/188 (19%)	5/29 (17%)
Week of First Observation	80	49
Life Table Tests (d)		P=0.312
Incidental Tumor Tests (d)		P=0.223N
Fisher Exact Test (d)		P<0.001N
Subcutaneous Tissue: Sarcoma or Fibrosarcoma		
Overall Rates (a)	11/250 (4%)	4/175 (2%)
Adjusted Rates (b)	5.4%	8.3%
Terminal Rates (c)	6/188 (3%)	1/29 (3%)
Week of First Observation	80	49
Life Table Tests (d)		P=0.261
Incidental Tumor Tests (d)		P=0.219N
Fisher Exact Test (d)		P=0.186N
Subcutaneous Tissue: Fibroma, Neurofibroma, Sarcoma, or Fibrosarcoma		
Overall Rates (a)	46/250 (18%)	11/175 (6%)
Adjusted Rates (b)	23.2%	26.3%
Terminal Rates (c)	39/188 (21%)	5/29 (17%)
Week of First Observation	80	49
Life Table Tests (d)		P=0.218
Incidental Tumor Tests (d)		P=0.177N
Fisher Exact Test (d)		P<0.001N
Integumentary System or Salivary Gland: Sarcoma or Fibrosarcoma		
Overall Rates (a)	15/250 (6%)	4/175 (2%)
Adjusted Rates (b)	7.5%	8.3%
Terminal Rates (c)	10/188(5%)	1/29 (3%)
Week of First Observation	80	49
Life Table Tests (d)		P=0.405
Incidental Tumor Tests (d)		P=0.148N
Fisher Exact Test (d)		P=0.053N
Integumentary System or Salivary Gland: Fibroma, Neurofibroma, Sarcoma, or Fibrosarcoma		
Overall Rates (a)	48/250 (19%)	11/175 (6%)
Adjusted Rates (b)	24.3%	26.3%
Terminal Rates (c)	41/188 (22%)	5/29(17%)
Week of First Observation	80	49
Life Table Tests (d)		P=0.253
Incidental Tumor Tests (d)		P=0.153N
Fisher Exact Test (d)		P<0.001N

TABLE A3c. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
Lung: Alveolar/Bronchiolar Carcinoma		
Overall Rates (e)	6/250 (2%)	2/175 (1%)
Adjusted Rates (b)	3.2%	6.9%
Terminal Rates (c)	6/188 (3%)	2/29 (7%)
Week of First Observation	117	117
Life Table Tests (d)		P=0.325
Incidental Tumor Tests (d)		P=0.342
Fisher Exact Test (d)		P=0.289N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma		
Overall Rates (e)	8/250 (3%)	3/175 (2%)
Adjusted Rates (b)	4.3%	7.5%
Terminal Rates (c)	8/188 (4%)	2/29 (7%)
Week of First Observation	117	70
Life Table Tests (d)		P=0.248
Incidental Tumor Tests (d)		P=0.421
Fisher Exact Test (d)		P=0.266N
Hematopoietic System: Leukemia		
Overall Rates (a)	107/250 (43%)	40/175 (23%)
Adjusted Rates (b)	50.0%	72.8%
Terminal Rates (c)	83/188 (44%)	17/29 (59%)
Week of First Observation	80	73
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.344
Fisher Exact Test (d)		P<0.001N
Liver: Neoplastic Nodule		
Overall Rates (e)	9/250 (4%)	27/175 (15%)
Adjusted Rates (b)	4.7%	54.2%
Terminal Rates (c)	8/188 (4%)	12/29 (41%)
Week of First Observation	101	69
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Liver: Hepatocellular Carcinoma		
Overall Rates (e)	3/250 (1%)	7/175 (4%)
Adjusted Rates (b)	1.6%	15.7%
Terminal Rates (c)	3/188 (2%)	2/29 (7%)
Week of First Observation	117	78
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.006
Fisher Exact Test (d)		P=0.062
Liver: Neoplastic Nodule or Hepatocellular Carcinoma		
Overall Rates (e)	12/250 (5%)	31/175 (18%)
Adjusted Rates (b)	6.3%	59.0%
Terminal Rates (c)	11/188 (6%)	13/29 (45%)
Week of First Observation	101	69
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Small Intestine: Adenocarcinoma		
Overall Rates (a)	0/250 (0%)	9/175 (5%)
Adjusted Rates (b)	0.0%	15.0%
Terminal Rates (c)	0/188 (0%)	2/29 (7%)
Week of First Observation		57
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.005
Fisher Exact Test (d)		P<0.001

TABLE A3c. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
Small Intestine: Mucinous Cystadenocarcinoma		
Overall Rates (a)	0/250 (0%)	7/175 (4%)
Adjusted Rates (b)	0.0%	9.0%
Terminal Rates (c)	0/188 (0%)	1/29 (3%)
Week of First Observation		60
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.045
Fisher Exact Test (d)		P=0.002
Small Intestine: Adenocarcinoma, Adenocarcinoma in Adenomatous Polyp, or Mucinous Cystadenocarcinoma		
Overall Rates (a)	1/250 (0%)	16/175 (9%)
Adjusted Rates (b)	0.5%	22.9%
Terminal Rates (c)	0/188 (0%)	3/29 (10%)
Week of First Observation	108	57
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.002
Fisher Exact Test (d)		P<0.001
Small Intestine: Adenomatous Polyp, Adenocarcinoma, Adenocarcinoma in Adenomatous Polyp, or Mucinous Cystadenocarcinoma		
Overall Rates (a)	1/250 (0%)	17/175 (10%)
Adjusted Rates (b)	0.5%	23.4%
Terminal Rates (c)	0/188 (0%)	3/29 (10%)
Week of First Observation	108	57
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.002
Fisher Exact Test (d)		P<0.001
Large Intestine: Signet Ring Carcinoma		
Overall Rates (a)	0/250 (0%)	5/175 (3%)
Adjusted Rates (b)	0.0%	8.3%
Terminal Rates (c)	0/188 (0%)	1/29 (3%)
Week of First Observation		74
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.080
Fisher Exact Test (d)		P=0.011
Large Intestine: Adenomatous Polyp		
Overall Rates (a)	3/250 (1%)	61/175 (35%)
Adjusted Rates (b)	1.5%	60.7%
Terminal Rates (c)	2/188 (1%)	8/29 (28%)
Week of First Observation	110	57
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Large Intestine: Adenocarcinoma		
Overall Rates (a)	0/250 (0%)	6/175 (3%)
Adjusted Rates (b)	0.0%	5.6%
Terminal Rates (c)	0/188 (0%)	0/29 (0%)
Week of First Observation		39
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.289
Fisher Exact Test (d)		P=0.005

TABLE A3c. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
Large Intestine: Adenocarcinoma in Adenomatous Polyp		
Overall Rates (a)	0/250 (0%)	45/175 (26%)
Adjusted Rates (b)	0.0%	50.9%
Terminal Rates (c)	0/188 (0%)	6/29 (21%)
Week of First Observation		51
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Large Intestine: Mucinous Cystadenocarcinoma		
Overall Rates (a)	0/250 (0%)	18/175 (10%)
Adjusted Rates (b)	0.0%	17.6%
Terminal Rates (c)	0/188 (0%)	1/29 (3%)
Week of First Observation		49
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.013
Fisher Exact Test (d)		P<0.001
Large Intestine: Adenocarcinoma, Adenocarcinoma in Adenomatous Polyp, or Mucinous Cystadenocarcinoma		
Overall Rates (a)	0/250 (0%)	65/175 (37%)
Adjusted Rates (b)	0.0%	60.5%
Terminal Rates (c)	0/188 (0%)	7/29 (24%)
Week of First Observation		39
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Large Intestine: Adenomatous Polyp, Adenocarcinoma, Mucinous Cystadenocarcinoma, and Adenocarcinoma in Adenomatous Polyp		
Overall Rates (a)	3/250 (1%)	106/175 (61%)
Adjusted Rates (b)	1.5%	81.1%
Terminal Rates (c)	2/188 (1%)	13/29 (45%)
Week of First Observation	110	39
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Pancreas: Acinar Cell Adenoma		
Overall Rates (a)	19/248 (8%)	5/175 (3%)
Adjusted Rates (b)	10.1%	14.5%
Terminal Rates (c)	19/188 (10%)	3/29 (10%)
Week of First Observation	117	103
Life Table Tests (d)		P=0.222
Incidental Tumor Tests (d)		P=0.424
Fisher Exact Test (d)		P=0.026N
Pancreas: Acinar Cell Adenoma or Carcinoma		
Overall Rates (a)	20/248 (8%)	5/175 (3%)
Adjusted Rates (b)	10.6%	14.5%
Terminal Rates (c)	20/188 (11%)	3/29 (10%)
Week of First Observation	117	103
Life Table Tests (d)		P=0.251
Incidental Tumor Tests (d)		P=0.457
Fisher Exact Test (d)		P=0.018N

TABLE A3c. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
Pituitary Gland: Adenoma		
Overall Rates (a)	41/249 (16%)	12/171 (7%)
Adjusted Rates (b)	20.9%	24.5%
Terminal Rates (c)	34/188 (18%)	4/29 (14%)
Week of First Observation	58	79
Life Table Tests (d)		P = 0.080
Incidental Tumor Tests (d)		P = 0.306N
Fisher Exact Test (d)		P = 0.003N
Pituitary Gland: Adenoma or Carcinoma		
Overall Rates (a)	45/249 (18%)	12/171 (7%)
Adjusted Rates (b)	22.8%	24.5%
Terminal Rates (c)	37/188 (20%)	4/29 (14%)
Week of First Observation	58	79
Life Table Tests (d)		P = 0.125
Incidental Tumor Tests (d)		P = 0.195N
Fisher Exact Test (d)		P = 0.001N
Adrenal Cortex: Cortical Adenoma		
Overall Rates (a)	5/250 (2%)	0/175 (0%)
Adjusted Rates (b)	2.7%	0.0%
Terminal Rates (c)	5/188 (3%)	0/29 (0%)
Week of First Observation	117	
Life Table Tests (d)		P = 0.412N
Incidental Tumor Tests (d)		P = 0.401N
Fisher Exact Test (d)		P = 0.069N
Adrenal Medulla: Pheochromocytoma		
Overall Rates (a)	65/250 (26%)	16/175 (9%)
Adjusted Rates (b)	33.9%	37.0%
Terminal Rates (c)	62/188 (33%)	8/29 (28%)
Week of First Observation	101	73
Life Table Tests (d)		P = 0.076
Incidental Tumor Tests (d)		P = 0.509N
Fisher Exact Test (d)		P < 0.001N
Adrenal Medulla: Malignant Pheochromocytoma		
Overall Rates (a)	5/250 (2%)	2/175 (1%)
Adjusted Rates (b)	2.3%	5.7%
Terminal Rates (c)	1/188 (1%)	0/29 (0%)
Week of First Observation	89	110
Life Table Tests (d)		P = 0.352
Incidental Tumor Tests (d)		P = 0.459N
Fisher Exact Test (d)		P = 0.393N
Adrenal Medulla: Pheochromocytoma or Malignant Pheochromocytoma		
Overall Rates (a)	68/250 (27%)	17/175 (10%)
Adjusted Rates (b)	34.8%	39.0%
Terminal Rates (c)	62/188 (33%)	8/29 (28%)
Week of First Observation	89	73
Life Table Tests (d)		P = 0.067
Incidental Tumor Tests (d)		P = 0.457N
Fisher Exact Test (d)		P < 0.001N
Thyroid Gland: Follicular Cell Adenoma		
Overall Rates (a)	13/246 (5%)	10/174 (6%)
Adjusted Rates (b)	7.0%	21.1%
Terminal Rates (c)	13/188 (7%)	4/29 (14%)
Week of First Observation	117	74
Life Table Tests (d)		P < 0.001
Incidental Tumor Tests (d)		P = 0.053
Fisher Exact Test (d)		P = 0.500

TABLE A3c. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
Thyroid Gland: Follicular Cell Carcinoma		
Overall Rates (a)	10/246 (4%)	3/174 (2%)
Adjusted Rates (b)	5.2%	9.0%
Terminal Rates (c)	9/188 (5%)	2/29 (7%)
Week of First Observation	96	106
Life Table Tests (d)		P=0.303
Incidental Tumor Tests (d)		P=0.551
Fisher Exact Test (d)		P=0.140N
Thyroid Gland: Follicular Cell Adenoma or Carcinoma		
Overall Rates (a)	23/246 (9%)	13/174 (7%)
Adjusted Rates (b)	12.1%	29.1%
Terminal Rates (c)	22/188 (12%)	6/29 (21%)
Week of First Observation	96	74
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.071
Fisher Exact Test (d)		P=0.311N
Thyroid Gland: C-Cell Adenoma		
Overall Rates (a)	26/246 (11%)	9/174 (5%)
Adjusted Rates (b)	13.6%	26.0%
Terminal Rates (c)	23/188 (12%)	7/29 (24%)
Week of First Observation	106	80
Life Table Tests (d)		P=0.035
Incidental Tumor Tests (d)		P=0.153
Fisher Exact Test (d)		P=0.034N
Thyroid Gland: C-Cell Carcinoma		
Overall Rates (a)	50/246 (20%)	10/174 (6%)
Adjusted Rates (b)	25.7%	24.7%
Terminal Rates (c)	44/188 (23%)	4/29 (14%)
Week of First Observation	65	98
Life Table Tests (d)		P=0.361
Incidental Tumor Tests (d)		P=0.214N
Fisher Exact Test (d)		P<0.001N
Thyroid Gland: C-Cell Adenoma or Carcinoma		
Overall Rates (a)	75/246 (30%)	19/174 (11%)
Adjusted Rates (b)	38.2%	47.2%
Terminal Rates (c)	67/188 (36%)	11/29 (38%)
Week of First Observation	65	80
Life Table Tests (d)		P=0.039
Incidental Tumor Tests (d)		P=0.552
Fisher Exact Test (d)		P<0.001N
Pancreatic Islets: Islet Cell Adenoma		
Overall Rates (a)	17/248 (7%)	3/175 (2%)
Adjusted Rates (b)	8.8%	6.8%
Terminal Rates (c)	14/188 (7%)	1/29 (3%)
Week of First Observation	103	99
Life Table Tests (d)		P=0.602
Incidental Tumor Tests (d)		P=0.279N
Fisher Exact Test (d)		P=0.010N
Pancreatic Islets: Islet Cell Carcinoma		
Overall Rates (a)	5/248 (2%)	3/175 (2%)
Adjusted Rates (b)	2.7%	7.4%
Terminal Rates (c)	5/188 (3%)	1/29 (3%)
Week of First Observation	117	103
Life Table Tests (d)		P=0.087
Incidental Tumor Tests (d)		P=0.309
Fisher Exact Test (d)		P=0.562N

**TABLE A3c. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY
OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)**

	1% Amosite	1% Amosite + DMH
Pancreatic Islets: Islet Cell Adenoma or Carcinoma		
Overall Rates (a)	22/248 (9%)	6/175 (3%)
Adjusted Rates (b)	11.4%	13.8%
Terminal Rates (c)	19/188 (10%)	2/29 (7%)
Week of First Observation	103	99
Life Table Tests (d)		P=0.211
Incidental Tumor Tests (d)		P=0.515N
Fisher Exact Test (d)		P=0.019N
Mammary Gland: Fibroadenoma		
Overall Rates (e)	27/250 (11%)	5/175 (3%)
Adjusted Rates (b)	14.4%	16.1%
Terminal Rates (c)	27/188 (14%)	4/29 (14%)
Week of First Observation	117	108
Life Table Tests (d)		P=0.454
Incidental Tumor Tests (d)		P=0.574
Fisher Exact Test (d)		P=0.001N
Preputial Gland: Carcinoma		
Overall Rates (a)	9/250 (4%)	4/175 (2%)
Adjusted Rates (b)	4.6%	8.2%
Terminal Rates (c)	7/188 (4%)	1/29 (3%)
Week of First Observation	106	97
Life Table Tests (d)		P=0.122
Incidental Tumor Tests (d)		P=0.598
Fisher Exact Test (d)		P=0.318N
Preputial Gland: Carcinoma or Squamous Cell Papilloma		
Overall Rates (a)	10/250 (4%)	4/175 (2%)
Adjusted Rates (b)	5.2%	8.2%
Terminal Rates (c)	8/188 (4%)	1/29 (3%)
Week of First Observation	106	97
Life Table Tests (d)		P=0.152
Incidental Tumor Tests (d)		P=0.631
Fisher Exact Test (d)		P=0.246N
Testis: Interstitial Cell Tumor		
Overall Rates (a)	240/250 (96%)	125/174 (72%)
Adjusted Rates (b)	99.2%	100.0%
Terminal Rates (c)	186/188 (99%)	29/29 (100%)
Week of First Observation	80	70
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.475
Fisher Exact Test (d)		P<0.001N
Zymbal Gland: Squamous Cell Papilloma		
Overall Rates (a)	2/250 (1%)	17/175 (10%)
Adjusted Rates (b)	1.0%	29.6%
Terminal Rates (c)	1/188 (1%)	4/29 (14%)
Week of First Observation	108	59
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Zymbal Gland: Carcinoma		
Overall Rates (a)	7/250 (3%)	35/175 (20%)
Adjusted Rates (b)	3.7%	42.0%
Terminal Rates (c)	6/188 (3%)	5/29 (17%)
Week of First Observation	113	57
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001

TABLE A3c. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
Zymbal Gland: Carcinoma or Squamous Cell Papilloma		
Overall Rates (a)	9/250 (4%)	52/175 (30%)
Adjusted Rates (b)	4.7%	60.6%
Terminal Rates (c)	7/188 (4%)	9/29 (31%)
Week of First Observation	108	57
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
All Sites: Mesothelioma		
Overall Rates (e)	10/250 (4%)	6/175 (3%)
Adjusted Rates (b)	5.2%	6.9%
Terminal Rates (c)	8/188 (4%)	0/29 (0%)
Week of First Observation	108	72
Life Table Tests (d)		P=0.054
Incidental Tumor Tests (d)		P=0.490N
Fisher Exact Test (d)		P=0.488N
All Sites: Benign Tumors		
Overall Rates (a)	244/250 (98%)	150/175 (86%)
Adjusted Rates (b)	100.0%	100%
Terminal Rates (c)	187/188 (99%)	29/29 (100%)
Week of First Observation	58	49
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.442
Fisher Exact Test (d)		P<0.001N
All Sites: Malignant Tumors		
Overall Rates (e)	201/250 (80%)	149/175 (85%)
Adjusted Rates (b)	96.0%	97.8%
Terminal Rates (c)	150/188 (80%)	26/29 (90%)
Week of First Observation	588	39
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.022
Fisher Exact Test (d)		P<0.128
All Sites: All Tumors		
Overall Rates (e)	249/250 (>99%)	173/175 (99%)
Adjusted Rates (b)	100.0%	100.0%
Terminal Rates (c)	188/188 (100%)	29/29 (100%)
Week of First Observation	58	39
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.774N
Fisher Exact Test (d)		P<0.369N

(a) Number of tumor-bearing animals/number of animals examined grossly at the site

(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality

(c) Observed tumor incidence in animals killed at the end of the study

(d) Beneath the 1% amosite + DMH group incidence are the P values corresponding to pairwise comparisons between that dosed group and the 1% amosite group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in a dosed group than in controls is indicated by (N).

(e) Number of tumor-bearing animals/number of animals examined microscopically at the site

TABLE A4a. INCIDENCE OF EPITHELIAL TUMORS OF THE LARGE INTESTINE IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Incidence	Diagnosis
SR Chrysotile	0/87 (0.0%)	
IR Chrysotile	0/85 (0.0%)	
Tremolite	1/118 (0.8%)	Adenomatous polyp, NOS
Crocidolite (a)	1/117 (0.8%)	Adenomatous polyp, NOS
Amosite	1/117 (0.8%)	Carcinoma, NOS
Amosite	0/117 (0.0%)	
TOTAL	2/524 (0.4%)	
SD (b)	0.47%	

(a) Both tumors occurred in the same animal

(b) Standard deviation

TABLE A4b. INCIDENCE OF EPITHELIAL TUMORS OF THE SMALL INTESTINE IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Incidence	Diagnosis
SR Chrysotile	1/88 (0.6%)	Mucinous cystadenocarcinoma
IR Chrysotile	0/85 (0.0%)	
Tremolite	0/118 (0.0%)	
Crocidolite	1/117 (0.9%)	Adenocarcinoma, NOS
Amosite	1/117 (0.9%)	Adenomatous polyp
Amosite	2/117 (1.7%)	Mucinous cystadenocarcinoma
TOTAL	5/524 (1.0%)	
SD (a)	1.05%	

(a) Standard deviation

TABLE A4c. INCIDENCE OF THYROID GLAND C-CELL TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Adenoma	Carcinoma	Adenoma or Carcinoma
SR Chrysotile	13/86 (15%)	11/86 (13%)	24/86 (28%)
IR Chrysotile	13/84 (15%)	19/84 (23%)	30/84 (36%)
Tremolite	11/117 (9%)	16/117 (14%)	27/117 (23%)
Crocidolite	13/116 (11%)	19/116 (16%)	32/116 (28%)
Amosite	16/117 (14%)	11/117 (9%)	27/117 (23%)
TOTAL	66/520 (12.7%)	76/520 (14.6%)	140/520 (26.9%)
SD (a)	2.61%	4.95%	5.17%

(a) Standard deviation

TABLE A4d. INCIDENCE OF LEUKEMIA IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Leukemia
SR Chrysotile	37/88 (42%)
IR Chrysotile	31/88 (35%)
Tremolite	43/118 (36%)
Crocidolite	43/118 (36%)
Amosite	38/117 (32%)
TOTAL	192/529 (36.3%)
SD (a)	3.48%

(a) Standard deviation

TABLE A4e. INCIDENCE OF ADRENAL MEDULLA TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Pheochromocytoma	Malignant Pheochromocytoma	Pheochromocytoma or Malignant Pheochromocytoma
SR Chrysotile	25/88 (28%)	1/88 (1%)	26/88 (30%)
IR Chrysotile	16/85 (19%)	1/85 (1%)	17/85 (20%)
Tremolite	38/118 (32%)	3/118 (3%)	41/118 (35%)
Crocidolite	33/117 (28%)	2/117 (2%)	35/117 (30%)
Amosite	39/117 (33%)	3/117 (3%)	39/117 (33%)
TOTAL	151/525 (28.8%)	10/525 (1.9%)	158/525 (30.1%)
SD (a)	5.71%	0.70%	5.76%

(a) Standard deviation

TABLE A4f. INCIDENCE OF THYROID GLAND FOLLICULAR CELL TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Adenoma	Carcinoma	Adenoma or Carcinoma
SR Chrysotile	4/86 (5%)	2/86 (2%)	6/86 (7%)
IR Chrysotile	1/84 (1%)	5/84 (6%)	6/84 (7%)
Tremolite	5/117 (4%)	6/117 (5%)	11/117 (9%)
Crocidolite	7/116 (6%)	3/116 (3%)	10/116 (9%)
Amosite	4/117 (3%)	7/117 (6%)	11/117 (9%)
TOTAL	21/520 (4.0%)	23/520 (4.4%)	44/520 (8.5%)
SD (a)	1.79%	1.81%	1.19%

(a) Standard deviation

TABLE A4g. INCIDENCE OF PREPUTIAL GLAND TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Adenoma	Carcinoma	Adenoma or Carcinoma
SR Chrysotile	0/88 (0%)	6/88 (7%)	6/88 (7%)
IR Chrysotile	1/88 (1%)	3/88 (3%)	4/88 (5%)
Tremolite	0/118 (0%)	7/118 (6%)	7/118 (6%)
Crocidolite	0/118 (0%)	3/118 (3%)	3/118 (3%)
Amosite	0/117 (0%)	6/117 (5%)	6/117 (5%)
TOTAL	1/529 (0.2%)	25/529 (4.7%)	26/529 (4.9%)
SD (a)	0.51%	1.77%	1.62%

(a) Standard deviation

TABLE A4h. INCIDENCE OF LIVER TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Neoplastic Nodule	Hepatocellular Carcinoma	Neoplastic Nodule or Hepatocellular Carcinoma
SR Chrysotile	12/88 (14%)	3/88 (3%)	15/88 (17%)
IR Chrysotile	6/85 (7%)	2/85 (2%)	8/85 (9%)
Tremolite	10/118 (8%)	6/118 (5%)	16/118 (14%)
Crocidolite	8/117 (7%)	4/117 (3%)	11/117 (9%)
Amosite	9/117 (8%)	1/117 (1%)	9/117 (8%)
TOTAL	45/525 (8.6%)	16/525 (3.0%)	59/525 (11.2%)
SD (a)	2.81%	1.56%	3.82%

(a) Standard deviation

TABLE A4i. INCIDENCE OF KIDNEY SARCOMAS AND MIXED TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

0/525

TABLE A4j. INCIDENCE OF ZYMBAL GLAND CARCINOMAS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Carcinomas
SR Chrysotile	4/88 (5%)
IR Chrysotile	2/88 (2%)
Tremolite	4/118 (3%)
Crocidolite	(a) 5/118 (4%)
Amosite	1/117 (1%)
TOTAL	16/529 (3.0%)
SD (b)	1.52%

(a) Includes a squamous cell carcinoma of the ear canal

(b) Standard deviation

TABLE A5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (a)

	Untreated Control	DMH	1% Amosite
Animals initially in study	117	125	250
Animals necropsied	117	125	250
Animals examined histopathologically	117	125	(249)
INTEGUMENTARY SYSTEM			
*Skin	(117)	(125)	(250)
Epidermal inclusion cyst	4 (3%)	6 (5%)	9 (4%)
Cystic ducts			1 (0%)
Effusion, serosanguineous			1 (0%)
Inflammation, acute focal	1 (1%)		
Abscess, NOS	1 (1%)		1 (0%)
Inflammation, chronic		1 (1%)	
Inflammation, chronic focal			2 (1%)
Fibrosis, focal			3 (1%)
Necrosis, focal			1 (0%)
Hyperplasia, NOS		1 (1%)	
Hyperkeratosis	5 (4%)	1 (1%)	8 (3%)
Acanthosis	5 (4%)		7 (3%)
*Subcut tissue	(117)	(125)	(250)
Abscess, NOS		1 (1%)	
Granuloma, NOS	1 (1%)		
Hyperkeratosis		1 (1%)	
RESPIRATORY SYSTEM			
#Trachea	(117)	(125)	(248)
Metaplasia, squamous			1 (0%)
#Lung/bronchus	(117)	(125)	(249)
Bronchiectasis	1 (1%)		2 (1%)
#Lung	(117)	(125)	(249)
Congestion, NOS	5 (4%)		6 (2%)
Edema, NOS	1 (1%)		
Hemorrhage	2 (2%)	2 (2%)	2 (1%)
Inflammation, interstitial	1 (1%)		1 (0%)
Pneumonia, aspiration			1 (0%)
Inflammation, acute focal			2 (1%)
Pneumonia, chronic murine		1 (1%)	
Inflammation, chronic	86 (74%)	108 (86%)	214 (86%)
Granuloma, NOS	3 (3%)	3 (2%)	5 (2%)
Pigmentation, NOS			5 (2%)
Hyperplasia, alveolar epithelium	3 (3%)	2 (2%)	9 (4%)
Metaplasia, osseous			1 (0%)
Histiocytosis			1 (0%)
#Lung/alveoli	(117)	(125)	(249)
Histiocytosis	2 (2%)		4 (2%)
HEMATOPOIETIC SYSTEM			
#Bone marrow	(117)	(110)	(249)
Congestion, NOS			1 (0%)
Hemorrhage			1 (0%)
Necrosis, focal			1 (0%)
Hypoplasia, NOS	1 (1%)		6 (2%)
Hyperplasia, NOS	2 (2%)	2 (2%)	7 (3%)
Myelofibrosis	1 (1%)		1 (0%)
#Spleen	(117)	(124)	(249)
Congestion, NOS			1 (0%)
Hemorrhage	1 (1%)	3 (2%)	3 (1%)
Fibrosis, focal	9 (8%)	1 (1%)	25 (10%)
Fibrosis, multifocal		1 (1%)	7 (3%)
Fibrosis, diffuse			1 (0%)

TABLE A5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
HEMATOPOIETIC SYSTEM			
Spleen (Continued)	(117)	(124)	(249)
Necrosis, NOS	1 (1%)	2 (2%)	
Necrosis, focal	1 (1%)	4 (3%)	4 (2%)
Amyloidosis			1 (0%)
Hemosiderosis	17 (15%)		45 (18%)
Hyperplasia, NOS	1 (1%)		
Hyperplasia, reticulum cell			2 (1%)
Hyperplasia, lymphoid	1 (1%)		
Hematopoiesis	22 (19%)	13 (10%)	26 (10%)
#Splenic capsule	(117)	(124)	(249)
Fibrosis, diffuse			1 (0%)
#Splenic follicles	(117)	(124)	(249)
Atrophy, NOS	3 (3%)	1 (1%)	6 (2%)
Atrophy, focal	1 (1%)		1 (0%)
#Mandibular l. node	(117)	(125)	(249)
Congestion, NOS	1 (1%)		
Hemorrhage	1 (1%)	1 (1%)	1 (0%)
Inflammation, acute	1 (1%)		
Pigmentation, NOS			1 (0%)
Hyperplasia, NOS	1 (1%)		
Angiectasis	1 (1%)		
Hyperplasia, lymphoid	18 (15%)	22 (18%)	21 (8%)
#Cervical lymph node	(117)	(125)	(249)
Congestion, NOS		1 (1%)	
Hemorrhage	1 (1%)		1 (0%)
Pigmentation, NOS			1 (0%)
#Mediastinal l. node	(117)	(125)	(249)
Congestion, NOS	2 (2%)	1 (1%)	
Hemorrhage	1 (1%)	5 (4%)	17 (7%)
Pigmentation, NOS	7 (6%)	3 (2%)	27 (11%)
Atrophy, NOS			1 (0%)
Erythrophagocytosis	3 (3%)		4 (2%)
Hyperplasia, reticulum cell	1 (1%)		1 (0%)
Hyperplasia, lymphoid		1 (1%)	4 (2%)
#Pancreatic lymph node	(117)	(125)	(249)
Hemorrhage			1 (0%)
Pigmentation, NOS	4 (3%)	1 (1%)	21 (8%)
Hyperplasia, reticulum cell	7 (6%)	5 (4%)	4 (2%)
Hyperplasia, lymphoid			1 (0%)
#Mesenteric lymph node	(117)	(125)	(249)
Hemorrhage	1 (1%)		4 (2%)
Pigmentation, NOS	3 (3%)		4 (2%)
Atrophy, NOS		1 (1%)	
Erythrophagocytosis	1 (1%)		2 (1%)
Hyperplasia, reticulum cell	43 (37%)	23 (18%)	67 (27%)
Hyperplasia, lymphoid	3 (3%)	3 (2%)	7 (3%)
#Ileocolic lymph node	(117)	(125)	(249)
Atrophy, NOS	1 (1%)		
Hyperplasia, reticulum cell		1 (1%)	1 (0%)
Hyperplasia, lymphoid	2 (2%)	2 (2%)	1 (0%)
#Renal lymph node	(117)	(125)	(249)
Pigmentation, NOS	2 (2%)	1 (1%)	1 (0%)
Hyperplasia, reticulum cell	1 (1%)		
#Iliac lymph node	(117)	(125)	(249)
Hyperplasia, lymphoid	1 (1%)		
#Inguinal lymph node	(117)	(125)	(249)
Hyperplasia, lymphoid			1 (0%)
#Liver	(117)	(125)	(249)
Leukocytosis, NOS	1 (1%)		7 (3%)
#Pancreas	(116)	(125)	(247)
Hyperplasia, reticulum cell		1 (1%)	

TABLE A5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
HEMATOPOIETIC SYSTEM (Continued)			
#Peyer's patch	(117)	(125)	(250)
Hyperplasia, lymphoid		1 (1%)	
#Thymus	(80)	(83)	(171)
Cyst, NOS			2 (1%)
Congestion, NOS		2 (2%)	
Hemorrhage		3 (4%)	
CIRCULATORY SYSTEM			
*Multiple organs	(117)	(125)	(250)
Lymphangiectasis	1 (1%)		
*Mediastinum	(117)	(125)	(250)
Periarteritis			1 (0%)
#Mandibular l. node	(117)	(125)	(249)
Lymphangiectasis	3 (3%)	12 (10%)	8 (3%)
#Mediastinal l. node	(117)	(125)	(249)
Lymphangiectasis			2 (1%)
#Pancreatic lymph node	(117)	(125)	(249)
Lymphangiectasis			2 (1%)
#Mesenteric lymph node	(117)	(125)	(249)
Lymphangiectasis	3 (3%)	2 (2%)	13 (5%)
#Ileocolic lymph node	(117)	(125)	(249)
Lymphangiectasis	7 (6%)	5 (4%)	12 (5%)
#Renal lymph node	(117)	(125)	(249)
Lymphangiectasis	1 (1%)		
#Iliac lymph node	(117)	(125)	(249)
Lymphangiectasis	1 (1%)		1 (0%)
#Lung	(117)	(125)	(249)
Thrombosis, NOS		3 (2%)	1 (0%)
#Heart	(117)	(125)	(249)
Thrombosis, NOS			1 (0%)
Inflammation, chronic focal	2 (2%)		
#Heart/atrium	(117)	(125)	(249)
Thrombosis, NOS	4 (3%)		3 (1%)
#Myocardium	(117)	(125)	(249)
Mineralization	2 (2%)	1 (1%)	2 (1%)
Inflammation, chronic		1 (1%)	
Inflammation, chronic focal	47 (40%)	42 (34%)	117 (47%)
Inflammation, chronic diffuse	35 (30%)	18 (14%)	67 (27%)
Fibrosis, focal	2 (2%)		3 (1%)
Fibrosis, multifocal	1 (1%)	3 (2%)	
Degeneration, NOS	3 (3%)	3 (2%)	2 (1%)
#Endocardium	(117)	(125)	(249)
Inflammation, chronic		1 (1%)	
#Cardiac valve	(117)	(125)	(249)
Inflammation, chronic	1 (1%)	1 (1%)	1 (0%)
Inflammation, chronic focal	1 (1%)	1 (1%)	
*Aorta	(117)	(125)	(250)
Mineralization	5 (4%)		1 (0%)
*Abdominal aorta	(117)	(125)	(250)
Mineralization	1 (1%)		1 (0%)
*Coronary artery	(117)	(125)	(250)
Calcification, focal			1 (0%)
*Pancreatic artery	(117)	(125)	(250)
Thrombosis, NOS	1 (1%)		
Periarteritis	1 (1%)		1 (0%)
*Mesenteric artery	(117)	(125)	(250)
Inflammation, chronic			1 (0%)
Periarteritis			1 (0%)
#Liver	(117)	(125)	(249)
Thrombosis, NOS	1 (1%)		1 (0%)

TABLE A5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
CIRCULATORY SYSTEM (Continued)			
#Pancreas	(116)	(125)	(247)
Periarteritis	2 (2%)		3 (1%)
*Mesentery	(117)	(125)	(250)
Periarteritis	2 (2%)		2 (1%)
#Prostate	(117)	(123)	(249)
Periarteritis			1 (0%)
#Testis	(117)	(123)	(249)
Periarteritis	4 (3%)		4 (2%)
#Adrenal	(117)	(125)	(249)
Thrombosis, NOS	1 (1%)		
DIGESTIVE SYSTEM			
*Oral mucous membrane	(117)	(125)	(250)
Fibrous osteodystrophy	1 (1%)		
Hyperkeratosis	1 (1%)		
Acanthosis	1 (1%)		
*Hard palate	(117)	(125)	(250)
Acanthosis			1 (0%)
#Salivary gland	(117)	(124)	(245)
Inflammation, acute diffuse	1 (1%)		
Abscess, NOS		1 (1%)	
Granuloma, NOS	1 (1%)		
Atrophy, focal			1 (0%)
#Parotid gland	(117)	(124)	(245)
Atrophy, focal			1 (0%)
#Submaxillary gland	(117)	(124)	(245)
Inflammation, chronic diffuse			1 (0%)
#Liver	(117)	(125)	(249)
Congestion, NOS			2 (1%)
Hemorrhage		1 (1%)	4 (2%)
Inflammation, acute focal			1 (0%)
Abscess, NOS		1 (1%)	
Inflammation, chronic			1 (0%)
Granuloma, NOS	9 (8%)	6 (5%)	11 (4%)
Hepatitis, toxic	15 (13%)	13 (10%)	41 (16%)
Degeneration, NOS	15 (13%)	9 (7%)	26 (10%)
Necrosis, NOS		4 (3%)	
Necrosis, focal	10 (9%)	22 (18%)	27 (11%)
Metamorphosis fatty	26 (22%)	36 (29%)	30 (12%)
Pigmentation, NOS	14 (12%)	3 (2%)	45 (18%)
Focal cellular change	44 (38%)	53 (42%)	67 (27%)
Angiectasis	4 (3%)	6 (5%)	2 (1%)
#Hepatic capsule	(117)	(125)	(249)
Granuloma, foreign body			1 (0%)
#Bile duct	(117)	(125)	(249)
Dilatation, NOS			3 (1%)
Cyst, NOS	1 (1%)		
Inflammation, chronic	24 (21%)	31 (25%)	32 (13%)
Fibrosis	17 (15%)	4 (3%)	1 (0%)
Hyperplasia, NOS	52 (44%)	63 (50%)	70 (28%)
Hyperplasia, focal	1 (1%)		
#Pancreas	(116)	(125)	(247)
Ectopia	5 (4%)	2 (2%)	12 (5%)
Inflammation, chronic focal			3 (1%)
Inflammation, chronic diffuse	1 (1%)		
Atrophy, NOS	1 (1%)	1 (1%)	
Atrophy, focal	10 (9%)	8 (6%)	48 (19%)
Atrophy, diffuse	6 (5%)	3 (2%)	5 (2%)
#Pancreatic acinus	(116)	(125)	(247)
Hyperplasia, focal	3 (3%)		13 (5%)

TABLE A5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
DIGESTIVE SYSTEM (Continued)			
#Esophagus	(115)	(124)	(248)
Inflammation, acute	1 (1%)		
Inflammation, chronic		1 (1%)	
Necrosis, diffuse	1 (1%)		
Hyperplasia, NOS		1 (1%)	
Hyperkeratosis	12 (10%)	11 (9%)	4 (2%)
Acanthosis		2 (2%)	
#Stomach	(117)	(125)	(249)
Mineralization	9 (8%)		2 (1%)
Edema, NOS	2 (2%)	1 (1%)	4 (2%)
Hemorrhage	3 (3%)		2 (1%)
Inflammation, acute focal			5 (2%)
Inflammation, chronic	6 (5%)	2 (2%)	4 (2%)
Inflammation, chronic focal	9 (8%)	5 (4%)	15 (6%)
Inflammation, chronic diffuse	5 (4%)	3 (2%)	38 (15%)
Granuloma, foreign body			1 (0%)
Ulcer, perforated	13 (11%)		25 (10%)
Fibrosis, diffuse			2 (1%)
Degeneration, NOS			1 (0%)
Necrosis, NOS	1 (1%)		
Necrosis, focal	22 (19%)	6 (5%)	41 (16%)
Hyperplasia, epithelial			1 (0%)
Hyperplasia, focal		1 (1%)	
Hyperkeratosis	22 (19%)	16 (13%)	41 (16%)
Acanthosis	31 (26%)	20 (16%)	62 (25%)
#Gastric mucosa	(117)	(125)	(249)
Hyperplasia, focal			1 (0%)
#Gastric submucosa	(117)	(125)	(249)
Edema, NOS		1 (1%)	3 (1%)
#Gastric muscularis	(117)	(125)	(249)
Degeneration, NOS	8 (7%)		3 (1%)
#Gastric fundus	(117)	(125)	(249)
Mineralization	1 (1%)		
Hyperplasia, epithelial	1 (1%)		
Hyperplasia, diffuse	6 (5%)		
#Small intestine	(117)	(125)	(249)
Parasitism			1 (0%)
#Duodenum	(117)	(125)	(249)
Hemorrhage	1 (1%)		
Inflammation, acute		1 (1%)	
Inflammation, acute focal	1 (1%)		
Inflammation, chronic focal			1 (0%)
Ulcer, perforated			1 (0%)
Necrosis, NOS		1 (1%)	
Necrosis, focal	1 (1%)		3 (1%)
Hyperplasia, cystic		1 (1%)	
Metaplasia, osseous		1 (1%)	
#Jejunum	(117)	(125)	(249)
Necrosis, NOS		1 (1%)	
#Ileum	(117)	(125)	(249)
Diverticulum			1 (0%)
Abscess, NOS			1 (0%)
Inflammation, acute/chronic		1 (1%)	
Necrosis, NOS		1 (1%)	
Necrosis, focal		1 (1%)	
Metaplasia, osseous			1 (0%)
#Ileal mucosa	(117)	(125)	(249)
Hyperplasia, focal	1 (1%)		
#Large intestine	(117)	(125)	(249)
Inflammation, acute		1 (1%)	1 (0%)
Parasitism			2 (1%)

TABLE A5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
DIGESTIVE SYSTEM (Continued)			
#Colon	(117)	(125)	(249)
Inflammation, acute focal	2 (2%)		1 (0%)
Inflammation, acute diffuse			1 (0%)
Inflammation, chronic focal		1 (1%)	1 (0%)
Inflammation, chronic diffuse		1 (1%)	
Parasitism	4 (3%)	6 (5%)	17 (7%)
Necrosis, focal	1 (1%)		2 (1%)
Hyperplasia, epithelial			1 (0%)
Hyperplasia, focal		2 (2%)	
Hyperplasia, papillary	1 (1%)		
#Colonic mucosa	(117)	(125)	(250)
Hyperplasia, focal		1 (1%)	
#Colonic submucosa	(117)	(125)	(250)
Granuloma, NOS		1 (1%)	
#Colonic muscularis p	(117)	(125)	(249)
Degeneration, NOS	2 (2%)		
#Cecum	(117)	(125)	(249)
Edema, NOS			1 (0%)
Hemorrhage			2 (1%)
Inflammation, acute		1 (1%)	
Inflammation, acute focal	1 (1%)	1 (1%)	1 (0%)
Inflammation, chronic focal	1 (1%)	1 (1%)	
Inflammation, chronic diffuse	1 (1%)	1 (1%)	1 (0%)
Fibrosis, diffuse		1 (1%)	
Parasitism		1 (1%)	2 (1%)
Necrosis, focal	3 (3%)	5 (4%)	2 (1%)
Necrosis, diffuse			1 (0%)
Hyperplasia, focal		3 (2%)	
#Ascending colon	(117)	(125)	(250)
Parasitism		2 (2%)	
#Transverse colon	(117)	(125)	(250)
Cyst, NOS		1 (1%)	
#Descending colon	(117)	(125)	(249)
Parasitism		4 (3%)	
Hyperplasia, epithelial			1 (0%)
*Rectum	(117)	(125)	(250)
Granuloma, pyogenic	1 (1%)		
Parasitism			1 (0%)
*Anus	(117)	(125)	(250)
Acanthosis			1 (0%)
*Intramuscular anal gland	(117)	(125)	(250)
Cystic ducts			1 (0%)
*Perianal tissue	(117)	(125)	(250)
Inflammation, chronic			1 (0%)
URINARY SYSTEM			
#Kidney	(117)	(125)	(248)
Hamartoma			1 (0%)
Mineralization			2 (1%)
Hydronephrosis	1 (1%)		1 (0%)
Inflammation, chronic	101 (86%)	95 (76%)	238 (96%)
Inflammation, chronic focal		2 (2%)	
Fibrosis, diffuse			1 (0%)
Infarct, NOS			1 (0%)
Metamorphosis fatty			2 (1%)
Pigmentation, NOS		1 (1%)	1 (0%)
Hyperplasia, tubular cell		1 (1%)	1 (0%)
#Kidney/cortex	(117)	(125)	(248)
Cyst, NOS	14 (12%)	1 (1%)	16 (6%)

TABLE A5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
URINARY SYSTEM (Continued)			
#Kidney/medulla	(117)	(125)	(248)
Inflammation, acute focal			1 (0%)
Necrosis, focal			1 (0%)
#Kidney/tubule	(117)	(125)	(248)
Cyst, NOS			2 (1%)
Necrosis, focal		1 (1%)	
Pigmentation, NOS	27 (23%)	17 (14%)	86 (35%)
Hyperplasia, focal			1 (0%)
#Urinary bladder	(116)	(124)	(249)
Hemorrhage	1 (1%)		5 (2%)
Inflammation, acute focal			1 (0%)
Inflammation, acute diffuse			4 (2%)
Inflammation, chronic focal			3 (1%)
Inflammation, chronic diffuse	2 (2%)		5 (2%)
Hyperplasia, epithelial	1 (1%)		4 (2%)
Hyperplasia, diffuse	1 (1%)		4 (2%)
Hyperplasia, papillary			1 (0%)
*Urethra	(117)	(125)	(250)
Metaplasia, squamous	1 (1%)		
*Urethral gland	(117)	(125)	(250)
Hyperplasia, NOS	1 (1%)		
ENDOCRINE SYSTEM			
#Pituitary	(117)	(122)	(248)
Embryonal rest	1 (1%)		
Cyst, NOS	2 (2%)	2 (2%)	3 (1%)
Hemorrhage	1 (1%)		1 (0%)
Hemorrhagic cyst	2 (2%)		
Abscess, NOS			1 (0%)
Necrosis, focal			1 (0%)
Hyperplasia, focal	2 (2%)	1 (1%)	6 (2%)
Angiectasis	7 (6%)	2 (2%)	11 (4%)
#Adrenal	(117)	(125)	(249)
Mineralization	1 (1%)		
Congestion, NOS			3 (1%)
Hemorrhage	1 (1%)		
Necrosis, focal	1 (1%)		1 (0%)
Metamorphosis fatty	1 (1%)	1 (1%)	1 (0%)
Hyperplasia, focal	1 (1%)		
Angiectasis	1 (1%)		1 (0%)
#Adrenal cortex	(117)	(125)	(249)
Congestion, NOS		1 (1%)	
Degeneration, NOS	1 (1%)		
Necrosis, NOS		1 (1%)	
Necrosis, diffuse	2 (2%)		
Metamorphosis fatty	43 (37%)	21 (17%)	61 (24%)
Hyperplasia, focal	2 (2%)	2 (2%)	15 (6%)
Angiectasis	3 (3%)	4 (3%)	2 (1%)
#Adrenal medulla	(117)	(125)	(249)
Hyperplasia, focal	43 (37%)	23 (18%)	92 (37%)
#Thyroid	(117)	(124)	(246)
Cystic follicles	1 (1%)		2 (1%)
Follicular cyst, NOS	4 (3%)	5 (4%)	16 (7%)
Pigmentation, NOS			1 (0%)
Hyperplasia, C-cell	21 (18%)	15 (12%)	58 (24%)
Hyperplasia, follicular cell			1 (0%)
#Parathyroid	(110)	(119)	(234)
Hyperplasia, NOS	36 (33%)	7 (6%)	28 (12%)

TABLE A5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
ENDOCRINE SYSTEM (Continued)			
#Pancreatic islets	(116)	(125)	(247)
Hyperplasia, focal	5 (4%)		5 (2%)
REPRODUCTIVE SYSTEM			
*Mammary gland	(117)	(125)	(250)
Galactocele	3 (3%)	1 (1%)	1 (0%)
Cystic ducts	9 (8%)	2 (2%)	8 (3%)
Hyperplasia, NOS	2 (2%)	1 (1%)	6 (2%)
Hyperplasia, diffuse	6 (5%)		12 (5%)
*Prepuce	(117)	(125)	(250)
Hyperkeratosis	1 (1%)		
*Preputial gland	(117)	(125)	(250)
Cystic ducts	3 (3%)	1 (1%)	10 (4%)
Inflammation, acute			1 (0%)
Abscess, NOS	1 (1%)		1 (0%)
Inflammation, chronic			1 (0%)
Atrophy, NOS			1 (0%)
Hyperplasia, NOS		1 (1%)	3 (1%)
Hyperplasia, focal	1 (1%)		
Hyperplasia, diffuse	1 (1%)		
Hyperkeratosis			4 (2%)
#Prostate	(117)	(123)	(249)
Cyst, NOS			1 (0%)
Hemorrhage			1 (0%)
Inflammation, acute focal		1 (1%)	3 (1%)
Inflammation, acute diffuse			6 (2%)
Abscess, NOS	6 (5%)		21 (8%)
Inflammation, acute/chronic			5 (2%)
Inflammation, chronic			3 (1%)
Inflammation, chronic focal	29 (25%)	20 (16%)	73 (29%)
Inflammation, chronic diffuse	12 (10%)		11 (4%)
Hyperplasia, focal	5 (4%)	3 (2%)	13 (5%)
#Prostatic gland	(117)	(123)	(249)
Cyst, NOS	1 (1%)		
*Seminal vesicle	(117)	(125)	(250)
Cyst, NOS	5 (4%)	2 (2%)	12 (5%)
Cystic ducts			2 (1%)
Edema, NOS			1 (0%)
Inflammation, acute diffuse			2 (1%)
Abscess, NOS			2 (1%)
Inflammation, chronic focal			1 (0%)
Inflammation, chronic diffuse			1 (0%)
Hyperplasia, epithelial			1 (0%)
Hyperplasia, focal		1 (1%)	2 (1%)
Hyperplasia, diffuse			6 (2%)
*Coagulating gland	(117)	(125)	(250)
Cyst, NOS	1 (1%)		
Cystic ducts			1 (0%)
#Testis	(117)	(123)	(249)
Hemorrhage		1 (1%)	1 (0%)
Degeneration, NOS	12 (10%)	16 (13%)	22 (9%)
Hyperplasia, interstitial cell	46 (39%)	68 (55%)	97 (39%)
*Epididymis	(117)	(125)	(250)
Inflammation, chronic			1 (0%)
Inflammation, chronic diffuse	1 (1%)		
Granuloma, spermatic		1 (1%)	2 (1%)
Fibrosis, focal			1 (0%)
Fibrosis, diffuse	1 (1%)		
Necrosis, fat	5 (4%)	2 (2%)	10 (4%)

TABLE A5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
NERVOUS SYSTEM			
#Brain/meninges	(117)	(125)	(250)
Inflammation, acute		1 (1%)	
#Lateral ventricle	(117)	(125)	(249)
Dilatation, NOS			1 (0%)
#Cerebrum	(117)	(125)	(249)
Gliosis		1 (1%)	
Necrosis, focal			1 (0%)
Angiectasis			1 (0%)
#Brain	(117)	(125)	(249)
Hemorrhage	1 (1%)		
#Cerebellum	(117)	(125)	(249)
Hemorrhage			1 (0%)
Abscess, NOS		1 (1%)	
#Medulla oblongata	(117)	(125)	(249)
Necrosis, focal			1 (0%)
*Spinal cord	(117)	(125)	(250)
Malacia			1 (0%)
SPECIAL SENSE ORGANS			
*Eye	(117)	(125)	(250)
Hemorrhage	6 (5%)		10 (4%)
Synechia, posterior	5 (4%)		7 (3%)
Cataract	25 (21%)		36 (14%)
Phthisis bulbi	2 (2%)		2 (1%)
*Eye anterior chamber	(117)	(125)	(250)
Empyema	1 (1%)		1 (0%)
*Vitreous body	(117)	(125)	(250)
Vascularization	1 (1%)		4 (2%)
*Eye/cornea	(117)	(125)	(250)
Mineralization	2 (2%)		
Inflammation, acute focal		1 (1%)	
Inflammation, chronic focal	9 (8%)		5 (2%)
Inflammation, chronic diffuse	2 (2%)		1 (0%)
Necrosis, focal	4 (3%)	1 (1%)	
*Eye/iris	(117)	(125)	(250)
Hemorrhage	1 (1%)		
*Eye/retina	(117)	(125)	(250)
Degeneration, NOS	42 (36%)	5 (4%)	76 (30%)
*Eye/crystalline lens	(117)	(125)	(250)
Rupture	1 (1%)		5 (2%)
*Ear canal	(117)	(125)	(250)
Hemorrhage		1 (1%)	
*Zymbal gland	(117)	(125)	(250)
Cystic ducts	34 (29%)	8 (6%)	42 (17%)
Inflammation, acute		1 (1%)	
Abscess, NOS		1 (1%)	2 (1%)
Inflammation, chronic focal	1 (1%)		
Hyperplasia, NOS		1 (1%)	1 (0%)
Hyperplasia, focal			1 (0%)
Hyperkeratosis		2 (2%)	1 (0%)
Acanthosis			1 (0%)

TABLE A5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
MUSCULOSKELETAL SYSTEM			
*Bone	(117)	(125)	(250)
Fibrous osteodystrophy	1 (1%)		
*Skull	(117)	(125)	(250)
Osteopetrosis	4 (3%)		2 (1%)
Fibrous osteodystrophy	3 (3%)		
*Maxilla	(117)	(125)	(250)
Osteopetrosis	1 (1%)		
Fibrous osteodystrophy	1 (1%)		
*Sternum	(117)	(125)	(250)
Osteopetrosis	1 (1%)		
Fibrous osteodystrophy	3 (3%)		
BODY CAVITIES			
*Mediastinum	(117)	(125)	(250)
Ectopia	1 (1%)		
*Abdominal cavity	(117)	(125)	(250)
Hemorrhage			1 (0%)
Steatitis	1 (1%)	1 (1%)	
Necrosis, fat	6 (5%)		5 (2%)
*Peritoneum	(117)	(125)	(250)
Inflammation, acute		1 (1%)	
*Pericardium	(117)	(125)	(250)
Pigmentation, NOS	1 (1%)		
*Mesentery	(117)	(125)	(250)
Inflammation, chronic			1 (0%)
Inflammation, chronic focal	2 (2%)	1 (1%)	7 (3%)
Granuloma, NOS			1 (0%)
Necrosis, fat			1 (0%)
ALL OTHER SYSTEMS			
*Multiple organs	(117)	(125)	(250)
Mineralization	3 (3%)		1 (0%)
Inflammation, chronic	15 (13%)	3 (2%)	8 (3%)
Inflammation, chronic focal	1 (1%)	1 (1%)	
Degeneration, NOS	1 (1%)		
Pigmentation, NOS			1 (0%)
Hyperplasia, NOS	1 (1%)		
Diaphragm			
Hernia, NOS	1		4
Adipose tissue			
Hemorrhage	1		
Mesentery of colon			
Hemorrhage	1		
Inflammation, chronic diffuse	1		
SPECIAL MORPHOLOGY SUMMARY			
Auto/necropsy/histo perf			1

(a) DMH indicates a group receiving five doses of 7.5 mg/kg 1,2-dimethylhydrazine dihydrochloride by gavage in pH 5 acetate buffer

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

Number of animals examined microscopically at this site

TABLE A5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (a)

	1% Amosite + PW	1% Amosite + DMH
Animals initially in study	100	175
Animals necropsied	100	175
Animals examined histopathologically	100	174
INTEGUMENTARY SYSTEM		
*Skin	(100)	(175)
Epidermal inclusion cyst	6 (6%)	13 (7%)
Abscess, NOS	1 (1%)	2 (1%)
Inflammation, chronic focal		1 (1%)
Hyperkeratosis	2 (2%)	3 (2%)
Acanthosis	3 (3%)	3 (2%)
*Subcut tissue	(100)	(175)
Hemorrhagic cyst		1 (1%)
Abscess, NOS	1 (1%)	4 (2%)
Granuloma, NOS	1 (1%)	
RESPIRATORY SYSTEM		
*Nasal cavity	(100)	(175)
Inflammation, chronic		1 (1%)
*Nasal turbinate	(100)	(175)
Inflammation, chronic		1 (1%)
#Lung/bronchus	(100)	(173)
Bronchiectasis	1 (1%)	
#Lung	(100)	(173)
Congestion, NOS	4 (4%)	
Edema, NOS	1 (1%)	
Hemorrhage	2 (2%)	1 (1%)
Pneumonia, aspiration	2 (2%)	
Inflammation, acute focal	1 (1%)	2 (1%)
Abscess, NOS	1 (1%)	
Inflammation, chronic	94 (94%)	150 (86%)
Granuloma, NOS	5 (5%)	
Granuloma, foreign body	1 (1%)	
Necrosis, focal	1 (1%)	1 (1%)
Pigmentation, NOS	1 (1%)	
Hyperplasia, alveolar epithelium	2 (2%)	2 (1%)
Metaplasia, osseous		1 (1%)
#Lung/alveoli	(100)	(173)
Histiocytosis	1 (1%)	
HEMATOPOIETIC SYSTEM		
#Bone marrow	(100)	(171)
Hyperplasia, NOS	5 (5%)	2 (1%)
#Spleen	(100)	(172)
Congestion, NOS	1 (1%)	
Hemorrhage		1 (1%)
Inflammation, chronic	1 (1%)	
Inflammation, chronic focal		1 (1%)
Fibrosis, focal	10 (10%)	4 (2%)
Fibrosis, diffuse		1 (1%)
Necrosis, NOS	1 (1%)	1 (1%)
Necrosis, focal		2 (1%)
Hemosiderosis	8 (8%)	1 (1%)
Metaplasia, osseous	1 (1%)	
Hematopoiesis	11 (11%)	20 (11%)
#Splenic follicles	(100)	(172)
Atrophy, NOS	1 (1%)	1 (1%)

TABLE A5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
HEMATOPOIETIC SYSTEM (Continued)		
#Mandibular l. node	(100)	(173)
Congestion, NOS	1 (1%)	
Hemorrhage		1 (1%)
Inflammation, chronic		1 (1%)
Hyperplasia, lymphoid	22 (22%)	33 (19%)
#Cervical lymph node	(100)	(173)
Necrosis, focal		1 (1%)
Hyperplasia, lymphoid		3 (2%)
#Mediastinal l. node	(100)	(173)
Hemorrhage	9 (9%)	3 (2%)
Pigmentation, NOS	22 (22%)	6 (3%)
Erythrophagocytosis	2 (2%)	
Hyperplasia, lymphoid	1 (1%)	6 (3%)
#Celiac lymph node	(100)	(173)
Hyperplasia, lymphoid		1 (1%)
#Hepatic lymph node	(100)	(173)
Hemorrhage		1 (1%)
Hyperplasia, lymphoid		1 (1%)
#Pancreatic lymph node	(100)	(173)
Necrosis, focal		1 (1%)
Pigmentation, NOS	4 (4%)	3 (2%)
Hyperplasia, reticulum cell		4 (2%)
Hyperplasia, lymphoid	2 (2%)	3 (2%)
#Mesenteric lymph node	(100)	(173)
Hemorrhage	2 (2%)	2 (1%)
Pigmentation, NOS	2 (2%)	2 (1%)
Atrophy, NOS		1 (1%)
Hyperplasia, reticulum cell	26 (26%)	14 (8%)
Hyperplasia, lymphoid	3 (3%)	4 (2%)
#Ileocolic lymph node	(100)	(173)
Hyperplasia, lymphoid		2 (1%)
#Renal lymph node	(100)	(173)
Pigmentation, NOS		2 (1%)
Hyperplasia, reticulum cell		1 (1%)
#Liver	(100)	(173)
Leukocytosis, NOS	3 (3%)	1 (1%)
#Peyer's patch	(100)	(173)
Hyperplasia, lymphoid		1 (1%)
#Ascending colon	(100)	(173)
Hyperplasia, lymphoid		1 (1%)
#Thymus	(78)	(134)
Cyst, NOS	2 (3%)	
Congestion, NOS	1 (1%)	
CIRCULATORY SYSTEM		
#Spleen	(100)	(172)
Thrombosis, NOS		1 (1%)
#Mandibular l. node	(100)	(173)
Lymphangiectasis	5 (5%)	4 (2%)
#Mediastinal l. node	(100)	(173)
Lymphangiectasis	1 (1%)	4 (2%)
#Celiac lymph node	(100)	(173)
Lymphangiectasis		1 (1%)
#Pancreatic lymph node	(100)	(173)
Lymphangiectasis		1 (1%)
#Mesenteric lymph node	(100)	(173)
Lymphangiectasis	1 (1%)	4 (2%)
#Ileocolic lymph node	(100)	(173)
Lymphangiectasis	3 (3%)	4 (2%)

TABLE A5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
CIRCULATORY SYSTEM (Continued)		
#Heart	(100)	(172)
Inflammation, chronic focal	1 (1%)	1 (1%)
#Heart/atrium	(100)	(172)
Thrombosis, NOS	2 (2%)	
#Myocardium	(100)	(172)
Mineralization	2 (2%)	
Inflammation, chronic		4 (2%)
Inflammation, chronic focal	60 (60%)	61 (35%)
Inflammation, chronic diffuse	22 (22%)	21 (12%)
Fibrosis, focal	1 (1%)	3 (2%)
Fibrosis, multifocal		2 (1%)
Fibrosis, diffuse	2 (2%)	
Degeneration, NOS		5 (3%)
#Cardiac valve	(100)	(172)
Inflammation, chronic focal		4 (2%)
*Aorta	(100)	(175)
Mineralization	1 (1%)	
*Mesenteric artery	(100)	(175)
Inflammation, chronic	1 (1%)	
Periarteritis	1 (1%)	
#Liver	(100)	(173)
Thrombosis, NOS	1 (1%)	1 (1%)
#Pancreas	(100)	(173)
Periarteritis	1 (1%)	2 (1%)
#Testis	(100)	(172)
Periarteritis	1 (1%)	2 (1%)
#Adrenal	(100)	(173)
Thrombosis, NOS	1 (1%)	
DIGESTIVE SYSTEM		
#Salivary gland	(100)	(171)
Cystic ducts	1 (1%)	
Abscess, NOS		1 (1%)
Inflammation, chronic	1 (1%)	1 (1%)
Atrophy, NOS		1 (1%)
Metaplasia, squamous		1 (1%)
#Liver	(100)	(173)
Cyst, NOS		1 (1%)
Congestion, NOS	1 (1%)	
Hemorrhage	1 (1%)	3 (2%)
Abscess, NOS		1 (1%)
Granuloma, NOS	5 (5%)	12 (7%)
Fibrosis, focal		1 (1%)
Adhesion, NOS	1 (1%)	
Hepatitis, toxic	15 (15%)	14 (8%)
Degeneration, NOS	5 (5%)	16 (9%)
Degeneration, cystic		5 (3%)
Necrosis, NOS		1 (1%)
Necrosis, focal	11 (11%)	28 (16%)
Metamorphosis fatty	4 (4%)	32 (18%)
Pigmentation, NOS	13 (13%)	6 (3%)
Focal cellular change	25 (25%)	67 (38%)
Hepatocytomegaly		1 (1%)
Angiectasis	3 (3%)	6 (3%)
#Bile duct	(100)	(173)
Cyst, NOS		1 (1%)
Multilocular cyst		1 (1%)
Inflammation, chronic	22 (22%)	24 (14%)
Fibrosis	3 (3%)	3 (2%)
Hyperplasia, NOS	41 (41%)	51 (29%)

TABLE A5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
DIGESTIVE SYSTEM (Continued)		
#Pancreas	(100)	(173)
Ectopia	5 (5%)	3 (2%)
Abscess, NOS	1 (1%)	
Inflammation, chronic focal	1 (1%)	2 (1%)
Inflammation, chronic diffuse	1 (1%)	
Atrophy, focal	15 (15%)	14 (8%)
Atrophy, diffuse	1 (1%)	2 (1%)
Hyperplasia, focal		1 (1%)
#Pancreatic acinus	(100)	(173)
Hyperplasia, focal	1 (1%)	
*Pharynx	(100)	(175)
Abscess, NOS		1 (1%)
#Esophagus	(100)	(173)
Hyperkeratosis	12 (12%)	9 (5%)
#Stomach	(100)	(173)
Mineralization	1 (1%)	
Cyst, NOS	1 (1%)	1 (1%)
Edema, NOS		2 (1%)
Abscess, NOS		1 (1%)
Inflammation, chronic	2 (2%)	4 (2%)
Inflammation, chronic focal	4 (4%)	1 (1%)
Inflammation, chronic diffuse	11 (11%)	3 (2%)
Ulcer, perforated	7 (7%)	1 (1%)
Parasitism	1 (1%)	
Necrosis, NOS		1 (1%)
Necrosis, focal	15 (15%)	8 (5%)
Hyperkeratosis	16 (16%)	13 (7%)
Acanthosis	21 (21%)	20 (11%)
#Gastric mucosa	(100)	(173)
Cyst, NOS		1 (1%)
Edema, NOS	1 (1%)	
#Duodenum	(100)	(173)
Inflammation, chronic focal	1 (1%)	1 (1%)
Hyperplasia, epithelial	1 (1%)	
Metaplasia, osseous	1 (1%)	
#Duodenal mucosa	(100)	(173)
Hyperplasia, diffuse	1 (1%)	
#Jejunum	(100)	(173)
Inflammation, chronic focal	1 (1%)	
#Ileum	(100)	(173)
Necrosis, focal		1 (1%)
#Colon	(100)	(173)
Mineralization	1 (1%)	
Inflammation, acute diffuse	1 (1%)	
Inflammation, chronic diffuse	1 (1%)	1 (1%)
Parasitism	4 (4%)	5 (3%)
Necrosis, focal	2 (2%)	1 (1%)
Necrosis, diffuse		1 (1%)
Hyperplasia, epithelial		1 (1%)
#Cecum	(100)	(173)
Edema, NOS	1 (1%)	
Hemorrhage	2 (2%)	2 (1%)
Inflammation, acute focal	1 (1%)	
Inflammation, chronic focal	2 (2%)	1 (1%)
Inflammation, chronic diffuse	1 (1%)	
Parasitism	1 (1%)	2 (1%)
Necrosis, focal	3 (3%)	2 (1%)
Hyperplasia, focal	1 (1%)	
#Ascending colon	(100)	(173)
Cyst, NOS		1 (1%)

TABLE A5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
DIGESTIVE SYSTEM (Continued)		
#Transverse colon	(100)	(173)
Parasitism		1 (1%)
Hyperplasia, epithelial		1 (1%)
#Descending colon	(100)	(173)
Parasitism		1 (1%)
URINARY SYSTEM		
#Kidney	(100)	(173)
Mineralization	3 (3%)	
Hydronephrosis		1 (1%)
Congestion, NOS	1 (1%)	
Inflammation, acute focal	1 (1%)	
Inflammation, chronic	97 (97%)	152 (87%)
Granuloma, NOS		1 (1%)
Fibrosis, diffuse		1 (1%)
Necrosis, focal	1 (1%)	
Infarct, NOS	1 (1%)	
Metamorphosis fatty	1 (1%)	
#Kidney/cortex	(100)	(173)
Cyst, NOS	5 (5%)	2 (1%)
#Kidney/tubule	(100)	(173)
Cyst, NOS		1 (1%)
Pigmentation, NOS	33 (33%)	34 (19%)
Hyperplasia, focal	1 (1%)	1 (1%)
#Urinary bladder	(100)	(172)
Hemorrhage	3 (3%)	
Inflammation, acute diffuse	1 (1%)	
Inflammation, chronic focal	2 (2%)	
Necrosis, focal	1 (1%)	
Necrosis, diffuse	1 (1%)	
Hyperplasia, epithelial	1 (1%)	
Hyperplasia, diffuse	1 (1%)	
*Urethra	(100)	(175)
Abscess, NOS	1 (1%)	
Hyperplasia, epithelial	1 (1%)	
ENDOCRINE SYSTEM		
#Pituitary	(99)	(169)
Cyst, NOS	3 (3%)	3 (2%)
Hemorrhage	2 (2%)	
Pigmentation, NOS	1 (1%)	
Hyperplasia, focal	5 (5%)	4 (2%)
Angiectasis	6 (6%)	1 (1%)
#Adrenal	(100)	(173)
Hemorrhage	1 (1%)	
Metamorphosis fatty	1 (1%)	1 (1%)
Pigmentation, NOS		1 (1%)
#Adrenal/capsule	(100)	(173)
Inflammation, chronic focal		1 (1%)
#Adrenal cortex	(100)	(173)
Congestion, NOS	1 (1%)	
Degeneration, NOS	1 (1%)	
Metamorphosis fatty	24 (24%)	16 (9%)
Hyperplasia, focal	3 (3%)	2 (1%)
#Adrenal medulla	(100)	(173)
Hyperplasia, focal	19 (19%)	29 (17%)

TABLE A5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
ENDOCRINE SYSTEM (Continued)		
#Thyroid	(100)	(172)
Cystic follicles		1 (1%)
Follicular cyst, NOS	1 (1%)	7 (4%)
Hyperplasia, C-cell	23 (23%)	33 (19%)
#Parathyroid	(99)	(168)
Hyperplasia, NOS	12 (12%)	1 (1%)
REPRODUCTIVE SYSTEM		
*Mammary gland	(100)	(175)
Galactocele		1 (1%)
Cystic ducts	9 (9%)	4 (2%)
Hemorrhagic cyst	1 (1%)	
Hyperplasia, NOS	4 (4%)	2 (1%)
*Penis	(100)	(175)
Epidermal inclusion cyst	1 (1%)	
*Prepuce	(100)	(175)
Epidermal inclusion cyst		1 (1%)
*Preputial gland	(100)	(175)
Cystic ducts	2 (2%)	2 (1%)
Hyperplasia, NOS		1 (1%)
#Prostate	(100)	(172)
Inflammation, acute focal		1 (1%)
Abscess, NOS	4 (4%)	1 (1%)
Inflammation, chronic focal	44 (44%)	43 (25%)
Inflammation, chronic diffuse	4 (4%)	1 (1%)
Hyperplasia, focal	1 (1%)	
*Seminal vesicle	(100)	(175)
Cyst, NOS	5 (5%)	4 (2%)
Abscess, NOS	1 (1%)	
Hyperplasia, epithelial	1 (1%)	
Hyperplasia, diffuse	3 (3%)	
*Coagulating gland	(100)	(175)
Inflammation, chronic focal	1 (1%)	
Hyperplasia, focal		1 (1%)
#Testis	(100)	(172)
Degeneration, NOS	7 (7%)	26 (15%)
Hyperplasia, interstitial cell	53 (53%)	117 (67%)
Hyperplasia, C-cell	1 (1%)	
*Epididymis	(100)	(175)
Granuloma, spermatic		1 (1%)
Necrosis, fat	4 (4%)	2 (1%)
NERVOUS SYSTEM		
#Cerebrum	(100)	(171)
Necrosis, focal	1 (1%)	
#Brain	(100)	(171)
Hydrocephalus, NOS	1 (1%)	
Hemorrhage	1 (1%)	
#Cerebellum	(100)	(171)
Abscess, NOS		1 (1%)
SPECIAL SENSE ORGANS		
*Eye	(100)	(175)
Hemorrhage	2 (2%)	
Inflammation, chronic	1 (1%)	
Synechia, posterior	1 (1%)	
Cataract	13 (13%)	6 (3%)

TABLE A5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
SPECIAL SENSE ORGANS (Continued)		
*Vitreous body	(100)	(175)
Vascularization	1 (1%)	
*Eye/cornea	(100)	(175)
Inflammation, acute focal	1 (1%)	
Inflammation, chronic		1 (1%)
Necrosis, focal		1 (1%)
*Eye/retina	(100)	(175)
Degeneration, NOS	35 (35%)	10 (6%)
*Eye/crystalline lens	(100)	(175)
Rupture	1 (1%)	
*Ear canal	(100)	(175)
Inflammation, chronic focal		1 (1%)
Hyperkeratosis		1 (1%)
Acanthosis		2 (1%)
*Zymbal's gland	(100)	(175)
Cystic ducts	11 (11%)	8 (5%)
Abscess, NOS		1 (1%)
Inflammation, chronic		1 (1%)
Hyperkeratosis		2 (1%)
MUSCULOSKELETAL SYSTEM		
*Skull	(100)	(175)
Osteopetrosis	1 (1%)	
*Rib	(100)	(175)
Degeneration, NOS	2 (2%)	
BODY CAVITIES		
*Mediastinum	(100)	(175)
Necrosis, focal		1 (1%)
*Abdominal cavity	(100)	(175)
Steatitis		1 (1%)
Necrosis, fat	1 (1%)	5 (3%)
*Mesentery	(100)	(175)
Hemorrhage	2 (2%)	
Inflammation, acute focal	1 (1%)	
Inflammation, chronic focal	3 (3%)	
ALL OTHER SYSTEMS		
*Multiple organs	(100)	(175)
Inflammation, acute	1 (1%)	
Inflammation, chronic	3 (3%)	2 (1%)
Diaphragm		
Hernia, NOS		2
Adipose tissue		
Hemorrhage	2	
SPECIAL MORPHOLOGY SUMMARY		
Auto/necropsy/histo perf		1

(a) DMH indicates a group receiving five doses of 7.5 mg/kg 1,2-dimethylhydrazine dihydrochloride by gavage in pH 5 acetate buffer; PW indicates a group administered 0.47 mg/g chrysotile asbestos daily by gavage for 3 weeks beginning at birth

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

Number of animals examined microscopically at this site

APPENDIX B

SUMMARY OF LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS

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TABLE B1a. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (a)

	Untreated Control	DMH	1% Amosite
Animals initially in study	117	125	250
Animals necropsied	117	125	250
Animals examined histopathologically	117	124	250
INTEGUMENTARY SYSTEM			
*Skin	(117)	(125)	(250)
Squamous cell papilloma	2 (2%)		3 (1%)
Squamous cell carcinoma	1 (1%)		1 (0%)
Basal cell tumor	1 (1%)		3 (1%)
Basal cell carcinoma	1 (1%)		
Keratoacanthoma			2 (1%)
Fibroma	1 (1%)		
Fibrosarcoma	2 (2%)	1 (1%)	1 (0%)
Osteosarcoma			1 (0%)
*Subcut tissue	(117)	(125)	(250)
Sarcoma, NOS			6 (2%)
Sarcoma, NOS, invasive	1 (1%)		
Fibroma	6 (5%)		8 (3%)
Fibrosarcoma	1 (1%)	1 (1%)	4 (2%)
Lipoma	3 (3%)		2 (1%)
Fibroadenoma	1 (1%)		
Neurofibroma			1 (0%)
Neurofibrosarcoma			1 (0%)
RESPIRATORY SYSTEM			
#Trachea	(116)	(122)	(249)
Follicular cell carcinoma, invas	1 (1%)		
#Lung	(116)	(124)	(250)
Carcinoma, NOS, metastatic		1 (1%)	
Squamous cell carcinoma	1 (1%)		
Squamous cell carcinoma, metasta			1 (0%)
Alveolar/bronchiolar adenoma	1 (1%)		
Alveolar/bronchiolar carcinoma			1 (0%)
Cortical carcinoma, metastatic			1 (0%)
C-cell carcinoma, metastatic	1 (1%)		2 (1%)
Pheochromocytoma, metastatic	1 (1%)		
Sarcoma, NOS, metastatic		1 (1%)	1 (0%)
Liposarcoma, metastatic			1 (0%)
Osteosarcoma, metastatic			1 (0%)
HEMATOPOIETIC SYSTEM			
*Multiple organs	(117)	(125)	(250)
Malig. lymphoma, histiocytic type	1 (1%)		1 (0%)
Myelomonocytic leukemia			78 (31%)
Monocytic leukemia	39 (33%)	34 (27%)	
#Spleen	(117)	(124)	(249)
Osteosarcoma	1 (1%)		
#Mandibular l. node	(117)	(124)	(250)
Adenocarcinoma, NOS, metastatic			1 (0%)
#Cervical lymph node	(117)	(124)	(250)
C-cell carcinoma, metastatic	2 (2%)		3 (1%)
#Mediastinal l. node	(117)	(124)	(250)
C-cell carcinoma, metastatic			1 (0%)
#Liver	(117)	(124)	(250)
Malig. lymphoma, histiocytic type			1 (0%)
Kupffer cell sarcoma			1 (0%)
Monocytic leukemia	1 (1%)	5 (4%)	4 (2%)
#Thymus	(79)	(96)	(210)
Adenocarcinoma, NOS			1 (0%)

TABLE B1a. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
CIRCULATORY SYSTEM			
#Endocardium	(116)	(122)	(250)
Sarcoma, NOS			1 (0%)
Neurilemoma, malignant			1 (0%)
*Aorta	(117)	(125)	(250)
Nonchromaffin paraganglioma			1 (0%)
#Uterus	(117)	(124)	(250)
Hemangiosarcoma	1 (1%)		
DIGESTIVE SYSTEM			
*Oral mucous membrane	(117)	(125)	(250)
Squamous cell carcinoma			1 (0%)
*Hard palate	(117)	(125)	(250)
Squamous cell papilloma	1 (1%)		1 (0%)
Squamous cell carcinoma			1 (0%)
*Tongue	(117)	(125)	(250)
Squamous cell papilloma			1 (0%)
#Salivary gland	(116)	(123)	(246)
Sarcoma, NOS	2 (2%)		1 (0%)
#Liver	(117)	(124)	(250)
Neoplastic nodule	4 (3%)	29 (23%)	10 (4%)
Hepatocellular carcinoma	1 (1%)	10 (8%)	
Sarcoma, NOS, metastatic		2 (2%)	
#Pancreas	(116)	(124)	(249)
Islet cell carcinoma			1 (0%)
Acinar cell adenoma	2 (2%)		
Sarcoma, NOS, invasive		1 (1%)	
Mixed tumor, benign			1 (0%)
#Stomach	(117)	(124)	(250)
Carcinoma, NOS	1 (1%)		
Squamous cell carcinoma			1 (0%)
Adenocarcinoma, NOS		2 (2%)	
Adenocarcinoma, NOS, invasive		1 (1%)	
Signet ring carcinoma		1 (1%)	
Leiomyosarcoma			1 (0%)
#Duodenum	(117)	(124)	(249)
Adenocarcinoma, NOS		1 (1%)	
Mucinous cystadenocarcinoma		1 (1%)	1 (0%)
Signet ring carcinoma		1 (1%)	
Leiomyosarcoma	1 (1%)		
#Jejunum	(117)	(124)	(249)
Adenoma, NOS			1 (0%)
Adenocarcinoma, NOS		3 (2%)	
Adenomatous polyp, NOS			1 (0%)
Mucinous cystadenocarcinoma		6 (5%)	
Signet ring carcinoma		2 (2%)	
Leiomyosarcoma			1 (0%)
#Colon	(117)	(124)	(250)
Adenocarcinoma, NOS		3 (2%)	
Adenomatous polyp, NOS		1 (1%)	
Signet ring carcinoma		1 (1%)	
Leiomyosarcoma			1 (0%)
Neurofibroma			1 (0%)
#Cecum	(117)	(124)	(250)
Adenocarcinoma, NOS		2 (2%)	
Mucinous cystadenocarcinoma		3 (2%)	
Signet ring carcinoma		2 (2%)	

TABLE B1a. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
DIGESTIVE SYSTEM (Continued)			
#Ascending colon	(117)	(124)	(250)
Adenocarcinoma, NOS		2 (2%)	
Adenomatous polyp, NOS		7 (6%)	
Adenocarcinoma in adenomatous polyp		4 (3%)	
Mucinous cystadenocarcinoma		3 (2%)	
Mucinous adenocarcinoma		1 (1%)	
Signet ring carcinoma		4 (3%)	
#Transverse colon	(117)	(124)	(250)
Adenomatous polyp, NOS		6 (5%)	
Adenocarcinoma in adenomatous polyp		9 (7%)	
#Descending colon	(117)	(124)	(250)
Adenomatous polyp, NOS	1 (1%)	27 (22%)	
Adenocarcinoma in adenomatous polyp		15 (12%)	
Mucinous cystadenocarcinoma		1 (1%)	
Lipoma			1 (0%)
URINARY SYSTEM			
#Kidney	(117)	(124)	(250)
Neoplasm, NOS, malignant		1 (1%)	
Tubular cell adenocarcinoma	1 (1%)	3 (2%)	
Sarcoma, NOS		23 (18%)	1 (0%)
Fibrosarcoma		4 (3%)	
Mixed tumor, benign			1 (0%)
Mixed tumor, malignant		9 (7%)	1 (0%)
#Perirenal tissue	(117)	(124)	(250)
Pheochromocytoma, invasive	1 (1%)		
#Urinary bladder	(117)	(121)	(248)
Transitional cell papilloma	1 (1%)		1 (0%)
Transitional cell carcinoma		1 (1%)	2 (1%)
ENDOCRINE SYSTEM			
#Pituitary	(117)	(123)	(249)
Carcinoma, NOS	2 (2%)		11 (4%)
Adenoma, NOS	50 (43%)	16 (13%)	07 (43%)
#Adrenal	(117)	(124)	(249)
Cortical adenoma	3 (3%)	2 (2%)	13 (5%)
Cortical carcinoma	1 (1%)		1 (0%)
Pheochromocytoma	17 (15%)		27 (11%)
Pheochromocytoma, malignant	1 (1%)		3 (1%)
Sarcoma, NOS, invasive		1 (1%)	
#Thyroid	(116)	(123)	(247)
Follicular cell adenoma	2 (2%)	4 (3%)	10 (4%)
Follicular cell carcinoma	7 (6%)	2 (2%)	3 (1%)
C-cell adenoma	14 (12%)	4 (3%)	37 (15%)
C-cell carcinoma	10 (9%)	1 (1%)	29 (12%)
#Parathyroid	(109)	(118)	(240)
Adenoma, NOS	1 (1%)		
#Pancreatic islets	(116)	(124)	(249)
Islet cell adenoma	2 (2%)		7 (3%)
Islet cell carcinoma	3 (3%)		6 (2%)

TABLE B1a. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
REPRODUCTIVE SYSTEM			
*Mammary gland	(117)	(125)	(250)
Carcinoma in-situ, NOS	1 (1%)		
Carcinoma, NOS	1 (1%)		
Adenoma, NOS	7 (6%)		13 (5%)
Adenocarcinoma, NOS	4 (3%)	3 (2%)	23 (9%)
Papillary adenocarcinoma			2 (1%)
Papillary cystadenoma, NOS	1 (1%)	1 (1%)	1 (0%)
Sarcoma, NOS, invasive	1 (1%)		
Fibroadenoma	72 (62%)	13 (10%)	35 (54%)
*Preputial gland	(117)	(125)	(250)
Carcinoma, NOS	6 (5%)	1 (1%)	14 (6%)
Adenoma, NOS			1 (0%)
Keratoacanthoma			1 (0%)
Sarcoma, NOS	1 (1%)		
Sarcoma, NOS, invasive			2 (1%)
*Vagina	(117)	(125)	(250)
Leiomyosarcoma, invasive	1 (1%)		
Endometrial stromal sarcoma, inv		1 (1%)	
#Uterus	(117)	(124)	(250)
Carcinoma, NOS			1 (0%)
Adenocarcinoma, NOS			1 (0%)
Papillary adenocarcinoma			1 (0%)
Leiomyoma			1 (0%)
Leiomyosarcoma			1 (0%)
Leiomyosarcoma, invasive	1 (1%)		
Endometrial stromal polyp	13 (11%)	10 (8%)	31 (12%)
Endometrial stromal sarcoma	5 (4%)	4 (3%)	4 (2%)
Mixed tumor, metastatic		1 (1%)	
#Cervix uteri	(117)	(124)	(250)
Leiomyosarcoma	1 (1%)	1 (1%)	
Endometrial stromal sarcoma, inv	2 (2%)	2 (2%)	2 (1%)
#Uterus/endometrium	(117)	(124)	(250)
Carcinoma, NOS			1 (0%)
Papillary adenoma			1 (0%)
#Ovary	(117)	(124)	(250)
Papillary cystadenoma, NOS			1 (0%)
Thecoma			1 (0%)
Granulosa cell tumor	1 (1%)		3 (1%)
Sertoli cell tumor	1 (1%)		
Mixed tumor, metastatic		1 (1%)	
Mesothelioma, NOS	1 (1%)		
NERVOUS SYSTEM			
#Cerebrum	(117)	(124)	(250)
Carcinoma, NOS, invasive	1 (1%)		5 (2%)
Granular cell tumor, NOS			1 (0%)
Glioma, NOS			1 (0%)
Astrocytoma	2 (2%)	1 (1%)	4 (2%)
#Cerebellum	(117)	(124)	(250)
Carcinoma, NOS, invasive			3 (1%)
Astrocytoma	2 (2%)		
Astrocytoma, invasive			1 (0%)
#Medulla oblongata	(117)	(124)	(250)
Astrocytoma, invasive			1 (0%)
*Trigeminal nerve	(117)	(125)	(250)
Squamous cell carcinoma, metasta			1 (0%)

TABLE B1a. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
SPECIAL SENSE ORGANS			
*Zymbal gland	(117)	(125)	(250)
Carcinoma, NOS	3 (3%)	20 (16%)	4 (2%)
Squamous cell papilloma		12 (10%)	3 (1%)
Keratoacanthoma	1 (1%)	2 (2%)	
MUSCULOSKELETAL SYSTEM			
*Skull	(117)	(125)	(250)
Osteosarcoma			1 (0%)
*Rib	(117)	(125)	(250)
Osteosarcoma			1 (0%)
*Femur	(117)	(125)	(250)
Osteosarcoma	1 (1%)		
BODY CAVITIES			
*Mediastinum	(117)	(125)	(250)
Squamous cell carcinoma, metasta	1 (1%)		
*Abdominal cavity	(117)	(125)	(250)
Mucinous cystadenoca, metastatic		1 (1%)	
Pheochromocytoma, invasive			1 (0%)
Sarcoma, NOS, invasive		1 (1%)	
Sarcoma, NOS, metastatic			1 (0%)
Endometrial stromal sarcoma, inv	1 (1%)		
*Abdominal wall	(117)	(125)	(250)
Endometrial stromal sarcoma, inv			1 (0%)
*Peritoneum	(117)	(125)	(250)
Fibrosarcoma			1 (0%)
*Mesentery	(117)	(125)	(250)
Mucinous cystadenoca, metastatic		1 (1%)	
Leiomyosarcoma, invasive			1 (0%)
Mesothelioma, malignant			1 (0%)
ALL OTHER SYSTEMS			
*Multiple organs	(117)	(125)	(250)
Carcinoma, NOS, invasive			1 (0%)
Squamous cell carcinoma, metasta			1 (0%)
Adenocarcinoma, NOS, metastatic		11 (9%)	
Mucinous cystadenocarcinoma, metastatic		6 (5%)	
Mucinous adenocarcinoma, metasta		1 (1%)	
Signet ring carcinoma, metastati		9 (7%)	
Sarcoma, NOS, invasive			2 (1%)
Sarcoma, NOS, metastatic			1 (0%)
Liposarcoma, metastatic			1 (0%)
Endometrial stromal sarcoma, met	1 (1%)	1 (1%)	
Mesothelioma, invasive			1 (0%)
Adipose tissue			
Sarcoma, NOS, invasive		1	

TABLE B1a. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	117	125	250
Natural death	16	22	24
Moribund sacrifice	91	90	195
Terminal sacrifice	10	13	27
Accidentally killed, nda			4
TUMOR SUMMARY			
Total animals with primary tumors**	113	121	240
Total primary tumors	316	326	663
Total animals with benign tumors	99	74	213
Total benign tumors	204	105	419
Total animals with malignant tumors	74	111	166
Total malignant tumors	106	192	230
Total animals with secondary tumors##	11	39	31
Total secondary tumors	16	44	38

(a) DMH indicates a group receiving five doses of 15 mg/kg 1,2-dimethylhydrazine dihydrochloride by gavage in pH 5 acetate buffer

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically

** Primary tumors: all tumors except secondary tumors

Number of animals examined microscopically at this site

Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE B1b. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, AND 1% AMOSITE + DMH (a)

	1% Amosite + PW	1% Amosite + DMH
Animals initially in study	100	175
Animals necropsied	100	175
Animals examined histopathologically	100	175
INTEGUMENTARY SYSTEM		
*Skin	(100)	(175)
Squamous cell papilloma		1 (1%)
Basal cell tumor	1 (1%)	
Basal cell carcinoma	1 (1%)	1 (1%)
Fibroma	1 (1%)	
Fibrosarcoma		1 (1%)
Carcinosarcoma		1 (1%)
*Subcut tissue	(100)	(175)
Carcinoma, NOS, invasive		1 (1%)
Sarcoma, NOS	1 (1%)	
Fibroma	2 (2%)	
Fibrosarcoma	1 (1%)	
RESPIRATORY SYSTEM		
#Trachea	(100)	(175)
C-cell carcinoma, invasive	2 (2%)	
#Lung	(100)	(175)
Carcinoma, NOS, metastatic	1 (1%)	
Alveolar/bronchiolar adenoma		1 (1%)
Alveolar/bronchiolar carcinoma	1 (1%)	1 (1%)
C-cell carcinoma, metastatic	1 (1%)	
Pheochromocytoma, metastatic		1 (1%)
Sarcoma, NOS, metastatic	1 (1%)	
Liposarcoma, metastatic		1 (1%)
Mixed tumor, metastatic		1 (1%)
Carcinosarcoma, metastatic		1 (1%)
HEMATOPOIETIC SYSTEM		
*Multiple organs	(100)	(175)
Myelomonocytic leukemia	1 (1%)	
Monocytic leukemia	33 (33%)	54 (31%)
#Spleen	(100)	(175)
Lipoma	1 (1%)	
#Celiac lymph node	(100)	(175)
Adenocarcinoma in adenomatous polyp, met		1 (1%)
#Mesenteric lymph node	(100)	(175)
Adenocarcinoma in adenomatous polyp, met		1 (1%)
Signet ring carcinoma, metastati		3 (2%)
#Ileocolic lymph node	(100)	(175)
Adenocarcinoma, NOS, metastatic		2 (1%)
Mucinous cystadenocarcinoma, metastatic		1 (1%)
Signet ring carcinoma, metastati		1 (1%)
#Liver	(100)	(175)
Monocytic leukemia	1 (1%)	7 (4%)
#Thymus	(81)	(139)
Carcinoma, NOS	1 (1%)	
#Thymic lymphocytes	(81)	(139)
Thymoma	1 (1%)	

TABLE B1b. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, AND 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
CIRCULATORY SYSTEM		
#Heart	(100)	(175)
Sarcoma, NOS	1 (1%)	
Mixed tumor, metastatic		1 (1%)
#Kidney	(100)	(175)
Hemangioma		1 (1%)
#Cervix uteri	(100)	(175)
Angioma		1 (1%)
DIGESTIVE SYSTEM		
*Tongue	(100)	(175)
Squamous cell papilloma		1 (1%)
#Salivary gland	(100)	(174)
Sarcoma, NOS	1 (1%)	
#Liver	(100)	(175)
Neoplastic nodule	4 (4%)	32 (18%)
Hepatocellular carcinoma		8 (5%)
Neurofibrosarcoma		1 (1%)
#Pancreas	(100)	(175)
Mixed tumor, invasive		1 (1%)
#Stomach	(100)	(175)
Squamous cell papilloma		1 (1%)
Signet ring carcinoma, metastatic		1 (1%)
Mixed tumor, invasive		1 (1%)
#Peyer's patch	(100)	(175)
Adenocarcinoma in adenomatous polyp, met		1 (1%)
#Duodenum	(100)	(175)
Adenocarcinoma, NOS		11 (6%)
Mucinous cystadenocarcinoma		1 (1%)
Signet ring carcinoma		7 (4%)
#Jejunum	(100)	(175)
Adenocarcinoma in adenomatous polyp		1 (1%)
Mucinous cystadenocarcinoma	1 (1%)	1 (1%)
Signet ring carcinoma		1 (1%)
#Ileum	(100)	(175)
Adenocarcinoma in adenomatous polyp		1 (1%)
Sarcoma, NOS	1 (1%)	
#Colon	(100)	(175)
Carcinoma in-situ, NOS		1 (1%)
Adenocarcinoma, NOS		2 (1%)
Mucinous cystadenocarcinoma, metastatic		1 (1%)
Signet ring carcinoma, metastatic		1 (1%)
#Cecum	(100)	(175)
Adenocarcinoma, NOS		2 (1%)
Mucinous cystadenocarcinoma		2 (1%)
Signet ring carcinoma		2 (1%)
#Ascending colon	(100)	(175)
Adenocarcinoma, NOS		3 (2%)
Adenomatous polyp, NOS		8 (5%)
Adenocarcinoma in adenomatous polyp		7 (4%)
Mucinous cystadenocarcinoma		5 (3%)
Signet ring carcinoma		6 (3%)
Signet ring carcinoma, metastatic		1 (1%)
#Transverse colon	(100)	(175)
Carcinoma, NOS	1 (1%)	
Adenocarcinoma, NOS		2 (1%)
Adenomatous polyp, NOS		22 (13%)
Adenocarcinoma in adenomatous polyp		20 (11%)

TABLE B1b. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, AND 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
DIGESTIVE SYSTEM (Continued)		
#Descending colon	(100)	(175)
Carcinoma in-situ, NOS		1 (1%)
Adenomatous polyp, NOS	1 (1%)	31 (18%)
Adenocarcinoma in adenomatous polyp		22 (13%)
Signet ring carcinoma		1 (1%)
*Rectum	(100)	(175)
Adenomatous polyp, NOS		1 (1%)
URINARY SYSTEM		
#Kidney	(100)	(175)
Tubular cell adenoma		1 (1%)
Tubular cell adenocarcinoma		2 (1%)
Sarcoma, NOS		19 (11%)
Mixed tumor, malignant	1 (1%)	35 (20%)
#Urinary bladder	(99)	(173)
Transitional cell papilloma	1 (1%)	
Endometrial stromal sarcoma, inv		1 (1%)
ENDOCRINE SYSTEM		
#Pituitary	(100)	(175)
Carcinoma, NOS	3 (3%)	1 (1%)
Adenoma, NOS	39 (39%)	19 (11%)
Ganglioneuroma	1 (1%)	
#Adrenal	(100)	(175)
Cortical adenoma	4 (4%)	4 (2%)
Pheochromocytoma	6 (6%)	3 (2%)
Pheochromocytoma, malignant		1 (1%)
Sarcoma, NOS, invasive		1 (1%)
Mixed tumor, invasive	1 (1%)	3 (2%)
Ganglioneuroma		1 (1%)
#Thyroid	(100)	(174)
Follicular cell adenoma	3 (3%)	6 (3%)
Follicular cell carcinoma	2 (2%)	1 (1%)
C-cell adenoma	15 (15%)	8 (5%)
C-cell carcinoma	14 (14%)	6 (3%)
#Pancreatic islets	(100)	(175)
Islet cell adenoma	1 (1%)	2 (1%)
REPRODUCTIVE SYSTEM		
*Mammary gland	(100)	(175)
Carcinoma, NOS	1 (1%)	
Adenoma, NOS	5 (5%)	2 (1%)
Adenocarcinoma, NOS	7 (7%)	
Papillary adenocarcinoma		1 (1%)
Fibrosarcoma	1 (1%)	
Fibroadenoma	52 (52%)	18 (10%)
*Preputial gland	(100)	(175)
Carcinoma, NOS	7 (7%)	3 (2%)
Keratoacanthoma		1 (1%)
#Uterus	(100)	(175)
Leiomyoma		1 (1%)
Endometrial stromal polyp	14 (14%)	19 (11%)
Endometrial stromal sarcoma		2 (1%)
#Cervix uteri	(100)	(175)
Squamous cell papilloma	1 (1%)	
Fibrosarcoma		1 (1%)
Endometrial stromal sarcoma, inv		2 (1%)

TABLE B1b. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, AND 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
REPRODUCTIVE SYSTEM (Continued)		
#Ovary	(99)	(175)
Papillary cystadenocarcinoma, NOS		1 (1%)
Granulosa cell tumor	2 (2%)	
Granulosa cell carcinoma	1 (1%)	
Sertoli cell tumor	1 (1%)	
NERVOUS SYSTEM		
#Cerebrum	(100)	(175)
Carcinoma, NOS, invasive	1 (1%)	
Astrocytoma	2 (2%)	
#Cerebellum	(100)	(175)
Carcinoma, NOS, invasive	1 (1%)	
#Medulla oblongata	(100)	(175)
Carcinoma, NOS, invasive	1 (1%)	
SPECIAL SENSE ORGANS		
*Eye/ciliary body	(100)	(175)
Leiomyosarcoma	1 (1%)	
*Ear canal	(100)	(175)
Squamous cell papilloma		2 (1%)
Squamous cell carcinoma		2 (1%)
*Zymbal gland	(100)	(175)
Carcinoma, NOS	3 (3%)	23 (13%)
Squamous cell papilloma		14 (8%)
Keratoacanthoma	1 (1%)	2 (1%)
MUSCULOSKELETAL SYSTEM		
*Mandible	(100)	(175)
Carcinoma, NOS, invasive		1 (1%)
*Vertebra	(100)	(175)
Osteosarcoma	1 (1%)	
BODY CAVITIES		
*Mediastinum	(100)	(175)
Signet ring carcinoma, metastatic		1 (1%)
Sarcoma, NOS, metastatic	1 (1%)	
*Abdominal cavity	(100)	(175)
Sarcoma, NOS, invasive		1 (1%)
Lipoma	1 (1%)	1 (1%)
Mixed tumor, invasive		1 (1%)
*Epicardium	(100)	(175)
Mesothelioma, NOS		1 (1%)
*Mesentery	(100)	(175)
Adenocarcinoma, NOS, metastatic		1 (1%)
Sarcoma, NOS, invasive		1 (1%)

TABLE B1b. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, AND 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
ALL OTHER SYSTEMS		
*Multiple organs	(100)	(175)
Adenocarcinoma, NOS, metastatic		10 (6%)
C-cell carcinoma, metastatic	2 (2%)	
Mucinous cystadenocarcinoma, metastatic		5 (3%)
Signet ring carcinoma, metastatic		7 (4%)
Sarcoma, NOS, invasive	1 (1%)	
Fibrosarcoma, invasive	1 (1%)	
Osteosarcoma, metastatic	1 (1%)	
Orbital region		
Sarcoma, NOS		1
ANIMAL DISPOSITION SUMMARY		
Animals initially in study	100	175
Natural death	14	30
Moribund sacrifice	77	117
Terminal sacrifice	9	28
TUMOR SUMMARY		
Total animals with primary tumors**	98	175
Total primary tumors	247	477
Total animals with benign tumors	79	102
Total benign tumors	152	172
Total animals with malignant tumors	68	164
Total malignant tumors	89	272
Total animals with secondary tumors###	10	46
Total secondary tumors	15	57
Total animals with tumors uncertain--benign or malignant	6	33
Total uncertain tumors	6	33

(a) DMH indicates a group receiving five doses of 15 mg/kg 1,2-dimethylhydrazine dihydrochloride in pH 5 acetate buffer; PW indicates a group administered 0.47 mg/g chrysotile asbestos daily by gavage for 3 weeks beginning at birth

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

Number of animals examined microscopically at this site

** Primary tumors: all tumors except secondary tumors

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

Number of animals examined microscopically at this site

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: CONTROL
(Continued)

ANIMAL NUMBER	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407	408		
WEEKS ON STUDY	071	071	103	106	113	113	113	113	117	117	117	117	117	117	117	117	117	117	117	117	117	117	117	117	117		
INTEGUMENTARY SYSTEM																											
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell papilloma																											
Squamous cell carcinoma																											
Basal cell tumor																											
Basal cell carcinoma																											
Fibroma																											
Fibrosarcoma																											
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS, invasive																											
Fibroma																											
Fibrosarcoma																											
Lipoma																											
Fibroadenoma																											
RESPIRATORY SYSTEM																											
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell carcinoma																											
Alveolar/bronchiolar adenoma																											
C-cell carcinoma, metastatic																											
Pheochromocytoma, metastatic																											
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Follicular cell carcinoma, invasive																											
HEMATOPOIETIC SYSTEM																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Osteosarcoma																											
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
C-cell carcinoma, metastatic																											
Thymus	+	+	+	+	+	-	-	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
CIRCULATORY SYSTEM																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
DIGESTIVE SYSTEM																											
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Squamous cell papilloma																											
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Neoplastic nodule																											
Hepatocellular carcinoma																											
Monocytic leukemia																											
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Acinar cell adenoma																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																											
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Leiomyosarcoma																											
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenomatous polyp, NOS																											
URINARY SYSTEM																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Tubular cell adenocarcinoma																											
Pheochromocytoma, invasive																											
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Transitional cell papilloma																											

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: CONTROL
(Continued)

ANIMAL NUMBER	3 4	3 5	3 6	3 7	3 8	3 9	3 0	3 1	3 2	3 3	3 4	3 5	3 6	3 7	3 8	3 9	3 0	3 1	3 2	3 3	3 4	3 5	3 6	3 7	3 8	3 9	
WEEKS ON STUDY	1 9	1 9	0 0	1 4	1 8	1 7	1 3	1 7	1 2	1 1	0 9																
ENDOCRINE SYSTEM																											
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS	X																										
Adenoma, NOS			X		X			X	X							X	X	X	X	X			X	X	X	X	
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Cortical adenoma						X																					
Cortical carcinoma																											
Pheochromocytoma																											
Pheochromocytoma, malignant																											
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Follicular cell adenoma			X		X																						
Follicular cell carcinoma							X	X						X	X								X				
C-cell adenoma							X			X																	
C cell carcinoma																X								X			
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenoma, NOS																											
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Islet cell adenoma																											
Islet cell carcinoma																X											
REPRODUCTIVE SYSTEM																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma in-situ, NOS																											
Carcinoma, NOS																											
Adenoma, NOS			X																								
Adenocarcinoma, NOS																											
Papillary cystadenoma, NOS																											
Sarcoma, NOS, invasive																											
Fibroadenoma	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Carcinoma, NOS																											
Sarcoma, NOS																											
Vagina	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Leiomyosarcoma, invasive																											
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Leiomyosarcoma																											
Leiomyosarcoma, invasive																											
Endometrial stromal polyp				X				X					X									X				X	
Endometrial stromal sarcoma									X																		
Endometrial stromal sarcoma, invasive																											
Hemangiosarcoma																											
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Granulosa cell tumor																											
Sertoli cell tumor																											
Mesothelioma, NOS																											
NERVOUS SYSTEM																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS, invasive																											
Astrocytoma																											
SPECIAL SENSE ORGANS																											
Zymbal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																											
Keratoacanthoma																											
MUSCULOSKELETAL SYSTEM																											
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Osteosarcoma																											
BODY CAVITIES																											
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Squamous cell carcinoma, metastatic																											
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Endometrial stromal sarcoma, invasive																											
ALL OTHER SYSTEMS																											
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Endometrial stromal sarcoma, metastatic																											
Malignant lymphoma, histiocytic type																											
Monocytic leukemia	X		X	X	X	X	X						X	X													

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: CONTROL
(Continued)

ANIMAL NUMBER	3 8 4	3 8 5	3 8 6	3 8 7	3 8 8	3 8 9	3 9 0	3 9 1	3 9 2	3 9 3	3 9 4	3 9 5	3 9 6	3 9 7	3 9 8	4 0 0	4 0 1	4 0 2	4 0 3	4 0 4	4 0 5	4 0 6	4 0 7	4 0 8			
WEEKS ON STUDY	0 7 1	0 7 1	1 3 3	0 9 6	1 3 0	1 3 5	1 3 6	1 3 5	0 5 0	1 5 5	1 4 0	1 4 6	0 9 8	0 8 3	1 1 0	1 1 7	1 1 5	0 4 9	0 8 2	1 1 1	1 1 4	0 5 4	1 2 3	1 1 4	1 1 6	1 1 9	1 1 1
ENDOCRINE SYSTEM																											
Pituitary	+																										
Carcinoma, NOS	+																										
Adenoma, NOS	+																										
Adrenal	+																										
Cortical adenoma	+																										
Cortical carcinoma	+																										
Pheochromocytoma	+																										
Pheochromocytoma, malignant	+																										
Thyroid	+																										
Follicular cell adenoma	+																										
Follicular cell carcinoma	+																										
C cell adenoma	+																										
C-cell carcinoma	+																										
Parathyroid	+																										
Adenoma, NOS	+																										
Pancreatic islets	+																										
Islet cell adenoma	+																										
Islet cell carcinoma	+																										
REPRODUCTIVE SYSTEM																											
Mammary gland	+																										
Carcinoma in-situ, NOS	+																										
Carcinoma, NOS	+																										
Adenoma, NOS	+																										
Adenocarcinoma, NOS	+																										
Papillary cystadenoma, NOS	+																										
Sarcoma, NOS, invasive	+																										
Fibroadenoma	+																										
Preputial/clitoral gland	+																										
Carcinoma, NOS	+																										
Sarcoma, NOS	+																										
Vagina	+																										
Leiomyosarcoma, invasive	+																										
Uterus	+																										
Leiomyosarcoma	+																										
Leiomyosarcoma, invasive	+																										
Endometrial stromal polyp	+																										
Endometrial stromal sarcoma	+																										
Endometrial stromal sarcoma, invasive	+																										
Hemangiosarcoma	+																										
Ovary	+																										
Granulosa cell tumor	+																										
Sertoli cell tumor	+																										
Mesothelioma, NOS	+																										
NERVOUS SYSTEM																											
Brain	+																										
Carcinoma, NOS, invasive	+																										
Astrocytoma	+																										
SPECIAL SENSE ORGANS																											
Zymbal gland	+																										
Carcinoma, NOS	+																										
Keratoacanthoma	+																										
MUSCULOSKELETAL SYSTEM																											
Bone	N																										
Osteosarcoma	N																										
BODY CAVITIES																											
Mediastinum	N																										
Squamous cell carcinoma, metastatic	N																										
Peritoneum	N																										
Endometrial stromal sarcoma, invasive	N																										
ALL OTHER SYSTEMS																											
Multiple organs, NOS	N																										
Endometrial stromal sarcoma, metastatic	N																										
Malignant lymphoma, histiocytic type	N																										
Monocytic leukemia	N																										

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE

ANIMAL NUMBER	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75
WEEKS ON STUDY	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Subcutaneous tissue	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, metastatic																									
Sarcoma, NOS, metastatic					X																				
Trachea	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule				X					X																
Hepatocellular carcinoma										X															
Sarcoma, NOS, metastatic	X																								
Monocytic leukemia																							X		
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS, invasive																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Adenocarcinoma, NOS, invasive																									
Signet ring carcinoma																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																							X		
Mucinous cystadenocarcinoma																								X	
Signet ring carcinoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Adenomatous polyp, NOS	X							X	X																
Adenocarcinoma in adenomatous polyp													X	X	X	X	X	X	X	X	X	X	X	X	X
Mucinous cystadenocarcinoma																									
Mucinous adenocarcinoma																									
Signet ring carcinoma																									
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS, malignant																									
Tubular cell adenocarcinoma										X															
Sarcoma, NOS																									
Fibrosarcoma																									
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Transitional cell carcinoma																									

@ Multiple occurrence of morphology

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80		
WEEKS ON STUDY	6	7	7	8	8	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
INTEGUMENTARY SYSTEM																											
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Fibrosarcoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Fibrosarcoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
RESPIRATORY SYSTEM																											
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Trachea	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMATOPOIETIC SYSTEM																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Thymus	+	+	-	+	+	+	+	-	+	-	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	
CIRCULATORY SYSTEM																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
DIGESTIVE SYSTEM																											
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Neoplastic nodule																											
Hepatocellular carcinoma																											
Sarcoma, NOS, metastatic																											
Monocytic leukemia																											
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS, invasive																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma, NOS																											
Adenocarcinoma, NOS, invasive																											
Signet ring carcinoma																											
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Adenocarcinoma, NOS																											
Mucinous cystadenocarcinoma																											
Signet ring carcinoma																											
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Adenocarcinoma, NOS																											
Adenomatous polyp, NOS																											
Adenocarcinoma in adenomatous polyp																											
Mucinous cystadenocarcinoma																											
Mucinous adenocarcinoma																											
Signet ring carcinoma																											
URINARY SYSTEM																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Neoplasm, NOS, malignant																											
Tubular cell adenocarcinoma																											
Sarcoma, NOS																											
Fibrosarcoma																											
Mixed tumor, malignant																											
Urinary bladder	X																										
Transitional cell carcinoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
WEEKS ON STUDY	95	98	99	74	97	79	87	74	96	55	77	73	68	99	00	68	35	77	00	66	77	66	68	88	80
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																					X				
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																						X			
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, metastatic																									
Sarcoma, NOS, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	-	-	+	+	+	+	+	-	-	-	+	+	+	-	+	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule	X						X	X	X		X					X	X				X				
Hepatocellular carcinoma																									
Sarcoma, NOS, metastatic																									
Monocytic leukemia																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS, invasive																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Adenocarcinoma, NOS, invasive																									
Signet ring carcinoma																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Mucinous cystadenocarcinoma																						X	X		
Signet ring carcinoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Adenomatous polyp, NOS		X	X				X	X	X			X				X	X			X	X			X	X
Adenocarcinoma in adenomatous polyp							X	X	X@X					X	X								X		
Mucinous cystadenocarcinoma																									
Mucinous adenocarcinoma																									
Signet ring carcinoma																									
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS, malignant																									
Tubular cell adenocarcinoma																									
Sarcoma, NOS																									
Fibrosarcoma																									
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Transitional cell carcinoma																									

@ Multiple occurrence of morphology

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	5 1	5 2	5 3	5 4	5 5	5 6	5 7	5 8	5 9	5 0	5 1	5 2	5 3	5 4	5 5	5 6	5 7	5 8	5 9	5 0	5 1	5 2	5 3	5 4	5 5	5 6	5 7	5 8	5 9	
WEEKS ON STUDY	6 8	5 3	3 8	7 4	7 8	9 5	9 2	9 3	0 8	0 3	0 1	0 6	0 8	0 7	0 7	0 6	0 7	0 8	0 6	0 5	0 9	0 5	0 6	0 7	0 8	0 6	0 7	0 8	0 9	
ENDOCRINE SYSTEM																														
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Adenoma, NOS										X						X			X								X			
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																														
Sarcoma, NOS, invasive																														
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Follicular cell adenoma							X																							
Follicular cell carcinoma								X																						
C-cell adenoma																														
C-cell carcinoma																														
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																														
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS											X																			X
Papillary cystadenoma, NOS																														
Fibroadenoma											X																	X	X	
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																														
Vagina	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Endometrial stromal sarcoma, invasive																														
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma																														
Endometrial stromal polyp											X																			
Endometrial stromal sarcoma																														
Endometrial stromal sarcoma, invasive																														
Mixed tumor, metastatic																														
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mixed tumor, metastatic																														
NERVOUS SYSTEM																														
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma																														
SPECIAL SENSE ORGANS																														
Zymbal gland	+	+	N	+	+	+	+	+	+	+	N	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS	X									X					X	X		X		X										X
Squamous cell papilloma	X																	X												
Keratoacanthoma																												X		
BODY CAVITIES																														
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mucinous cystadenocarcinoma, metastatic																														
Sarcoma, NOS, invasive																														
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mucinous cystadenocarcinoma, metastatic																														
ALL OTHER SYSTEMS																														
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenocarcinoma, NOS, metastatic	X																										X			X
Mucinous cystadenocarcinoma, metastatic																														
Mucinous adenocarcinoma, metastatic							X					X														X				
Signet ring carcinoma, metastatic																										X				
Endometrial stromal sarcoma, metastatic				X				X																						
Monocytic leukemia																														X
Adipose tissue																														
Sarcoma, NOS, invasive																														

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	601	602	603	604	605	606	607	608	609	610	611	612	613	614	615	616	617	618	619	620	621	622	623	624	625
WEEKS ON STUDY	95	84	96	74	93	78	77	84	76	58	85	15	83	69	00	63	85	77	30	67	06	77	66	88	88
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS											X												X		
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma		X																							
Sarcoma, NOS, invasive																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																									
C-cell adenoma																							X		
C-cell carcinoma																									
Parathyroid	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Papillary cystadenoma, NOS																									
Fibroadenoma																									
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	X	X	N	N	N	N	N	N	N	N
Carcinoma, NOS	X																								
Vagina	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Endometrial stromal sarcoma, invasive																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma																									
Endometrial stromal polyp			X	X	X							X													
Endometrial stromal sarcoma																									
Endometrial stromal sarcoma, invasive																									
Mixed tumor, metastatic																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mixed tumor, metastatic																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma																									
SPECIAL SENSE ORGANS																									
Zymbal gland	+	N	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+
Carcinoma, NOS			X	X		X				X															
Squamous cell papilloma																									
Keratoacanthoma																									
BODY CAVITIES																									
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mucinous cystadenocarcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mucinous cystadenocarcinoma, metastatic																									
ALL OTHER SYSTEMS																									
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenocarcinoma, NOS, metastatic																									
Mucinous cystadenocarcinoma, metastatic																									
Mucinous adenocarcinoma, metastatic																									
Signet ring carcinoma, metastatic																									
Endometrial stromal sarcoma, metastatic																									
Monocytic leukemia	X	X	X	X							X											X			X
Adipose tissue																									
Sarcoma, NOS, invasive																									

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE (Continued)

ANIMAL NUMBER	90	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	
WEEKS ON STUDY	18	11	11	17	09	05	06	02	02	05	00	02	01	09	08	04	06	00	05	04	05	04	05	04	05	00	05	07	07	07	07	
INTEGUMENTARY SYSTEM																																
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell papilloma																																
Squamous cell carcinoma			X																													
Basal cell tumor																																
Keratoacanthoma																																
Fibrosarcoma																																
Osteosarcoma																																
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS																																
Fibroma																																
Fibrosarcoma						X																										
Lipoma																																
Neurofibroma																																
Neurofibrosarcoma																																
RESPIRATORY SYSTEM																																
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell carcinoma, metastatic			X																													
Alveolar/bronchiolar carcinoma																																
Cortical carcinoma, metastatic																																
C cell carcinoma, metastatic																																
Sarcoma, NOS, metastatic																																
Liposarcoma, metastatic																																
Osteosarcoma, metastatic																																
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMATOPOIETIC SYSTEM																																
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma, NOS, metastatic																																
C cell carcinoma, metastatic																																
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma, NOS																																
CIRCULATORY SYSTEM																																
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS																																
Neurilemoma, malignant																																
Blood vessels	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Nonchromaffin paraganglioma																																
DIGESTIVE SYSTEM																																
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Squamous cell papilloma																																
Squamous cell carcinoma																																
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS																																
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Neoplastic nodule	X																															
Malignant lymphoma, histiocytic type																																
Kupffer cell sarcoma																																
Monocytic leukemia																																
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Islet cell carcinoma																																
Mixed tumor, benign																																
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell carcinoma																																
Leiomyosarcoma																																
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenoma, NOS																																
Adenomatous polyp, NOS																																
Mucinous cystadenocarcinoma																																
Leiomyosarcoma																																
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lipoma																																
Leiomyosarcoma																																
Neurofibroma																																
URINARY SYSTEM																																
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma, NOS																																
Mixed tumor, benign																																
Mixed tumor, malignant																																
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Transitional cell papilloma																																
Transitional cell carcinoma																																

@ Multiple occurrence of morphology

**TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	975	976	977	978	979	980	981	982	983	984	985	986	987	988	989	990	991	992	993	994	995	996	997	998	999	1000	TOTAL TISSUES TUMORS
WEEKS ON STUDY	123	123	127	121	099	125	126	123	084	124	123	121	121	124	020	129	123	122	124	120	122	124	126	127	128	120	
INTEGUMENTARY SYSTEM																											
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*250
Squamous cell papilloma														X													3
Squamous cell carcinoma																											1
Basal cell tumor																											3
Keratoacanthoma																											2
Fibrosarcoma																											1
Osteosarcoma																											1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*250
Sarcoma, NOS																											6
Fibroma																											8
Fibrosarcoma																											4
Lipoma																											2
Neurofibroma																											1
Neurofibrosarcoma																											1
RESPIRATORY SYSTEM																											
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Squamous cell carcinoma, metastatic																											1
Alveolar/bronchiolar carcinoma																											1
Cortical carcinoma, metastatic																											1
C cell carcinoma, metastatic										X	X																2
Sarcoma, NOS, metastatic																											1
Liposarcoma, metastatic																											1
Osteosarcoma, metastatic																											1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
HEMATOPOIETIC SYSTEM																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Adenocarcinoma, NOS, metastatic																											1
C-cell carcinoma, metastatic														X													3
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	210
Adenocarcinoma, NOS																											1
CIRCULATORY SYSTEM																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Sarcoma, NOS																											1
Neurileioma, malignant																											1
Blood vessels	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*250
Nonchromaffin paraganglioma																											1
DIGESTIVE SYSTEM																											
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*250
Squamous cell papilloma																											2
Squamous cell carcinoma																											2
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	246
Sarcoma, NOS																											1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Neoplastic nodule																											10
Malignant lymphoma, histiocytic type																											1
Kupffer cell sarcoma																											1
Monocytic leukemia																											4
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*250
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Islet cell carcinoma																											1
Mixed tumor, benign																											1
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	246
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Squamous cell carcinoma																											1
Leiomyosarcoma																											1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Adenoma, NOS																											1
Adenomatous polyp, NOS																											1
Mucinous cystadenocarcinoma																											1
Leiomyosarcoma																											1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Lipoma																											1
Leiomyosarcoma																											1
Neurofibroma																											1
URINARY SYSTEM																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Sarcoma, NOS																											1
Mixed tumor, benign																											1
Mixed tumor, malignant																											1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	248
Transitional cell papilloma																											1
Transitional cell carcinoma																											2

* Animals necropsied

**TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	WEEKS ON STUDY																									
	1	1	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	0	1	0	1	0	1	0	1
	2	2	2	2	3	3	3	3	3	3	3	3	3	3	4	4	4	4	4	4	4	4	4	4	4	4
	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	
ENDOCRINE SYSTEM																										
Pituitary																										
Carcinoma, NOS																										
Adenoma, NOS	X						X	X	X		X	X	X	X			X				X				X	
Adrenal																										
Cortical adenoma	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Cortical carcinoma																										
Pheochromocytoma																										
Pheochromocytoma, malignant																										
Thyroid																										
Follicular cell adenoma				X																						
Follicular cell carcinoma																										
C cell adenoma																										
C-cell carcinoma	X		X							X	X					X	X	X			X				X	
Parathyroid																										
Pancreatic islets																										
Islet cell adenoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Islet cell carcinoma																										
REPRODUCTIVE SYSTEM																										
Mammary gland																										
Adenoma, NOS																										
Adenocarcinoma, NOS																										
Papillary adenocarcinoma																										
Papillary cystadenoma, NOS																										
Fibroadenoma	N	X	X				X		X	X		X	X	X	X		X	X	X						X	
Preputial/clitoral gland																										
Carcinoma, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Adenoma, NOS																										
Keratoacanthoma																										
Sarcoma, NOS, invasive																										
Uterus																										
Carcinoma, NOS																										
Adenocarcinoma, NOS																										
Papillary adenoma																										
Papillary adenocarcinoma																										
Leiomyoma																										
Leiomyosarcoma																										
Endometrial stromal polyp			X		X			X												X					X	
Endometrial stromal sarcoma																										
Endometrial stromal sarcoma, invasive																										
Ovary																										
Papillary cystadenoma, NOS																										
Thecoma																										
Granulosa cell tumor	X																									
NERVOUS SYSTEM																										
Nerves																										
Squamous cell carcinoma, metastatic	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Brain																										
Carcinoma, NOS, invasive																										
Granular cell tumor, NOS																										
Glioma, NOS																										
Astrocytoma																										
Astrocytoma, invasive																										
SPECIAL SENSE ORGANS																										
Zymbal gland																										
Carcinoma, NOS																										
Squamous cell papilloma																							N		+	+
MUSCULOSKELETAL SYSTEM																										
Bone																										
Osteosarcoma	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
BODY CAVITIES																										
Peritoneum																										
Pheochromocytoma, invasive																										
Sarcoma, NOS, metastatic																										
Fibrosarcoma																										
Endometrial stromal sarcoma, invasive																										
Mesentery																										
Leiomyosarcoma, invasive																										
Mesothelioma, malignant																										
ALL OTHER SYSTEMS																										
Multiple organs, NOS																										
Carcinoma, NOS, invasive																										
Squamous cell carcinoma, metastatic																										
Sarcoma, NOS, invasive																										
Sarcoma, NOS, metastatic																										
Liposarcoma, metastatic																										
Mesothelioma, invasive																										
Myelomonocytic leukemia																										
Monocytic leukemia				X		X		X	X							X	X			X	X	X	X			

**TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	0500	0501	0502	0503	0504	0505	0506	0507	0508	0509	0510	0511	0512	0513	0514	0515	0516	0517	0518	0519	0520	0521	0522	0523	0524	0525	0526	0527	0528	0529	0530	0531	0532	0533	0534	0535		
WEEKS ON STUDY	1138	1139	1140	1141	1142	1143	1144	1145	1146	1147	1148	1149	1150	1151	1152	1153	1154	1155	1156	1157	1158	1159	1160	1161	1162	1163	1164	1165	1166	1167	1168	1169	1170	1171	1172	1173	1174	1175
ENDOCRINE SYSTEM																																						
Pituitary	+																																					
Carcinoma, NOS																																						
Adenoma, NOS				X	X	X		X	X	X	X	X		X	X		X	X																			X	
Adrenal	+																																					
Cortical adenoma				X																																		
Cortical carcinoma																																						
Pheochromocytoma							X				X				X																							
Pheochromocytoma, malignant																																						
Thyroid	+																																					
Follicular cell adenoma																																						
Follicular cell carcinoma																																						
C cell adenoma																																						
C-cell carcinoma			X	X					X																												X	
Parathyroid	+																																					
Pancreatic islets																																						
Islet cell adenoma																																						
Islet cell carcinoma					X																																	
REPRODUCTIVE SYSTEM																																						
Mammary gland	+																																					
Adenoma, NOS					X	X			X																													
Adenocarcinoma, NOS																																						
Papillary adenocarcinoma																																						
Papillary cystadenoma, NOS																																						
Fibroadenoma		X	X	X	X				X	X	X	X		X				X			X	X																
Preputial/choral gland	N																																					
Carcinoma, NOS																																						
Adenoma, NOS																																						
Keratoacanthoma																																						
Sarcoma, NOS, invasive																																						
Uterus	+																																					
Carcinoma, NOS																																						
Adenocarcinoma, NOS																																						
Papillary adenoma																																						
Papillary adenocarcinoma																																						
Leiomyoma																																						
Leiomyosarcoma																																						
Endometrial stromal polyp																																						
Endometrial stromal sarcoma																																					X	
Endometrial stromal sarcoma, invasive																																						X
Ovary	+																																					
Papillary cystadenoma, NOS																																						
Thecoma																																						
Granulosa cell tumor																																						X
NERVOUS SYSTEM																																						
Nerves	N																																					
Squamous cell carcinoma, metastatic																																						
Brain	+																																					
Carcinoma, NOS, invasive																																						
Granular cell tumor, NOS																																						
Glioma, NOS																																						
Astrocytoma																																						
Astrocytoma, invasive																																						
SPECIAL SENSE ORGANS																																						
Zymbal gland	+																																					
Carcinoma, NOS																																						
Squamous cell papilloma																																						
MUSCULOSKELETAL SYSTEM																																						
Bone	N																																					
Osteosarcoma																																						
BODY CAVITIES																																						
Pertoneum	N																																					
Pheochromocytoma, invasive																																						
Sarcoma, NOS, metastatic																																						
Fibrosarcoma																																						
Endometrial stromal sarcoma, invasive																																						X
Mesentery	N																																					
Leiomyosarcoma, invasive																																						
Mesothelioma, malignant																																						
ALL OTHER SYSTEMS																																						
Multiple organs, NOS	N																																					
Carcinoma, NOS, invasive																																						
Squamous cell carcinoma, metastatic																																						
Sarcoma, NOS, invasive																																						
Sarcoma, NOS, metastatic																																						
Liposarcoma, metastatic			X																																			
Mesothelioma, invasive																																						
Myelomonocytic leukemia					X	X	X			X	X																										X	
Monocytic leukemia																																						X

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE
(Continued)

ANIMAL NUMBER	075	076	077	078	079	080	081	082	083	084	085	086	087	088	089	090	091	092	093	094	095	096	097	098	099
WEEKS ON STUDY	12	14	15	19	21	22	23	26	26	30	32	33	33	37	37	41	42	43	43	47	47	51	51	52	52
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS	X		X		X	X	X	X						X						X	X			X	
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Cortical carcinoma								X						X											
Pheochromocytoma																									
Pheochromocytoma, malignant																									X
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma														X											
C cell adenoma	X		X																						
C cell carcinoma	X									X						X						X			X
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
Islet cell carcinoma								X																	
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS																									
Papillary adenocarcinoma																									
Papillary cystadenoma, NOS																									
Fibroadenoma																									
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
Adenoma, NOS																									
Keratoacanthoma																									
Sarcoma, NOS, invasive																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenocarcinoma, NOS																									
Papillary adenoma																									
Papillary adenocarcinoma																									
Leiomyoma																									
Leiomyosarcoma																									
Endometrial stromal polyp																									
Endometrial stromal sarcoma																									
Endometrial stromal sarcoma, invasive																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papillary cystadenoma, NOS																									
Thecoma																									
Granulosa cell tumor																									
NERVOUS SYSTEM																									
Nerves	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Squamous cell carcinoma, metastatic																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Granular cell tumor, NOS																									
Glioma, NOS																									
Astrocytoma																									
Astrocytoma, invasive																									
SPECIAL SENSE ORGANS																									
Zymbal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
MUSCULOSKELETAL SYSTEM																									
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Osteosarcoma																									
BODY CAVITIES																									
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pheochromocytoma, invasive																									
Sarcoma, NOS, metastatic																									
Fibrosarcoma																									
Endometrial stromal sarcoma, invasive																									
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leiomyosarcoma, invasive																									
Mesothelioma, malignant																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS, invasive																									
Squamous cell carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Sarcoma, NOS, metastatic																									
Liposarcoma, metastatic																									
Mesothelioma, invasive																									
Myelomonocytic leukemia																									
Monocytic leukemia	X		X		X																				

@ Multiple occurrence of morphology

**TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE
(Continued)**

ANIMAL NUMBER	9 7 5	9 7 6	9 7 7	9 7 8	9 7 9	9 8 0	9 8 1	9 8 2	9 8 3	9 8 4	9 8 5	9 8 6	9 8 7	9 8 8	9 8 9	9 9 0	9 9 1	9 9 2	9 9 3	9 9 4	9 9 5	9 9 6	9 9 7	9 9 8	9 9 9	TOTAL: TISSUES TUMORS			
WEEKS ON STUDY	1 2 3	1 2 3	1 2 7	1 3 1	0 8 9	1 4 5	1 2 6	1 4 2	0 8 2	1 4 2	1 4 3	1 4 2	1 4 3	1 4 5	1 4 2	0 9 5	1 4 2	1 4 2	1 4 2	1 4 3	1 4 4	1 4 5	1 4 6	1 4 7	1 4 8	0 7 0			
ENDOCRINE SYSTEM																													
Pituitary	+																										249		
Carcinoma, NOS	+																										11		
Adenoma, NOS	X		X																									107	
Adrenal	+																										249		
Cortical adenoma	+																										13		
Cortical carcinoma	+																										1		
Pheochromocytoma	+																										27		
Pheochromocytoma, malignant					X																							3	
Thyroid	+																										247		
Follicular cell adenoma	+																										10		
Follicular cell carcinoma			X																									3	
C-cell adenoma		X																										37	
C cell carcinoma							X		X																			29	
Parathyroid	+																										240		
Pancreatic islets	+																										249		
Islet cell adenoma	+																										7		
Islet cell carcinoma																									X			6	
REPRODUCTIVE SYSTEM																													
Mammary gland	+																										*250		
Adenoma, NOS	X																												13
Adenocarcinoma, NOS																													23
Papillary adenocarcinoma																													2
Papillary cystadenoma, NOS																													1
Fibroadenoma	X	X	X	X	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		135
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		*250
Carcinoma, NOS																													14
Adenoma, NOS																													1
Keratoacanthoma																													1
Sarcoma, NOS, invasive																													2
Uterus	+																										250		
Carcinoma, NOS	+																										2		
Adenocarcinoma, NOS	+																										1		
Papillary adenoma	+																										1		
Papillary adenocarcinoma	+																										1		
Leiomyoma	+																										1		
Leiomyosarcoma	+																										1		
Endometrial stromal polyp	+																										31		
Endometrial stromal sarcoma																													4
Endometrial stromal sarcoma, invasive					X																								2
Ovary	+																										250		
Papillary cystadenoma, NOS	+																										1		
Thecoma	+																										1		
Granulosa cell tumor																													3
NERVOUS SYSTEM																													
Nerves	N																										*250		
Squamous cell carcinoma, metastatic	N																										1		
Brain	+																										250		
Carcinoma, NOS, invasive	+																										8		
Granular cell tumor, NOS																													1
Ghoma, NOS																													1
Astrocytoma																													4
Astrocytoma, invasive							X							X															1
SPECIAL SENSE ORGANS																													
Zymbal gland	+																										*250		
Carcinoma, NOS																													4
Squamous cell papilloma				X																									3
MUSCULOSKELETAL SYSTEM																													
Bone	N																										*250		
Osteosarcoma																													2
BODY CAVITIES																													
Peritoneum	N																										*250		
Pheochromocytoma, invasive	N																										1		
Sarcoma, NOS, metastatic	N																										1		
Fibrosarcoma	N																										1		
Endometrial stromal sarcoma, invasive	N																										1		
Mesentery	N																										*250		
Leiomyosarcoma, invasive	N																										1		
Mesothelioma, malignant	N																										1		
ALL OTHER SYSTEMS																													
Multiple organs, NOS	N																										*250		
Carcinoma, NOS, invasive	N																										1		
Squamous cell carcinoma, metastatic	N																										1		
Sarcoma, NOS, invasive																													2
Sarcoma, NOS, metastatic																													1
Liposarcoma, metastatic																													1
Mesothelioma, invasive																													1
Myelomonocytic leukemia																													1
Monocytic leukemia	X	X					X	X																		X	X	X	78

* Animals necropsied

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: 1% AMOSITE AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE

ANIMAL NUMBER	3 5 1	3 5 2	3 5 3	3 5 4	3 5 5	3 5 6	3 5 7	3 5 8	3 5 9	3 5 0	3 5 1	3 5 2	3 5 3	3 5 4	3 5 5	3 5 6	3 5 7	3 5 8	3 5 9	3 5 0	3 5 1	3 5 2	3 5 3	3 5 4	3 5 5	3 5 6	3 5 7	3 5 8	3 5 9	3 5 0	3 5 1	3 5 2	3 5 3	3 5 4	3 5 5	3 5 6	3 5 7	3 5 8	3 5 9			
WEEKS ON STUDY	0 8 3	0 9 7	1 0 0	1 0 6	1 0 6	0 8 7	1 0 6	1 0 6	0 6 9	0 6 4	0 6 9	0 6 0	1 0 2	1 0 2	1 0 2	0 5 5	0 6 4	0 6 7	0 6 8	0 6 6	0 6 3	0 6 5	0 6 5	0 6 5	0 6 4	0 6 5	0 6 5	0 6 4	0 6 8	0 6 5	0 6 5	0 6 5	0 6 5	0 6 4	0 6 5	0 6 5	0 6 4	0 6 5	0 6 5	0 6 7	0 6 8	0 6 9
INTEGUMENTARY SYSTEM																																										
Skin	+																																									
Squamous cell papilloma	+																																									
Basal cell carcinoma	+																																									
Fibrosarcoma	+																																									
Carcinosarcoma	+																																									
Subcutaneous tissue	+																																									
Carcinoma, NOS, invasive	+																																									
RESPIRATORY SYSTEM																																										
Lungs and bronchi	+																																									
Alveolar/bronchiolar adenoma	+																																									
Alveolar/bronchiolar carcinoma	+																																									
Pheochromocytoma, metastatic	+																																									
Liposarcoma, metastatic	+																																									
Mixed tumor, metastatic	+																																									
Carcinosarcoma, metastatic	+																																									
Trachea	+																																									
HEMATOPOIETIC SYSTEM																																										
Bone marrow	+																																									
Spleen	+																																									
Lymph nodes	+																																									
Adenocarcinoma, NOS, metastatic	+																																									
Adenocarcinoma in adenomatous polyp, metastatic	+																																									
Mucinous cystadenocarcinoma, metastatic	+																																									
Signet ring carcinoma, metastatic	+																																									
Thymus	+																																									
CIRCULATORY SYSTEM																																										
Heart	+																																									
Mixed tumor, metastatic	+																																									
DIGESTIVE SYSTEM																																										
Oral cavity	N																																									
Squamous cell papilloma	+																																									
Salivary gland	+																																									
Liver	+																																									
Neoplastic nodule	+																																									
Hepatocellular carcinoma	+																																									
Neurofibrosarcoma	+																																									
Monocytic leukemia	+																																									
Bile duct	+																																									
Gallbladder & common bile duct	+																																									
Pancreas	+																																									
Mixed tumor, invasive	+																																									
Esophagus	+																																									
Stomach	+																																									
Squamous cell papilloma	+																																									
Signet ring carcinoma, metastatic	+																																									
Mixed tumor, invasive	+																																									
Small intestine	+																																									
Adenocarcinoma, NOS	+																																									
Adenocarcinoma in adenomatous polyp	+																																									
Adenocarcinoma in adenomatous polyp, metastatic	+																																									
Mucinous cystadenocarcinoma	+																																									
Signet ring carcinoma	+																																									
Large intestine	+																																									
Carcinoma in situ, NOS	+																																									
Adenocarcinoma, NOS	+																																									
Adenomatous polyp, NOS	+																																									
Adenocarcinoma in adenomatous polyp	+																																									
Mucinous cystadenocarcinoma	+																																									
Mucinous cystadenocarcinoma, metastatic	+																																									
Signet ring carcinoma	+																																									
Signet ring carcinoma, metastatic	+																																									
Rectum	+																																									
Adenomatous polyp, NOS	+																																									
URINARY SYSTEM																																										
Kidney	+																																									
Tubular cell adenoma	+																																									
Tubular cell adenocarcinoma	+																																									
Sarcoma, NOS	+																																									
Mixed tumor, malignant	+																																									
Hemangioma	+																																									
Urinary bladder	+																																									
Endometrial stromal sarcoma, invasive	-																																									

@ Multiple occurrence of morphology

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	4
WEEKS ON STUDY	6	7	7	7	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	9
INTEGUMENTARY SYSTEM																								
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																								
Basal cell carcinoma																								
Fibrosarcoma																								
Carcinosarcoma																								
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																								
RESPIRATORY SYSTEM																								
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																								
Alveolar/bronchiolar carcinoma																								
Pheochromocytoma, metastatic																								
Liposarcoma, metastatic																								
Mixed tumor, metastatic																								
Carcinosarcoma, metastatic																								
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																								
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic							X																	
Adenocarcinoma in adenomatous polyp, metastatic																	X							
Mucinous cystadenocarcinoma, metastatic																								
Signet ring carcinoma, metastatic																								X
Thymus	+	+	-	+	+	+	-	-	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	-
CIRCULATORY SYSTEM																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mixed tumor, metastatic																								
DIGESTIVE SYSTEM																								
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Squamous cell papilloma																								
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule						X					X													
Hepatocellular carcinoma									X		X													
Neurofibrosarcoma																								
Monocytic leukemia																								
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mixed tumor, invasive																								
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																								
Signet ring carcinoma, metastatic																								
Mixed tumor, invasive																								
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																								
Adenocarcinoma in adenomatous polyp																								
Adenocarcinoma in adenomatous polyp, metastatic																								
Mucinous cystadenocarcinoma																								
Signet ring carcinoma																								
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma in situ, NOS																								
Adenocarcinoma, NOS																								
Adenomatous polyp, NOS																								
Adenocarcinoma in adenomatous polyp	X	X																						X
Mucinous cystadenocarcinoma																								X
Mucinous cystadenocarcinoma, metastatic																								
Signet ring carcinoma																								
Signet ring carcinoma, metastatic																								
Rectum	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS																								
URINARY SYSTEM																								
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																								
Tubular cell adenocarcinoma																								
Sarcoma, NOS	X																							
Mixed tumor, malignant			X																					
Hemangioma																								
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrial stromal sarcoma, invasive																								

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70
WEEKS ON STUDY	071	107	008	009	015	000	000	006	007	011	011	000	011	011	011	000	011	011	000	011	000	011	000	011	010
INTEGUMENTARY SYSTEM																									
Skin																									
Squamous cell papilloma																									
Basal cell carcinoma																									
Fibrosarcoma																									
Carcinosarcoma																									
Subcutaneous tissue																									
Carcinoma, NOS, invasive																									
RESPIRATORY SYSTEM																									
Lungs and bronchi																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic																									
Mixed tumor, metastatic																									
Carcinosarcoma, metastatic																									
Trachea																									
HEMATOPOIETIC SYSTEM																									
Bone marrow																									
Spleen																									
Lymph nodes																									
Adenocarcinoma, NOS, metastatic																									
Adenocarcinoma in adenomatous polyp, metastatic																									
Mucinous cystadenocarcinoma, metastatic																									
Signet ring carcinoma, metastatic																									
Thymus																									
CIRCULATORY SYSTEM																									
Heart																									
Mixed tumor, metastatic																									
DIGESTIVE SYSTEM																									
Oral cavity																									
Squamous cell papilloma																									
Salivary gland																									
Liver																									
Neoplastic nodule																									
Hepatocellular carcinoma																									
Neurofibrosarcoma																									
Monocytic leukemia																									
Bile duct																									
Gallbladder & common bile duct																									
Pancreas																									
Mixed tumor, invasive																									
Esophagus																									
Stomach																									
Squamous cell papilloma																									
Signet ring carcinoma, metastatic																									
Mixed tumor, invasive																									
Small intestine																									
Adenocarcinoma, NOS																									
Adenocarcinoma in adenomatous polyp																									
Adenocarcinoma in adenomatous polyp, metastatic																									
Mucinous cystadenocarcinoma																									
Signet ring carcinoma																									
Large intestine																									
Carcinoma in situ, NOS																									
Adenocarcinoma, NOS																									
Adenomatous polyp, NOS																									
Adenocarcinoma in adenomatous polyp																									
Mucinous cystadenocarcinoma																									
Mucinous cystadenocarcinoma, metastatic																									
Signet ring carcinoma																									
Signet ring carcinoma, metastatic																									
Rectum																									
Adenomatous polyp, NOS																									
URINARY SYSTEM																									
Kidney																									
Tubular cell adenoma																									
Tubular cell adenocarcinoma																									
Sarcoma, NOS																									
Mixed tumor, malignant																									
Hemangioma																									
Urinary bladder																									
Endometrial stromal sarcoma, invasive																									

@ Multiple occurrence of morphology

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	3151	3152	3153	3154	3155	3156	3157	3158	3159	3160	3161	3162	3163	3164	3165	3166	3167	3168	3169	3170	3171	3172	3173	3174	3175
WEEKS ON STUDY	083	097	100	116	116	008	116	116	006	007	007	007	112	112	112	005	007	007	009	008	006	007	007	009	007
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS	X			X	X				X			X		X											
Adrenal	+	+	+	+	+				+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma								X								X						X			
Pheochromocytoma																									
Pheochromocytoma, malignant																									
Sarcoma, NOS, invasive																									
Mixed tumor, invasive																									
Ganglioneuroma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																									
C-cell adenoma																									
C-cell carcinoma						X																			X
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									X
Papillary adenocarcinoma																									
Fibroadenoma					X																				
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
Keratoacanthoma																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Leiomyoma																									
Endometrial stromal polyp					X																				
Endometrial stromal sarcoma																	X						X		X
Endometrial stromal sarcoma, invasive																									
Angioma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papillary cystadenocarcinoma, NOS																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Ear	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Zymbal gland	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS	X											X									X				
Squamous cell papilloma														X											
Keratoacanthoma																									
MUSCULOSKELETAL SYSTEM																									
Bone	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS, invasive																									
BODY CAVITIES																									
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Signet ring carcinoma, metastatic																									
Pericardium	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, NOS																									
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Sarcoma, NOS, invasive																									
Lipoma					X																				
Mixed tumor, invasive																									
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenocarcinoma, NOS, metastatic																									
Sarcoma, NOS, invasive																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenocarcinoma, NOS, metastatic	X							X															X	N	N
Mucinous cystadenocarcinoma, metastatic																							X	X	X
Signet ring carcinoma, metastatic																									
Monocytic leukemia		X	X		X	X						X	X						X						
Orbital region																									
Sarcoma, NOS																									

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	376	377	378	379	380	381	382	383	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	
WEEKS ON STUDY	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075	076	077	078	079	080
ENDOCRINE SYSTEM																										
Pituitary																										
Carcinoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																		X	X							
Adrenal																										
Cortical adenoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma																										
Pheochromocytoma, malignant																										
Sarcoma, NOS, invasive																										
Mixed tumor, invasive																										
Ganglioneuroma																										
Thyroid																										
Follicular cell adenoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma																										
C-cell adenoma																										
C-cell carcinoma																										
Parathyroid																										
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																										
Mammary gland																										
Adenoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papillary adenocarcinoma																										
Fibroadenoma																										
Preputial/clitoral gland																										
Carcinoma, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Keratoacanthoma																										
Uterus																										
Fibrosarcoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyoma																										
Endometrial stromal polyp																										
Endometrial stromal sarcoma																										
Endometrial stromal sarcoma, invasive																										
Angioma																										
Ovary																										
Papillary cystadenocarcinoma, NOS																										
NERVOUS SYSTEM																										
Brain																										
SPECIAL SENSE ORGANS																										
Ear																										
Squamous cell papilloma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																										
Zymbal gland																										
Carcinoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																										
Keratoacanthoma																										
MUSCULOSKELETAL SYSTEM																										
Bone																										
Carcinoma, NOS, invasive	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
BODY CAVITIES																										
Mediastinum																										
Signet ring carcinoma, metastatic	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pericardium																										
Mesothelioma, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Peritoneum																										
Sarcoma, NOS, invasive	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Lipoma																										
Mixed tumor, invasive																										
Mesentery																										
Adenocarcinoma, NOS, metastatic	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Sarcoma, NOS, invasive																										
ALL OTHER SYSTEMS																										
Multiple organs, NOS																										
Adenocarcinoma, NOS, metastatic	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mucinous cystadenocarcinoma, metastatic																										
Signet ring carcinoma, metastatic																										
Monocytic leukemia																										
Orbital region																										
Sarcoma, NOS																										

**TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE AND
i,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)**

ANIMAL NUMBER	420	421	422	423	424	425	426	427	428	429	430	431	432	433	434	435	436	437	438	439	440
WEEKS ON STUDY	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ENDOCRINE SYSTEM																					
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																					
Adenoma, NOS																					
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																					
Pheochromocytoma																					
Pheochromocytoma, malignant																					
Sarcoma, NOS, invasive																					
Mixed tumor, invasive																					
Ganglioneuroma																					
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																					
Follicular cell carcinoma																					
C-cell adenoma																					
C-cell carcinoma																					
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																					
REPRODUCTIVE SYSTEM																					
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																					
Papillary adenocarcinoma																					
Fibroadenoma																					
Pregutal/choral gland																					
Carcinoma, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Keratoacanthoma																					
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																					
Leiomyoma																					
Endometrial stromal polyp																					
Endometrial stromal sarcoma																					
Endometrial stromal sarcoma, invasive																					
Angioma																					
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papillary cystadenocarcinoma, NOS																					
NERVOUS SYSTEM																					
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																					
Ear	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																					
Squamous cell carcinoma																					
Zymbal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS	X																				
Squamous cell papilloma																					
Keratoacanthoma																					
MUSCULOSKELETAL SYSTEM																					
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS, invasive																					
BODY CAVITIES																					
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Signet ring carcinoma, metastatic																					
Pericardium	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, NOS																					
Pertoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Sarcoma, NOS, invasive																					
Lipoma																					
Mixed tumor, invasive																					
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenocarcinoma, NOS, metastatic																					
Sarcoma, NOS, invasive																					
ALL OTHER SYSTEMS																					
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenocarcinoma, NOS, metastatic																					
Mucinous cystadenocarcinoma, metastatic																					
Signet ring carcinoma, metastatic																					
Monocytic leukemia	X																				
Orbital region																					
Sarcoma, NOS																					

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	496	497	498	499	500
WEEKS ON STUDY	071	103	078	079	080	106	081	082	083	084	110	111	087	112	113	114	089	115	116	094	117	095	118	119	120
ENDOCRINE SYSTEM																									
Pituitary																									
Carcinoma, NOS																									
Adenoma, NOS																									
Adrenal																									
Cortical adenoma																									
Pheochromocytoma																									
Pheochromocytoma, malignant																									
Sarcoma, NOS, invasive																									
Mixed tumor, invasive																									
Ganglioneuroma																									
Thyroid																									
Follicular cell adenoma																									
Follicular cell carcinoma																									
C cell adenoma																									
C-cell carcinoma																									
Parathyroid																									
Pancreatic islets																									
Islet cell adenoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland																									
Adenoma, NOS																									
Papillary adenocarcinoma																									
Fibroadenoma																									
Pregutal/choral gland																									
Carcinoma, NOS																									
Keratoacanthoma																									
Uterus																									
Fibrosarcoma																									
Leiomyoma																									
Endometrial stromal polyp																									
Endometrial stromal sarcoma																									
Endometrial stromal sarcoma, invasive																									
Angioma																									
Ovary																									
Papillary cystadenocarcinoma, NOS																									
NERVOUS SYSTEM																									
Brain																									
SPECIAL SENSE ORGANS																									
Ear																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Zymbal gland																									
Carcinoma, NOS																									
Squamous cell papilloma																									
Keratoacanthoma																									
MUSCULOSKELETAL SYSTEM																									
Bone																									
Carcinoma, NOS, invasive																									
BODY CAVITIES																									
Mediastinum																									
Signet ring carcinoma, metastatic																									
Pericardium																									
Mesothelioma, NOS																									
Peritoneum																									
Sarcoma, NOS, invasive																									
Lipoma																									
Mixed tumor, invasive																									
Mesentery																									
Adenocarcinoma, NOS, metastatic																									
Sarcoma, NOS, invasive																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS																									
Adenocarcinoma, NOS, metastatic																									
Mucinous cystadenocarcinoma, metastatic																									
Signet ring carcinoma, metastatic																									
Monocytic leukemia																									
Orbital region																									
Sarcoma, NOS																									

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE AND PREWEANING GAVAGE (Continued)

ANIMAL NUMBER	676	677	678	679	680	681	682	683	684	685	686	687	688	689	690	691	692	693	694	695	696	697	698	699	700	
WEEKS ON STUDY	06	13	22	31	40	47	54	62	70	77	85	92	100	107	115	122	130	137	145	152	160	167	175	182	190	197
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell tumor																										
Basal cell carcinoma																										
Fibroma																										
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																										
Fibroma																										
Fibrosarcoma																										
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, metastatic																										
Alveolar/bronchiolar carcinoma																										
C cell carcinoma, metastatic																										
Sarcoma, NOS, metastatic																										
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C cell carcinoma, invasive																										
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lipoma																										
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																										
Thymoma																										
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																										
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																										
Monocytic leukemia																										
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma																										
Sarcoma, NOS																										
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																										
Adenomatous polyp, NOS																										
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mixed tumor, malignant																										
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Transitional cell papilloma																										

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE AND PREWEANING GAVAGE (Continued)

ANIMAL NUMBER	7 0 1	7 0 2	7 0 3	7 0 4	7 0 5	7 0 6	7 0 7	7 0 8	7 0 9	7 0 0	7 1 1	7 1 2	7 1 3	7 1 4	7 1 5	7 1 6	7 1 7	7 1 8	7 1 9	7 2 0	7 2 1	7 2 2	7 2 3	7 2 4	7 2 5	TOTAL TISSUES TUMORS		
WEEKS ON STUDY	1 2	1 7	1 1	0 4	1 8	1 7	0 8	1 6	1 0	1 7	1 1	0 5	1 5	0 0	1 2	0 6	1 9	1 3	1 8	1 0	1 7	1 2	0 1	1 4	0 9	1 1	0 5	1 0
INTEGUMENTARY SYSTEM																												
Skin																												
Basal cell tumor	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*100	
Basal cell carcinoma																											1	
Fibroma																											1	
Subcutaneous tissue	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*100	
Sarcoma, NOS																											1	
Fibroma	X																									2		
Fibrosarcoma																											1	
RESPIRATORY SYSTEM																												
Lungs and bronchi																												
Carcinoma, NOS, metastatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	100	
Alveolar/bronchiolar carcinoma																									X		1	
C-cell carcinoma, metastatic																									X		1	
Sarcoma, NOS, metastatic																											1	
Trachea																												
C cell carcinoma, invasive	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	
																											2	
HEMATOPOIETIC SYSTEM																												
Bone marrow																												
	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	
Spleen																												
Lipoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	
Thymus	+	+	-	+	+	+	-	+	+	+	+	+	+	+	-	+	+	-	-	+	-	+	+	+	+	+	81	
Carcinoma, NOS																											1	
Thymoma																											1	
CIRCULATORY SYSTEM																												
Heart																												
Sarcoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	
																											1	
DIGESTIVE SYSTEM																												
Salivary gland																												
Sarcoma, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+	+	+	+	100	
																											1	
Liver																												
Neoplastic nodule	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	
Monocytic leukemia																						X					4	
Bile duct																												
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	100	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	
Small intestine																												
Mucinous cystadenocarcinoma	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	
Sarcoma, NOS																											1	
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	
Carcinoma, NOS						X																					1	
Adenomatous polyp, NOS																											1	
URINARY SYSTEM																												
Kidney																												
Mixed tumor, malignant	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	1	
Transitional cell papilloma							X																				99	
																											1	

* Animals necropsied

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1% AMOSITE AND PREWEANING GAVAGE (Continued)

ANIMAL NUMBER	6676	6677	6678	6679	6680	6681	6682	6683	6684	6685	6686	6687	6688	6689	6690	6691	6692	6693	6694	6695	6696	6697	6698	6699	6700
WEEKS ON STUDY	106	103	102	103	100	101	104	102	102	100	104	109	101	100	102	104	101	102	103	102	102	101	102	100	101
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																						X			
Adenoma, NOS			X	X		X			X	X		X		X	X	X							X		
Ganglioglioma	X																								
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma																									
Mixed tumor, invasive								X	X								X								
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																								X	
C cell adenoma		X		X					X					X											
C-cell carcinoma																									
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS			X				X																		
Adenocarcinoma, NOS																						X		X	
Fibrosarcoma																									
Fibroadenoma		X	X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																						X			X
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Endometrial stromal polyp																							X		X
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor																									
Granulosa cell carcinoma																									
Sertoli cell tumor	X																								
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Astrocytoma																									
SPECIAL SENSE ORGANS																									
Eye	N	+	N	N	N	N	+	N	N	N	+	N	N	+	N	+	N	N	N	+	+	+	+	N	N
Leiomyosarcoma																									
Zymbal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Keratoacanthoma																									X
MUSCULOSKELETAL SYSTEM																									
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Osteosarcoma																									
BODY CAVITIES																									
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Sarcoma, NOS, metastatic																									
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Lipoma																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
C cell carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Fibrosarcoma, invasive																									
Osteosarcoma, metastatic																									
Myelomonocytic leukemia																									
Monocytic leukemia			X	X	X		X							X						X		X	X		X

TABLE B3a. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Skin: Squamous Cell Papilloma or Carcinoma				
Overall Rates (a)	3/117 (3%)	4/250 (2%)	0/100 (0%)	
Adjusted Rates (b)	18.2%	5.8%	0.0%	
Terminal Rates (c)	2/13 (15%)	1/30 (3%)	0/9 (0%)	
Week of First Observation	136	121		
Life Table Test (d)		P=0.357N	P=0.195N	
Incidental Tumor Test (d)		P=0.337N	P=0.154N	
Fisher Exact Test (d)		P=0.396N	P=0.155N	
Subcutaneous Tissue: Lipoma				
Overall Rates (a)	3/117 (3%)	2/250 (1%)	0/100 (0%)	
Adjusted Rates (b)	16.1%	1.6%	0.0%	
Terminal Rates (c)	2/13 (15%)	0/30 (0%)	0/9 (0%)	
Week of First Observation	84	111		
Life Table Test (d)		P=0.171N	P=0.179N	
Incidental Tumor Test (d)		P=0.196N	P=0.171N	
Fisher Exact Test (d)		P=0.187N	P=0.155N	
Subcutaneous Tissue: Fibroma				
Overall Rates (a)	7/117 (6%)	8/250 (3%)	3/100 (3%)	
Adjusted Rates (b)	26.8%	16.3%	8.4%	
Terminal Rates (c)	2/13 (12%)	4/30 (13%)	0/9 (0%)	
Week of First Observation	96	90	102	
Life Table Tests (d)		P=0.138N	P=0.341N	P=0.576
Incidental Tumor Tests (d)		P=0.178N	P=0.269N	P=0.593N
Fisher Exact Test (d)		P=0.165N	P=0.238N	P=0.612N
Subcutaneous Tissue: Fibroma or Neurofibroma				
Overall Rates (a)	7/117 (6%)	9/250 (4%)	3/100 (3%)	
Adjusted Rates (b)	26.8%	17.2%	8.4%	
Terminal Rates (c)	2/13 (12%)	4/30 (13%)	0/9 (0%)	
Week of First Observation	96	90	102	
Life Table Tests (d)		P=0.189N	P=0.341N	P=0.622N
Incidental Tumor Tests (d)		P=0.233N	P=0.269N	P=0.521N
Fisher Exact Test (d)		P=0.218N	P=0.238N	P=0.536N
Subcutaneous Tissue: Sarcoma				
Overall Rates (a)	0/117 (0%)	6/250 (2%)	1/100 (1%)	
Adjusted Rates (b)	0.0%	11.0%	2.0%	
Terminal Rates (c)	0/13 (0%)	2/30 (7%)	0/9 (0%)	
Week of First Observation		112	123	
Life Table Tests (d)		P=0.123	P=0.478	P=0.421N
Incidental Tumor Tests (d)		P=0.100	P=0.550	P=0.348N
Fisher Exact Test (d)		P=0.098	P=0.461	P=0.358N
Subcutaneous Tissue: Fibrosarcoma				
Overall Rates (a)	3/117 (3%)	5/250 (2%)	1/100 (1%)	
Adjusted Rates (b)	6.9%	5.7%	1.3%	
Terminal Rates (c)	0/13 (0%)	0/30 (0%)	0/9 (0%)	
Week of First Observation	105	124	109	
Life Table Tests (d)		P=0.452N	P=0.358N	P=0.498N
Incidental Tumor Tests (d)		P=0.503N	P=0.447N	P=0.412N
Fisher Exact Test (d)		P=0.497N	P=0.372N	P=0.450N
Subcutaneous Tissue: Fibroma or Fibrosarcoma				
Overall Rates (a)	10/117 (9%)	12/250 (5%)	4/100 (4%)	
Adjusted Rates (b)	31.8%	19.4%	0.6%	
Terminal Rates (c)	2/13 (15%)	4/30 (13%)	0/9 (0%)	
Week of First Observation	96	90	102	
Life Table Tests (d)		P=0.089N	P=0.207N	P=0.608N
Incidental Tumor Tests (d)		P=0.125N	P=0.189N	P=0.471N
Fisher Exact Test (d)		P=0.122N	P=0.139N	P=0.499N

TABLE B3a. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Subcutaneous Tissue: Sarcoma, Fibrosarcoma, or Neurofibrosarcoma				
Overall Rates (a)	3/117 (3%)	11/250 (4%)	2/100 (2%)	
Adjusted Rates (b)	6.9%	15.1%	3.3%	
Terminal Rates (c)	0/13 (0%)	2/30 (7%)	0/9 (0%)	
Week of First Observation	105	112	109	
Life Table Tests (d)		P=0.352	P=0.559N	P=0.312N
Incidental Tumor Tests (d)		P=0.286	P=0.612N	P=0.226N
Fisher Exact Test (d)		P=0.296	P=0.574N	P=0.230N
Subcutaneous Tissue: Fibroma, Neurofibroma, Sarcoma, Fibrosarcoma, or Neurofibrosarcoma				
Overall Rates (a)	10/117 (9%)	19/250 (8%)	5/100 (5%)	
Adjusted Rates (b)	31.8%	29.0%	11.3%	
Terminal Rates (c)	2/13 (15%)	6/30 (20%)	0/9 (0%)	
Week of First Observation	96	90	102	
Life Table Tests (d)		P=0.380N	P=0.305N	P=0.395N
Incidental Tumor Tests (d)		P=0.472N	P=0.271N	P=0.262N
Fisher Exact Test (d)		P=0.450N	P=0.226N	P=0.269N
Integumentary System or Salivary Gland: Sarcoma, Fibrosarcoma, or Neurofibrosarcoma				
Overall Rates (a)	5/117 (4%)	12/250 (5%)	3/100 (3%)	
Adjusted Rates (b)	15.8%	17.3%	5.9%	
Terminal Rates (c)	1/13 (8%)	3/30 (10%)	0/9 (0%)	
Week of First Observation	105	112	109	
Life Table Tests (d)		P=0.594N	P=0.457N	P=0.437N
Incidental Tumor Tests (d)		P=0.529	P=0.482N	P=0.332N
Fisher Exact Test (d)		P=0.529	P=0.451N	P=0.336N
Integumentary System or Salivary Gland: Fibroma, Neurofibroma, Sarcoma, Fibrosarcoma, or Neurofibrosarcoma				
Overall Rates (a)	11/117 (9%)	20/250 (8%)	6/100 (6%)	
Adjusted Rates (b)	33.2%	31.9%	13.7%	
Terminal Rates (c)	2/13 (15%)	7/30 (23%)	0/9 (0%)	
Week of First Observation	96	90	102	
Life Table Tests (d)		P=0.324N	P=0.333N	P=0.490N
Incidental Tumor Tests (d)		P=0.410N	P=0.297N	P=0.343N
Fisher Exact Test (d)		P=0.395N	P=0.251N	P=0.347N
Hematopoietic System: Leukemia				
Overall Rates (e)	40/117 (34%)	83/250 (33%)	35/100 (35%)	
Adjusted Rates (b)	82.4%	70.3%	70.5%	
Terminal Rates (c)	8/13 (62%)	13/30 (43%)	1/9 (11%)	
Week of First Observation	86	80	77	
Life Table Test (d)		P=0.275N	P=0.394	P=0.197
Incidental Tumor Test (d)		P=0.408N	P=0.558N	P=0.441
Fisher Exact Test (d)		P=0.471N	P=0.507	P=0.420
Oral Cavity: Squamous Cell Papilloma or Carcinoma				
Overall Rates (e)	1/117 (1%)	4/250 (2%)	0/100 (0%)	
Adjusted Rates (b)	2.4%	3.4%	0.0%	
Terminal Rates (c)	0/13 (0%)	0/30 (0%)	0/9 (0%)	
Week of First Observation	131	115		
Life Table Tests (d)		P=0.510	P=0.574N	
Incidental Tumor Tests (d)		P=0.541	P=0.535N	
Fisher Exact Test (d)		P=0.489	P=0.539N	

TABLE B3a. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Liver: Neoplastic Nodule				
Overall Rates (e)	4/117 (3%)	10/250 (4%)	4/100 (4%)	
Adjusted Rates (b)	9.6%	16.0%	20.4%	
Terminal Rates (c)	0/13 (0%)	2/30 (7%)	1/9 (11%)	
Week of First Observation	101	116	129	
Life Table Test (d)		P=0.577	P=0.468	P=0.484
Incidental Tumor Test (d)		P=0.600	P=0.556	P=0.585
Fisher Exact Test (d)		P=0.522	P=0.549	P=0.603
Liver: Neoplastic Nodule or Hepatocellular Carcinoma				
Overall Rates (e)	5/117 (4%)	10/250 (4%)	4/100 (4%)	
Adjusted Rates (b)	11.9%	16.0%	20.4%	
Terminal Rates (c)	0/13 (0%)	2/30 (7%)	1/9 (11%)	
Week of First Observation	101	116	129	
Life Table Test (d)		P=0.497N	P=0.561	P=0.484
Incidental Tumor Test (d)		P=0.472N	P=0.596N	P=0.585
Fisher Exact Test (d)		P=0.550N	P=0.597N	P=0.603
Pituitary Gland: Adenoma				
Overall Rates (e)	50/117 (43%)	107/249 (43%)	39/100 (39%)	
Adjusted Rates (b)	79.1%	80.4%	83.8%	
Terminal Rates (c)	6/13 (46%)	16/30 (53%)	5/9 (56%)	
Week of First Observation	71	73	94	
Life Table Test (d)		P=0.308N	P=0.469N	P=0.398
Incidental Tumor Test (d)		P=0.507N	P=0.266N	P=0.313N
Fisher Exact Test (d)		P=0.529	P=0.338N	P=0.288N
Pituitary Gland: Carcinoma				
Overall Rates (e)	2/117 (2%)	11/249 (4%)	3/100 (3%)	
Adjusted Rates (b)	2.2%	10.4%	4.7%	
Terminal Rates (c)	0/13 (0%)	1/30 (3%)	0/9 (0%)	
Week of First Observation	101	85	110	
Life Table Test (d)		P=0.194	P=0.467	P=0.457N
Incidental Tumor Test (d)		P=0.127	P=0.363	P=0.362N
Fisher Exact Test (d)		P=0.158	P=0.426	P=0.394N
Pituitary Gland: Adenoma or Carcinoma				
Overall Rates (e)	52/117 (44%)	118/249 (47%)	42/100 (42%)	
Adjusted Rates (b)	79.6%	83.1%	84.6%	
Terminal Rates (c)	6/13 (46%)	17/30 (57%)	5/9 (56%)	
Week of First Observation	71	73	94	
Life Table Test (d)		P=0.443N	P=0.521N	P=0.453
Incidental Tumor Test (d)		P=0.369	P=0.355N	P=0.229N
Fisher Exact Test (d)		P=0.340	P=0.411N	P=0.214N
Adrenal Cortex: Cortical Adenoma				
Overall Rates (e)	3/117 (3%)	13/249 (5%)	4/100 (4%)	
Adjusted Rates (b)	10.2%	18.6%	20.2%	
Terminal Rates (c)	1/13 (8%)	3/30 (10%)	1/9 (11%)	
Week of First Observation	101	115	117	
Life Table Tests (d)		P=0.256	P=0.389	P=0.563N
Incidental Tumor Tests (d)		P=0.260	P=0.451	P=0.455N
Fisher Exact Test (d)		P=0.190	P=0.414	P=0.433N
Adrenal Cortex: Cortical Adenoma or Carcinoma				
Overall Rates (e)	4/117 (3%)	14/249 (6%)	4/100 (4%)	
Adjusted Rates (b)	11.6%	19.2%	20.2%	
Terminal Rates (c)	1/13 (8%)	3/30 (10%)	1/9 (11%)	
Week of First Observation	101	115	117	
Life Table Tests (d)		P=0.344	P=0.533	P=0.505N
Incidental Tumor Tests (d)		P=0.369	P=0.615	P=0.393N
Fisher Exact Test (d)		P=0.264	P=0.549	P=0.375N

TABLE B3a. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Adrenal Medulla: Pheochromocytoma				
Overall Rates (e)	17/117 (15%)	27/249 (11%)	6/100 (6%)	
Adjusted Rates (b)	51.4%	40.3%	29.6%	
Terminal Rates (c)	4/13 (31%)	7/30 (23%)	1/9 (11%)	
Week of First Observation	103	107	117	
Life Table Test (d)		P=0.125N	P=0.067N	P=0.269N
Incidental Tumor Test (d)		P=0.146N	P=0.034N	P=0.141N
Fisher Exact Test (d)		P=0.199N	P=0.033N	P=0.113N
Adrenal Medulla: Pheochromocytoma or Malignant Pheochromocytoma				
Overall Rates (e)	18/117 (15%)	30/249 (12%)	6/100 (6%)	
Adjusted Rates (b)	51.8%	44.0%	29.6%	
Terminal Rates (c)	4/13 (31%)	8/30 (27%)	1/9 (11%)	
Week of First Observation	87	107	117	
Life Table Test (d)		P=0.150N	P=0.049N	P=0.191N
Incidental Tumor Test (d)		P=0.180N	P=0.025N	P=0.085N
Fisher Exact Test (d)		P=0.235N	P=0.022N	P=0.064N
Thyroid Gland: Follicular Cell Adenoma				
Overall Rates (e)	2/116 (2%)	10/247 (4%)	3/100 (3%)	
Adjusted Rates (b)	4.4%	14.4%	7.2%	
Terminal Rates (c)	0/13 (0%)	1/30 (3%)	0/9 (0%)	
Week of First Observation	117	120	114	
Life Table Test (d)		P=0.258	P=0.396	P=0.577N
Incidental Tumor Test (d)		P=0.290	P=0.537	P=0.466N
Fisher Exact Test (d)		P=0.204	P=0.430	P=0.456N
Thyroid Gland: Follicular Cell Carcinoma				
Overall Rates (e)	7/116 (6%)	3/247 (1%)	2/100 (2%)	
Adjusted Rates (b)	26.0%	5.7%	11.0%	
Terminal Rates (c)	1/13 (8%)	1/30 (3%)	0/9 (0%)	
Week of First Observation	111	121	124	
Life Table Test (d)		P=0.007N	P=0.171N	P=0.388
Incidental Tumor Test (d)		P=0.008N	P=0.114N	P=0.456
Fisher Exact Test (d)		P=0.014N	P=0.127N	P=0.448
Thyroid Gland: Follicular Cell Adenoma or Carcinoma				
Overall Rates (e)	9/116 (8%)	13/247 (5%)	5/100 (5%)	
Adjusted Rates (b)	29.3%	19.4%	17.4%	
Terminal Rates (c)	1/13 (8%)	2/30 (7%)	0/9 (0%)	
Week of First Observation	111	120	114	
Life Table Test (d)		P=0.171N	P=0.370N	P=0.484
Incidental Tumor Test (d)		P=0.151N	P=0.223N	P=0.602N
Fisher Exact Test (d)		P=0.240N	P=0.296N	P=0.579N
Thyroid Gland: C-Cell Adenoma				
Overall Rates (e)	14/116 (12%)	37/247 (15%)	15/100 (15%)	
Adjusted Rates (b)	43.1%	44.8%	49.5%	
Terminal Rates (c)	2/13 (15%)	7/30 (23%)	1/9 (11%)	
Week of First Observation	108	73	99	
Life Table Test (d)		P=0.412	P=0.203	P=0.304
Incidental Tumor Test (d)		P=0.383	P=0.362	P=0.504
Fisher Exact Test (d)		P=0.284	P=0.333	P=0.558
Thyroid Gland: C-Cell Carcinoma				
Overall Rates (e)	10/116 (9%)	29/247 (12%)	14/100 (14%)	
Adjusted Rates (b)	35.3%	38.6%	48.8%	
Terminal Rates (c)	3/13 (23%)	5/30 (17%)	2/9 (22%)	
Week of First Observation	107	75	106	
Life Table Test (d)		P=0.346	P=0.119	P=0.169
Incidental Tumor Test (d)		P=0.282	P=0.156	P=0.305
Fisher Exact Test (d)		P=0.241	P=0.150	P=0.339

TABLE B3a. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Thyroid Gland: C-Cell Adenoma or Carcinoma				
Overall Rates (e)	24/116 (21%)	65/247 (26%)	29/100 (29%)	
Adjusted Rates (b)	65.4%	68.1%	75.4%	
Terminal Rates (c)	5/13 (38%)	12/30 (40%)	3/9 (33%)	
Week of First Observation	107	73	99	
Life Table Test (d)		P=0.311	P=0.057	P=0.107
Incidental Tumor Test (d)		P=0.246	P=0.111	P=0.271
Fisher Exact Test (d)		P=0.151	P=0.105	P=0.351
Pancreatic Islets: Islet Cell Adenoma				
Overall Rates (e)	2/116 (2%)	7/249 (3%)	1/100 (1%)	
Adjusted Rates (b)	10.4%	8.0%	1.1%	
Terminal Rates (c)	0/13 (0%)	0/30 (0%)	0/9 (0%)	
Week of First Observation	141	111	96	
Life Table Tests (d)		P=0.443	P=0.583N	P=0.322N
Incidental Tumor Tests (d)		P=0.362	P=0.588N	P=0.255N
Fisher Exact Test (d)		P=0.414	P=0.556N	P=0.280N
Pancreatic Islets: Islet Cell Carcinoma				
Overall Rates (e)	3/116 (3%)	(f) 7/249 (3%)	0/100 (0%)	
Adjusted Rates (b)	15.8%	10.0%	0.0%	
Terminal Rates (c)	1/13 (8%)	1/30 (3%)	0/9 (0%)	
Week of First Observation	138	121		
Life Table Tests (d)		P=0.624N	P=0.195N	P=0.141N
Incidental Tumor Tests (d)		P=0.587N	P=0.154N	P=0.104N
Fisher Exact Test (d)		P=0.602	P=0.153N	P=0.092N
Pancreatic Islets: Islet Cell Adenoma or Carcinoma				
Overall Rates (e)	5/116 (4%)	(f) 14/249 (6%)	1/100 (1%)	
Adjusted Rates (b)	24.5%	17.2%	1.1%	
Terminal Rates (c)	1/13 (8%)	1/30 (3%)	0/9 (0%)	
Week of First Observation	138	111	96	
Life Table Tests (d)		P=0.470	P=0.192N	P=0.086N
Incidental Tumor Tests (d)		P=0.440	P=0.162N	P=0.051N
Fisher Exact Test (d)		P=0.403	P=0.145N	P=0.041N
Mammary Gland: Adenoma				
Overall Rates (a)	(g) 8/117 (7%)	(g) 14/250 (6%)	5/100 (5%)	
Adjusted Rates (b)	23.6%	14.2%	28.9%	
Terminal Rates (c)	2/13 (15%)	1/30 (3%)	1/9 (11%)	
Week of First Observation	96	70	116	
Life Table Test (d)		P=0.333N	P=0.456N	P=0.575
Incidental Tumor Test (d)		P=0.364N	P=0.398N	P=0.571N
Fisher Exact Test (d)		P=0.400N	P=0.392N	P=0.528N
Mammary Gland: Fibroadenoma				
Overall Rates (a)	72/117 (62%)	135/250 (54%)	52/100 (52%)	
Adjusted Rates (b)	98.4%	91.5%	95.3%	
Terminal Rates (c)	12/13 (92%)	21/30 (70%)	7/9 (78%)	
Week of First Observation	70	70	99	
Life Table Test (d)		P=0.053N	P=0.354N	P=0.192
Incidental Tumor Test (d)		P=0.016N	P=0.041N	P=0.507N
Fisher Exact Test (d)		P=0.106N	P=0.101N	P=0.412N
Mammary Gland: Adenocarcinoma				
Overall Rates (a)	(h) 6/117 (5%)	(i) 25/250 (10%)	7/100 (7%)	
Adjusted Rates (b)	25.0%	34.0%	28.9%	
Terminal Rates (c)	1/13 (8%)	5/30 (17%)	1/9 (11%)	
Week of First Observation	71	85	118	
Life Table Test (d)		P=0.137	P=0.325	P=0.436N
Incidental Tumor Test (d)		P=0.148	P=0.430	P=0.287N
Fisher Exact Test (d)		P=0.083	P=0.383	P=0.255N

TABLE B3a. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Clitoral Gland: Carcinoma				
Overall Rates (e)	6/117 (5%)	14/250 (6%)	7/100 (7%)	
Adjusted Rates (b)	14.4%	14.4%	19.8%	
Terminal Rates (c)	0/13 (0%)	1/30 (3%)	1/9 (11%)	
Week of First Observation	101	69	65	
Life Table Tests (d)		P=0.584N	P=0.381	P=0.285
Incidental Tumor Tests (d)		P=0.459	P=0.395	P=0.391
Fisher Exact Test (d)		P=0.535	P=0.383	P=0.390
Clitoral Gland: Adenoma or Carcinoma				
Overall Rates (e)	6/117 (5%)	15/250 (6%)	7/100 (7%)	
Adjusted Rates (b)	14.4%	16.8%	19.8%	
Terminal Rates (c)	0/13 (0%)	1/30 (3%)	1/9 (11%)	
Week of First Observation	101	69	65	
Life Table Tests (d)		P=0.547	P=0.381	P=0.333
Incidental Tumor Tests (d)		P=0.403	P=0.395	P=0.444
Fisher Exact Test (d)		P=0.473	P=0.283	P=0.446
Uterus: Endometrial Stromal Polyp				
Overall Rates (e)	13/117 (11%)	31/250 (12%)	14/100 (14%)	
Adjusted Rates (b)	40.0%	32.3%	39.0%	
Terminal Rates (c)	3/13 (23%)	5/30 (17%)	1/9 (11%)	
Week of First Observation	86	68	25	
Life Table Test (d)		P=0.532	P=0.286	P=0.273
Incidental Tumor Test (d)		P=0.489	P=0.315	P=0.398
Fisher Exact Test (d)		P=0.434	P=0.330	P=0.403
Uterus: Endometrial Stromal Sarcoma				
Overall Rates (e)	5/117 (4%)	4/250 (2%)	0/100 (0%)	
Adjusted Rates (b)	8.1%	1.8%	0.0%	
Terminal Rates (c)	0/13 (0%)	0/30 (0%)	0/9 (0%)	
Week of First Observation	88	77		
Life Table Test (d)		P=0.107N	P=0.065N	
Incidental Tumor Test (d)		P=0.195N	P=0.055N	
Fisher Exact Test (d)		P=0.121N	P=0.044N	
Ovary: Granulosa Cell Tumor or Carcinoma				
Overall Rates (e)	1/117 (1%)	3/250 (1%)	3/100 (3%)	
Adjusted Rates (b)	7.7%	6.7%	5.5%	
Terminal Rates (c)	1/13 (8%)	1/30 (3%)	0/9 (0%)	
Week of First Observation	145	125	94	
Life Table Tests (d)		P=0.626	P=0.249	P=0.191
Incidental Tumor Tests (d)		P=0.650	P=0.260	P=0.239
Fisher Exact Test (d)		P=0.619	P=0.254	P=0.228
Ovary: Thecoma, Granulosa Cell Tumor, or Granulosa Cell Carcinoma				
Overall Rates (e)	1/117 (1%)	4/250 (2%)	3/100 (3%)	
Adjusted Rates (b)	7.7%	7.4%	5.5%	
Terminal Rates (c)	1/13 (8%)	1/30 (3%)	0/9 (0%)	
Week of First Observation	145	123	94	
Life Table Tests (d)		P=0.504	P=0.249	P=0.279
Incidental Tumor Tests (d)		P=0.541	P=0.260	P=0.340
Fisher Exact Test (d)		P=0.489	P=0.254	P=0.320
Brain: Astrocytoma				
Overall Rates (e)	4/117 (3%)	4/250 (2%)	2/100 (2%)	
Adjusted Rates (b)	4.0%	2.4%	10.3%	
Terminal Rates (c)	0/13 (0%)	0/30 (0%)	0/9 (0%)	
Week of First Observation	75	82	131	
Life Table Tests (d)		P=0.225N	P=0.425N	P=0.546
Incidental Tumor Tests (d)		P=0.357N	P=0.505N	P=0.559
Fisher Exact Test (d)		P=0.227N	P=0.418N	P=0.550

TABLE B3a. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS (Continued)

	Untreated Control	1% Amosite	1% Amosite + PW	1% Amosite vs. 1% Amosite + PW
Brain: Glioma or Astrocytoma				
Overall Rates (e)	4/117 (3%)	5/250 (2%)	2/100 (2%)	
Adjusted Rates (b)	4.0%	2.9%	10.3%	
Terminal Rates (c)	0/13 (0%)	0/30 (0%)	0/9 (0%)	
Week of First Observation	75	82	131	
Life Table Tests (d)		P=0.312N	P=0.425N	P=0.639
Incidental Tumor Tests (d)		P=0.485N	P=0.505N	P=0.661
Fisher Exact Test (d)		P=0.313N	P=0.418N	P=0.642
Zymbal Gland: Carcinoma				
Overall Rates (e)	3/117 (3%)	4/250 (2%)	3/100 (3%)	
Adjusted Rates (b)	3.9%	3.3%	5.1%	
Terminal Rates (c)	0/13 (0%)	0/30 (0%)	0/9 (0%)	
Week of First Observation	99	121	105	
Life Table Tests (d)		P=0.359N	P=0.614	P=0.278
Incidental Tumor Tests (d)		P=0.403N	P=0.619	P=0.349
Fisher Exact Test (d)		P=0.396N	P=0.582	P=0.320
Zymbal Gland: Carcinoma or Squamous Cell Papilloma				
Overall Rates (e)	3/117 (3%)	7/250 (3%)	3/100 (3%)	
Adjusted Rates (b)	3.9%	7.9%	5.1%	
Terminal Rates (c)	0/13 (0%)	0/30 (0%)	0/9 (0%)	
Week of First Observation	99	121	105	
Life Table Tests (d)		P=0.628N	P=0.614	P=0.494
Incidental Tumor Tests (d)		P=0.606	P=0.619	P=0.596
Fisher Exact Test (d)		P=0.599	P=0.582	P=0.581
All Sites: Benign Tumors				
Overall Rates (a)	99/117 (85%)	213/250 (85%)	79/100 (79%)	
Adjusted Rates (b)	100.0%	99.5%	100.0%	
Terminal Rates (c)	13/13 (100%)	29/30 (97%)	9/9 (100%)	
Week of First Observation	70	68	25	
Life Table Test (d)		P=0.230N	P=0.517N	P=0.267
Incidental Tumor Test (d)		P=0.320N	P=0.123N	P=0.144N
Fisher Exact Test (d)		P=0.499	P=0.185N	P=0.107N
All Sites: Malignant Tumors				
Overall Rates (a)	74/117 (63%)	166/250 (66%)	68/100 (68%)	
Adjusted Rates (b)	96.0%	93.0%	93.9%	
Terminal Rates (c)	11/13 (85%)	21/30 (70%)	6/9 (67%)	
Week of First Observation	71	69	56	
Life Table Test (d)		P=0.399N	P=0.245	P=0.136
Incidental Tumor Test (d)		P=0.284	P=0.274	P=0.434
Fisher Exact Test (d)		P=0.317	P=0.278	P=0.438
All Sites: All Tumors				
Overall Rates (a)	113/117 (97%)	240/250 (96%)	98/100 (98%)	
Adjusted Rates (b)	100.0%	100.0%	100.0%	
Terminal Rates (c)	13/13 (100%)	30/30 (100%)	9/9 (100%)	
Week of First Observation	70	68	25	
Life Table Test (d)		P=0.192N	P=0.350	P=0.081
Incidental Tumor Test (d)		P=0.571N	P=0.379	P=0.257
Fisher Exact Test (d)		P=0.522N	P=0.418	P=0.284

**TABLE B3a. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY
OF AMOSITE ASBESTOS (Continued)**

- (a) Number of tumor-bearing animals/number of animals examined grossly at the site
- (b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
- (c) Observed tumor incidence in animals killed at the end of the study
- (d) Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in a dosed group than in controls is indicated by (N). The P values for the comparison of the 1% amosite group with the 1% amosite + PW group are presented in the last column for sites with a tumor incidence of at least 2% in at least one of the two groups.
- (e) Number of tumor-bearing animals/number of animals examined microscopically at the site
- (f) Includes one islet cell carcinoma of the pancreas
- (g) Includes one papillary cystadenoma, NOS
- (h) Includes one carcinoma in situ, NOS, and one carcinoma, NOS
- (i) Includes two papillary adenocarcinomas

TABLE B3b. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. Amosite + DMH
Skin: Squamous Cell Papilloma or Carcinoma				
Overall Rates (a)	3/117 (3%)	0/125 (0%)	1/175 (1%)	
Adjusted Rates (b)	3.2%	0.0%	2.8%	
Terminal Rates (c)	3/94 (3%)	0/15 (0%)	1/36 (3%)	
Week of First Observation	136		106	
Life Table Tests (d)		P=0.559N	P=0.671N	
Incidental Tumor Tests (d)		P=0.329N	P=0.430N	
Fisher Exact Test (d)		P=0.112N	P=0.178N	
Subcutaneous Tissue: Fibroma				
Overall Rates (a)	7/117 (6%)	0/125 (0%)	0/175 (0%)	
Adjusted Rates (b)	7.3%	0.0%	0.0%	
Terminal Rates (c)	6/94 (6%)	0/15 (0%)	0/36 (0%)	
Week of First Observation	96			
Life Table Tests (d)		P=0.288N	P=0.101N	
Incidental Tumor Tests (d)		P=0.104N	P=0.029N	
Fisher Exact Test (d)		P=0.006N	P=0.001N	
Subcutaneous Tissue: Fibrosarcoma				
Overall Rates (a)	3/117 (3%)	2/125 (2%)	1/175 (1%)	
Adjusted Rates (b)	3.2%	8.1%	1.1%	
Terminal Rates (c)	3/94 (3%)	1/15 (7%)	0/36 (0%)	
Week of First Observation	105	77	83	
Life Table Tests (d)		P=0.245	P=0.598N	
Incidental Tumor Tests (d)		P=0.690N	P=0.220N	
Fisher Exact Test (d)		P=0.469N	P=0.178N	
Integumentary System: Fibroma or Fibrosarcoma				
Overall Rates (a)	10/117 (9%)	2/125 (2%)	1/175 (1%)	
Adjusted Rates (b)	10.5%	8.1%	1.1%	
Terminal Rates (c)	9/94 (10%)	1/15 (7%)	0/36 (0%)	
Week of First Observation	96	77	83	
Life Table Tests (d)		P=0.640	P=0.114N	
Incidental Tumor Tests (d)		P=0.153N	P=0.010N	
Fisher Exact Test (d)		P=0.013N	P<0.001N	
Integumentary System or Salivary Gland: Sarcoma or Fibrosarcoma				
Overall Rates (a)	5/117 (4%)	2/125 (2%)	1/175 (1%)	
Adjusted Rates (b)	5.3%	8.1%	1.1%	
Terminal Rates (c)	5/94 (5%)	1/15 (7%)	0/36 (0%)	
Week of First Observation	103	77	83	
Life Table Tests (d)		P=0.377	P=0.383N	
Incidental Tumor Tests (d)		P=0.465N	P=0.087N	
Fisher Exact Test (d)		P=0.197N	P=0.040N	
Integumentary System or Salivary Gland: Fibroma, Sarcoma, or Fibrosarcoma				
Overall Rates (a)	11/117 (9%)	2/125 (2%)	1/175 (1%)	
Adjusted Rates (b)	11.5%	8.1%	1.1%	
Terminal Rates (c)	10/94 (11%)	1/15 (7%)	0/36 (0%)	
Week of First Observation	96	77	83	
Life Table Tests (d)		P=0.634N	P=0.090N	
Incidental Tumor Tests (d)		P=0.121N	P=0.006N	
Fisher Exact Test (d)		P=0.007N	P<0.001N	
Hematopoietic System: Leukemia				
Overall Rates (a)	40/117 (34%)	39/125 (31%)	61/175 (35%)	
Adjusted Rates (b)	41.0%	81.7%	79.7%	
Terminal Rates (c)	37/94 (39%)	9/15 (60%)	23/36 (64%)	
Week of First Observation	86	65	62	
Life Table Tests (d)		P<0.001	P<0.001	P=0.075N
Incidental Tumor Tests (d)		P=0.017	P=0.002	P=0.382N
Fisher Exact Test (d)		P=0.360N	P=0.504	P=0.296

TABLE B3b. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. Amosite + DMH
Liver: Neoplastic Nodule				
Overall Rates (e)	4/117 (3%)	29/125 (23%)	32/175 (18%)	
Adjusted Rates (b)	4.2%	73.6%	48.7%	
Terminal Rates (c)	3/94 (3%)	8/43 (53%)	11/36 (31%)	
Week of First Observation	101	66	69	
Life Table Tests (d)		P<0.001	P<0.001	P=0.006N
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.038N
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.185N
Liver: Hepatocellular Carcinoma				
Overall Rates (e)	1/117 (1%)	10/125 (8%)	8/175 (5%)	
Adjusted Rates (b)	1.1%	28.7%	12.8%	
Terminal Rates (c)	1/94 (1%)	3/15 (20%)	2/36 (6%)	
Week of First Observation	133	60	59	
Life Table Tests (d)		P<0.001	P=0.002	P=0.040N
Incidental Tumor Tests (d)		P=0.001	P=0.021	P=0.125N
Fisher Exact Test (d)		P=0.007	P=0.067	P=0.162N
Liver: Neoplastic Nodule or Hepatocellular Carcinoma				
Overall Rates (e)	5/117 (4%)	33/125 (26%)	38/175 (22%)	
Adjusted Rates (b)	5.2%	75.5%	54.8%	
Terminal Rates (c)	4/94 (4%)	9/15 (60%)	13/36 (36%)	
Week of First Observation	101	60	59	
Life Table Tests (d)		P<0.001	P<0.001	P=0.007N
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.054N
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.210N
Small Intestine: Adenocarcinoma				
Overall Rates (a)	0/117 (0%)	4/125 (3%)	11/175 (6%)	
Adjusted Rates (b)	0.0%	6.9%	15.1%	
Terminal Rates (c)	0/94 (0%)	0/15 (0%)	3/36 (8%)	
Week of First Observation		75	43	
Life Table Tests (d)		P=0.012	P<0.001	P=0.335
Incidental Tumor Tests (d)		P=0.233	P=0.025	P=0.184
Fisher Exact Test (d)		P=0.070	P=0.003	P=0.174
Small Intestine: Mucinous Cystadenocarcinoma				
Overall Rates (a)	0/117 (0%)	7/125 (6%)	2/175 (1%)	
Adjusted Rates (b)	0.0%	19.6%	2.0%	
Terminal Rates (c)	0/94 (0%)	2/15 (13%)	0/36 (0%)	
Week of First Observation		56	73	
Life Table Tests (d)		P<0.001	P=0.218	P=0.010N
Incidental Tumor Tests (d)		P=0.018	P=0.393	P=0.026N
Fisher Exact Test (d)		P=0.009	P=0.358	P=0.030N
Small Intestine: Adenocarcinoma, Mucinous Cystadenocarcinoma, or Adenocarcinoma in Adenomatous Polyp				
Overall Rates (a)	0/117 (0%)	11/125 (9%)	15/175 (9%)	
Adjusted Rates (b)	0.0%	25.1%	20.0%	
Terminal Rates (c)	0/94 (0%)	2/15 (13%)	4/36 (11%)	
Week of First Observation		56	43	
Life Table Tests (d)		P<0.001	P<0.001	P=0.287N
Incidental Tumor Tests (d)		P=0.005	P=0.005	P=0.513N
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.551N
Small Intestine: Signet Ring Carcinoma				
Overall Rates (a)	0/117 (0%)	3/125 (2%)	8/175 (5%)	
Adjusted Rates (b)	0.0%	8.0%	7.8%	
Terminal Rates (c)	0/94 (0%)	0/15 (0%)	0/36 (0%)	
Week of First Observation		83	62	
Life Table Tests (d)		P=0.012	P=0.005	P=0.394
Incidental Tumor Tests (d)		P=0.070	P=0.121	P=0.242
Fisher Exact Test (d)		P=0.136	P=0.016	P=0.254

TABLE B3b. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. Amosite + DMH
Large Intestine: Signet Ring Carcinoma				
Overall Rates (a)	0/117 (0%)	7/125 (6%)	9/175 (5%)	
Adjusted Rates (b)	0.0%	8.5%	11.0%	
Terminal Rates (c)	0/94 (0%)	0/15 (0%)	2/36 (6%)	
Week of First Observation		29	48	
Life Table Tests (d)		P=0.004	P=0.002	P=0.387N
Incidental Tumor Tests (d)		P=0.205	P=0.056	P=0.513
Fisher Exact Test (d)		P=0.009	P=0.009	P=0.529N
Large Intestine: Adenomatous Polyp				
Overall Rates (a)	1/117 (1%)	38/125 (30%)	59/175 (34%)	
Adjusted Rates (b)	1.1%	67.4%	66.1%	
Terminal Rates (c)	1/94 (1%)	6/15 (40%)	15/36 (42%)	
Week of First Observation	103	51	49	
Life Table Tests (d)		P<0.001	P<0.001	P=0.156N
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.494
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.316
Large Intestine: Adenocarcinoma				
Overall Rates (a)	0/117 (0%)	7/125 (6%)	9/175 (5%)	
Adjusted Rates (b)	0.0%	16.8%	12.2%	
Terminal Rates (c)	0/94 (0%)	1/15 (7%)	2/36 (6%)	
Week of First Observation		35	63	
Life Table Tests (d)		P<0.001	P<0.001	P=0.315N
Incidental Tumor Tests (d)		P=0.063	P=0.027	P=0.540N
Fisher Exact Test (d)		P=0.009	P=0.009	P=0.529N
Large Intestine: Mucinous Cystadenocarcinoma				
Overall Rates (a)	0/117 (0%)	7/125 (6%)	7/175 (4%)	
Adjusted Rates (b)	0.0%	14.5%	5.7%	
Terminal Rates (c)	0/94 (0%)	1/15 (7%)	0/36 (0%)	
Week of First Observation		35	60	
Life Table Tests (d)		P=0.001	P=0.015	P=0.236N
Incidental Tumor Tests (d)		P=0.063	P=0.265	P=0.453N
Fisher Exact Test (d)		P=0.009	P=0.026	P=0.352N
Large Intestine: Adenocarcinoma in Adenomatous Polyp				
Overall Rates (a)	0/117 (0%)	26/125 (21%)	46/175 (26%)	
Adjusted Rates (b)	0.0%	66.3%	48.4%	
Terminal Rates (c)	0/94 (0%)	6/15 (40%)	7/36 (19%)	
Week of First Observation		67	55	
Life Table Tests (d)		P<0.001	P<0.001	P=0.390N
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.277
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.169
Large Intestine: Adenocarcinoma, Mucinous Adenocarcinoma, Mucinous Cystadenocarcinoma, or Adenocarcinoma in Adenomatous Polyp				
Overall Rates (a)	0/117 (0%)	39/125 (31%)	59/175 (34%)	
Adjusted Rates (b)	0.0%	77.6%	56.7%	
Terminal Rates (c)	0/94 (0%)	8/15 (53%)	9/36 (25%)	
Week of First Observation		35	55	
Life Table Tests (d)		P<0.001	P<0.001	P=0.153N
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.462
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.370

TABLE B3b. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. Amosite + DMH
Large Intestine: Adenomatous Polyp, Adenocarcinoma, Mucinous Adenocarcinoma, Mucinous Cystadenocarcinoma, or Adenocarcinoma in Adenomatous Polyp				
Overall Rates (a)	1/117 (1%)	66/125 (53%)	96/175 (55%)	
Adjusted Rates (b)	1.1%	92.0%	81.8%	
Terminal Rates (c)	1/94 (1%)	11/15 (73%)	20/36 (56%)	
Week of First Observation	136	35	49	
Life Table Tests (d)		P < 0.001	P < 0.001	P = 0.039N
Incidental Tumor Tests (d)		P < 0.001	P < 0.001	P = 0.477N
Fisher Exact Test (d)		P < 0.001	P < 0.001	P = 0.407
Kidney: Tubular Cell Adenocarcinoma				
Overall Rates (e)	1/117 (1%)	3/125 (2%)	2/175 (1%)	
Adjusted Rates (b)	1.1%	10.6%	5.6%	
Terminal Rates (c)	1/94 (1%)	0/15 (0%)	2/36 (6%)	
Week of First Observation	127	78	106	
Life Table Tests (d)		P = 0.018	P = 0.192	P = 0.180N
Incidental Tumor Tests (d)		P = 0.183	P = 0.386	P = 0.258N
Fisher Exact Test (d)		P = 0.333	P = 0.648	P = 0.346N
Kidney: Tubular Cell Adenoma or Adenocarcinoma				
Overall Rates (e)	1/117 (1%)	3/125 (2%)	3/175 (2%)	
Adjusted Rates (b)	1.1%	10.6%	8.3%	
Terminal Rates (c)	1/94 (1%)	0/15 (0%)	3/36 (8%)	
Week of First Observation	127	78	106	
Life Table Tests (d)		P = 0.018	P = 0.058	P = 0.281N
Incidental Tumor Tests (d)		P = 0.183	P = 0.199	P = 0.365N
Fisher Exact Test (d)		P = 0.333	P = 0.473	P = 0.490N
Kidney: Sarcoma				
Overall Rates (e)	0/117 (0%)	23/125 (18%)	19/175 (11%)	
Adjusted Rates (b)	0.0%	27.5%	13.2%	
Terminal Rates (c)	0/94 (0%)	0/15 (0%)	0/36 (0%)	
Week of First Observation		52	39	
Life Table Tests (d)		P < 0.001	P < 0.001	P = 0.019N
Incidental Tumor Tests (d)		P = 0.018	P = 0.210	P = 0.142N
Fisher Exact Test (d)		P < 0.001	P < 0.001	P = 0.046N
Kidney: Fibrosarcoma				
Overall Rates (e)	0/117 (0%)	4/125 (3%)	0/175 (0%)	
Adjusted Rates (b)	0.0%	5.7%	0.0%	
Terminal Rates (c)	0/94 (0%)	0/15 (0%)	0/36 (0%)	
Week of First Observation		67		
Life Table Tests (d)		P = 0.021	(f)	P = 0.019N
Incidental Tumor Tests (d)		P = 0.609	(f)	P = 0.036N
Fisher Exact Test (d)		P = 0.068	(f)	P = 0.029N
Kidney: Mixed Tumor Malignant				
Overall Rates (e)	0/117 (0%)	9/125 (7%)	35/175 (20%)	
Adjusted Rates (b)	0.0%	20.3%	34.0%	
Terminal Rates (c)	0/94 (0%)	1/15 (7%)	2/36 (6%)	
Week of First Observation		52	54	
Life Table Tests (d)		P < 0.001	P < 0.001	P = 0.027
Incidental Tumor Tests (d)		P = 0.017	P < 0.001	P = 0.001
Fisher Exact Test (d)		P = 0.002	P < 0.001	P = 0.001

TABLE B3b. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. Amosite + DMH
Pituitary Gland: Adenoma				
Overall Rates (e)	50/117 (43%)	16/124 (13%)	19/175 (11%)	
Adjusted Rates (b)	48.8%	46.0%	34.0%	
Terminal Rates (c)	42/94 (45%)	5/15 (33%)	8/36 (22%)	
Week of First Observation	71	60	69	
Life Table Tests (d)		P=0.119	P=0.278N	P=0.063N
Incidental Tumor Tests (d)		P=0.015N	P<0.001N	P=0.184N
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.357N
Pituitary Gland: Adenoma or Carcinoma				
Overall Rates (e)	52/117 (44%)	16/124 (13%)	20/175 (11%)	
Adjusted Rates (b)	50.3%	46.0%	34.8%	
Terminal Rates (c)	43/94 (46%)	5/15 (33%)	8/36 (22%)	
Week of First Observation	71	60	69	
Life Table Tests (d)		P=0.144	P=0.283N	P=0.084N
Incidental Tumor Tests (d)		P=0.007N	P<0.001N	P=0.235N
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.416N
Adrenal Cortex: Adenoma				
Overall Rates (e)	3/117 (3%)	2/125 (2%)	4/175 (2%)	
Adjusted Rates (b)	3.1%	5.3%	8.7%	
Terminal Rates (c)	3/94 (3%)	0/15 (0%)	2/36 (6%)	
Week of First Observation	101	84	77	
Life Table Tests (d)		P=0.257	P=0.142	P=0.643N
Incidental Tumor Tests (d)		P=0.690N	P=0.480	P=0.586
Fisher Exact Test (d)		P=0.473N	P=0.583N	P=0.510
Adrenal Cortex: Adenoma or Carcinoma				
Overall Rates (e)	4/117 (3%)	2/125 (2%)	4/175 (2%)	
Adjusted Rates (b)	4.2%	5.3%	8.7%	
Terminal Rates (c)	3/94 (2%)	0/15 (0%)	2/36 (6%)	
Week of First Observation	101	84	77	
Life Table Tests (d)		P=0.324	P=0.215	P=0.643N
Incidental Tumor Tests (d)		P=0.570N	P=0.608	P=0.586
Fisher Exact Test (d)		P=0.311N	P=0.407N	P=0.510
Adrenal Medulla: Pheochromocytoma				
Overall Rates (e)	17/117 (15%)	0/125 (0%)	3/175 (2%)	
Adjusted Rates (b)	18.1%	0.0%	6.1%	
Terminal Rates (c)	17/94 (18%)	0/15 (0%)	1/36 (3%)	
Week of First Observation	103		82	
Life Table Tests (d)		P=0.080N	P=0.119N	
Incidental Tumor Tests (d)		P=0.007N	P=0.005N	
Fisher Exact Test (d)		P<0.001N	P<0.001N	
Adrenal Medulla: Pheochromocytoma or Malignant Pheochromocytoma				
Overall Rates (e)	18/117 (15%)	0/125 (0%)	4/175 (2%)	
Adjusted Rates (b)	18.8%	0.0%	8.8%	
Terminal Rates (c)	17/94 (18%)	0/15 (0%)	2/36 (6%)	
Week of First Observation	87		82	
Life Table Tests (d)		P=0.063N	P=0.166N	P=0.215
Incidental Tumor Tests (d)		P=0.006N	P=0.008N	P=0.166
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.114

TABLE B3b. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. Amosite + DMH
Thyroid Gland: Follicular Cell Adenoma				
Overall Rates (e)	2/116 (2%)	4/124 (3%)	6/174 (3%)	
Adjusted Rates (b)	2.1%	13.5%	10.5%	
Terminal Rates (c)	2/94 (2%)	1/15 (7%)	2/36 (6%)	
Week of First Observation	117	70	83	
Life Table Tests (d)		P=0.012	P=0.019	P=0.445N
Incidental Tumor Tests (d)		P=0.122	P=0.185	P=0.563N
Fisher Exact Test (d)		P=0.370	P=0.312	P=0.593
Thyroid Gland: Follicular Cell Carcinoma				
Overall Rates (e)	7/116 (6%)	2/124 (2%)	1/174 (1%)	
Adjusted Rates (b)	7.4%	9.4%	2.8%	
Terminal Rates (c)	7/94 (7%)	1/15 (7%)	1/36 (3%)	
Week of First Observation	111	92	106	
Life Table Tests (d)		P=0.441	P=0.281N	
Incidental Tumor Tests (d)		P=0.499N	P=0.087N	
Fisher Exact Test (d)		P=0.072N	P=0.008N	
Thyroid Gland: Follicular Cell Adenoma or Carcinoma				
Overall Rates (e)	9/116 (8%)	6/124 (5%)	7/174 (4%)	
Adjusted Rates (b)	9.6%	22.1%	13.2%	
Terminal Rates (c)	9/94 (10%)	2/15 (13%)	3/36 (8%)	
Week of First Observation	111	70	83	
Life Table Tests (d)		P=0.021	P=0.194	P=0.225N
Incidental Tumor Tests (d)		P=0.335	P=0.446N	P=0.319N
Fisher Exact Test (d)		P=0.258N	P=0.136N	P=0.473N
Thyroid Gland: C-Cell Adenoma				
Overall Rates (e)	14/116 (12%)	4/124 (3%)	8/174 (5%)	
Adjusted Rates (b)	14.9%	17.6%	14.8%	
Terminal Rates (c)	14/94 (15%)	2/15 (13%)	3/36 (8%)	
Week of First Observation	103	77	78	
Life Table Tests (d)		P=0.311	P=0.358	P=0.572N
Incidental Tumor Tests (d)		P=0.259N	P=0.203N	P=0.543
Fisher Exact Test (d)		P=0.009N	P=0.018N	P=0.390N
Thyroid Gland: C-Cell Carcinoma				
Overall Rates (e)	10/116 (9%)	1/124 (1%)	6/174 (3%)	
Adjusted Rates (b)	10.6%	6.7%	13.5%	
Terminal Rates (c)	10/94 (11%)	1/15 (7%)	3/36 (8%)	
Week of First Observation	107	103	91	
Life Table Tests (d)		P=0.495N	P=0.310	P=0.311
Incidental Tumor Tests (d)		P=0.139N	P=0.453N	P=0.246
Fisher Exact Test (d)		P=0.004N	P=0.053N	P=0.136
Thyroid Gland: C-Cell Adenoma or Carcinoma				
Overall Rates (e)	24/116 (21%)	5/124 (4%)	14/174 (8%)	
Adjusted Rates (b)	25.5%	23.9%	27.0%	
Terminal Rates (c)	24/94 (26%)	3/15 (20%)	6/36 (17%)	
Week of First Observation	107	77	78	
Life Table Tests (d)		P=0.455	P=0.205	P=0.423
Incidental Tumor Tests (d)		P=0.070N	P=0.178N	P=0.276
Fisher Exact Test (d)		P<0.001N	P=0.002N	P=0.122
Pancreatic Islets: Islet Cell Carcinoma				
Overall Rates (e)	3/116 (3%)	0/125 (0%)	0/175 (0%)	
Adjusted Rates (b)	3.2%	0.0%	0.0%	
Terminal Rates (c)	3/94 (3%)	0/15 (0%)	0/36 (0%)	
Week of First Observation	138			
Life Table Tests (d)		P=0.559N	P=0.334N	
Incidental Tumor Tests (d)		P=0.326N	P=0.186N	
Fisher Exact Test (d)		P=0.111N	P=0.062N	

TABLE B3b. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. Amosite + DMH
Pancreatic Islets: Islet Cell Adenoma or Carcinoma				
Overall Rates (e)	5/116 (4%)	0/125 (0%)	2/175 (1%)	
Adjusted Rates (b)	5.3%	0.0%	5.2%	
Terminal Rates (c)	5/94 (5%)	0/15 (0%)	1/36 (3%)	
Week of First Observation	138		102	
Life Table Tests (d)		P=0.402N	P=0.653	
Incidental Tumor Tests (d)		P=0.402N	P=0.533N	
Fisher Exact Test (d)		P=0.025N	P=0.092N	
Mammary Gland: Adenoma				
Overall Rates (a)	(g) 8/117 (7%)	1/125 (1%)	2/175 (1%)	
Adjusted Rates (b)	8.4%	6.7%	3.7%	
Terminal Rates (c)	7/94 (7%)	1/15 (7%)	0/36 (0%)	
Week of First Observation	96	103	94	
Life Table Tests (d)		P=0.584N	P=0.372N	
Incidental Tumor Tests (d)		P=0.216N	P=0.135N	
Fisher Exact Test (d)		P=0.014N	P=0.011N	
Mammary Gland: Fibroadenoma				
Overall Rates (a)	72/117 (62%)	13/125 (10%)	18/175 (10%)	
Adjusted Rates (b)	71.8%	45.1%	38.8%	
Terminal Rates (c)	66/94 (70%)	4/15 (27%)	12/36 (33%)	
Week of First Observation	70	67	77	
Life Table Tests (d)		P=0.428N	P=0.003N	P=0.126N
Incidental Tumor Tests (d)		P<0.001N	P<0.001N	P=0.252N
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.560
Mammary Gland: Adenocarcinoma				
Overall Rates (a)	(h) 6/117 (5%)	3/125 (2%)	(i) 1/175 (1%)	
Adjusted Rates (b)	6.1%	15.3%	1.2%	
Terminal Rates (c)	5/94 (5%)	2/15 (13%)	0/36 (0%)	
Week of First Observation	71	87	84	
Life Table Tests (d)		P=0.224	P=0.239N	P=0.098N
Incidental Tumor Tests (d)		P=0.605N	P=0.016N	P=0.126N
Fisher Exact Test (d)		P=0.218N	P=0.018N	P=0.197N
Clitoral Gland: Carcinoma				
Overall Rates (e)	6/117 (5%)	1/125 (1%)	3/175 (2%)	
Adjusted Rates (b)	6.3%	4.0%	8.3%	
Terminal Rates (c)	5/94 (5%)	0/15 (0%)	3/36 (8%)	
Week of First Observation	101	95	106	
Life Table Tests (d)		P=0.698N	P=0.503	
Incidental Tumor Tests (d)		P=0.344N	P=0.428N	
Fisher Exact Test (d)		P=0.050N	P=0.097N	
Uterus: Endometrial Stromal Polyp				
Overall Rates (a)	13/117 (11%)	10/125 (8%)	19/175 (11%)	
Adjusted Rates (b)	13.2%	27.5%	30.0%	
Terminal Rates (c)	10/94 (11%)	2/15 (13%)	7/36 (19%)	
Week of First Observation	86	65	69	
Life Table Tests (d)		P=0.008	P=0.003	P=0.536N
Incidental Tumor Tests (d)		P=0.552N	P=0.502	P=0.404
Fisher Exact Test (d)		P=0.279N	P=0.545N	P=0.267
Uterus: Endometrial Stromal Sarcoma				
Overall Rates (a)	5/117 (4%)	4/125 (3%)	2/175 (1%)	
Adjusted Rates (b)	5.0%	7.8%	4.9%	
Terminal Rates (c)	3/94 (3%)	0/15 (0%)	1/36 (3%)	
Week of First Observation	88	57	99	
Life Table Tests (d)		P=0.186	P=0.595N	P=0.098N
Incidental Tumor Tests (d)		P=0.513N	P=0.370N	P=0.206N
Fisher Exact Test (d)		P=0.464N	P=0.094N	P=0.201N

TABLE B3b. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. Amosite + DMH
Brain: Astrocytoma				
Overall Rates (e)	4/117 (3%)	1/125 (1%)	0/175 (0%)	
Adjusted Rates (b)	4.0%	3.3%	0.0%	
Terminal Rates (c)	2/94 (2%)	0/15 (0%)	0/36 (0%)	
Week of First Observation	75	93		
Life Table Tests (d)		P=0.707N	P=0.171N	
Incidental Tumor Tests (d)		P=0.283N	P=0.029N	
Fisher Exact Test (d)		P=0.165N	P=0.025N	
Ear Canal: Squamous Cell Papilloma or Carcinoma				
Overall Rates (e)	0/117 (0%)	0/125 (0%)	4/175 (2%)	
Adjusted Rates (b)	0.0%	0.0%	7.3%	
Terminal Rates (c)	0/94 (0%)	0/15 (0%)	1/36 (3%)	
Week of First Observation			82	
Life Table Tests (d)		(f)	P=0.015	P=0.210
Incidental Tumor Tests (d)		(f)	P=0.069	P=0.145
Fisher Exact Test (d)		(f)	P=0.127	P=0.114
Zymbal Gland: Squamous Cell Papilloma				
Overall Rates (e)	0/117 (0%)	12/125 (10%)	14/175 (8%)	
Adjusted Rates (b)	0.0%	30.9%	20.2%	
Terminal Rates (c)	0/94 (0%)	2/15 (13%)	4/36 (11%)	
Week of First Observation		54	49	
Life Table Tests (d)		P<0.001	P<0.001	P=0.144N
Incidental Tumor Tests (d)		P<0.001	P=0.005	P=0.336N
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.388N
Zymbal Gland: Carcinoma				
Overall Rates (e)	3/117 (3%)	20/125 (16%)	23/175 (13%)	
Adjusted Rates (b)	3.1%	41.3%	23.5%	
Terminal Rates (c)	2/94 (2%)	1/15 (7%)	1/36 (3%)	
Week of First Observation	99	40	49	
Life Table Tests (d)		P<0.001	P<0.001	P=0.082
Incidental Tumor Tests (d)		P<0.001	P=0.016	P=0.374N
Fisher Exact Test (d)		P<0.001	P=0.001	P=0.297N
Zymbal Gland: Carcinoma or Squamous Cell Papilloma				
Overall Rates (e)	3/117 (3%)	31/125 (25%)	37/175 (21%)	
Adjusted Rates (b)	3.1%	59.4%	39.2%	
Terminal Rates (c)	2/94 (2%)	3/15 (20%)	5/36 (14%)	
Week of First Observation	99	40	49	
Life Table Tests (d)		P<0.001	P<0.001	P=0.041N
Incidental Tumor Tests (d)		P<0.001	P<0.001	P=0.297N
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.271N
All Sites: Benign Tumors				
Overall Rates (a)	99/117 (85%)	74/125 (59%)	102/175 (58%)	
Adjusted Rates (b)	90.8%	96.5%	91.1%	
Terminal Rates (c)	84/94 (89%)	13/15 (87%)	28/36 (78%)	
Week of First Observation	70	51	49	
Life Table Test (d)		P<0.001	P<0.001	P=0.007N
Incidental Tumor Test (d)		P=0.032N	P<0.001N	P=0.167N
Fisher Exact Test (d)		P<0.001N	P<0.001N	P=0.485N
All Sites: Malignant Tumors				
Overall Rates (a)	74/117 (63%)	111/125 (89%)	164/175 (94%)	
Adjusted Rates (b)	69.6%	98.0%	98.1%	
Terminal Rates (c)	62/94 (66%)	13/15 (87%)	33/36 (92%)	
Week of First Observation	71	29	39	
Life Table Test (d)		P<0.001	P<0.001	P=0.023N
Incidental Tumor Test (d)		P<0.001	P<0.001	P=0.082
Fisher Exact Test (d)		P<0.001	P<0.001	P=0.096

TABLE B3b. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DIMETHYLHYDRAZINE (DMH) (Continued)

	Untreated Control	DMH	1% Amosite + DMH	DMH vs. Amosite + DMH
All Sites: All Tumors				
Overall Rates (a)	113/117 (97%)	121/125 (97%)	175/175 (100%)	
Adjusted Rates (b)	98.3%	100.0%	100.0%	
Terminal Rates (c)	92/94 (98%)	15/15 (100%)	36/36 (100%)	
Week of First Observation	70	29	39	
Life Table Test (d)		P<0.001	P<0.001	P=0.010N
Incidental Tumor Test (d)		P=0.366	P=0.028	P=0.046
Fisher Exact Test (d)		P=0.602	P=0.025	P=0.029

(a) Number of tumor-bearing animals/number of animals examined grossly at the site

(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality

(c) Observed tumor incidence in animals killed at the end of the study

(d) Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in a dosed group than in controls is indicated by (N). The P values for the comparison of the DMH group with the 1% amosite + DMH group are presented in the last column for sites with a tumor incidence of at least 2% in at least one of the two groups.

(e) Number of tumor-bearing animals/number of animals examined microscopically at the site

(f) No P value is reported because no tumors were observed in the dosed and control groups.

(g) Includes one papillary cystadenoma

(h) Includes one carcinoma in situ, NOS, and one carcinoma, NOS

(i) Papillary adenocarcinoma

TABLE B3c. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH)

	1% Amosite	1% Amosite + DMH
Subcutaneous Tissue: Fibroma		
Overall Rates (a)	8/250 (3%)	0/175 (0%)
Adjusted Rates (b)	3.8%	0.0%
Terminal Rates (c)	6/206 (3%)	0/36 (0%)
Week of First Observation	90	
Life Table Tests (d)		P = 0.216N
Incidental Tumor Tests (d)		P = 0.065N
Fisher Exact Test (d)		P = 0.014N
Subcutaneous Tissue: Fibroma or Neurofibroma		
Overall Rates (a)	9/250 (4%)	0/175 (0%)
Adjusted Rates (b)	4.2%	0.0%
Terminal Rates (c)	7/206 (3%)	0/36 (0%)
Week of First Observation	90	
Life Table Tests (d)		P = 0.189N
Incidental Tumor Tests (d)		P = 0.058N
Fisher Exact Test (d)		P = 0.008N
Subcutaneous Tissue: Fibrosarcoma		
Overall Rates (a)	5/250 (2%)	1/175 (1%)
Adjusted Rates (b)	2.4%	1.1%
Terminal Rates (c)	5/206 (2%)	0/36 (0%)
Week of First Observation	103	83
Life Table Tests (d)		P = 0.702N
Incidental Tumor Tests (d)		P = 0.463N
Fisher Exact Test (d)		P = 0.214N
Subcutaneous Tissue: Fibroma or Fibrosarcoma		
Overall Rates (a)	12/250 (5%)	1/175 (1%)
Adjusted Rates (b)	5.7%	1.1%
Terminal Rates (c)	10/206 (5%)	0/36 (0%)
Week of First Observation	90	83
Life Table Tests (d)		P = 0.302N
Incidental Tumor Tests (d)		P = 0.060N
Fisher Exact Test (d)		P = 0.009N
Subcutaneous Tissue: Sarcoma		
Overall Rates (a)	6/250 (2%)	0/175 (0%)
Adjusted Rates (b)	2.9%	0.0%
Terminal Rates (c)	6/206 (3%)	0/36 (0%)
Week of First Observation	103	
Life Table Tests (d)		P = 0.325N
Incidental Tumor Tests (d)		P = 0.325N
Fisher Exact Test (d)		P = 0.040N
Subcutaneous Tissue: Sarcoma, Fibrosarcoma, or Neurofibrosarcoma		
Overall Rates (a)	11/250 (4%)	1/175 (1%)
Adjusted Rates (b)	5.3%	1.1%
Terminal Rates (c)	11/206 (5%)	0/36 (0%)
Week of First Observation	103	83
Life Table Tests (d)		P = 0.370N
Incidental Tumor Tests (d)		P = 0.211N
Fisher Exact Test (d)		P = 0.015N
Subcutaneous Tissue: Fibroma, Neurofibroma, Sarcoma, Fibrosarcoma, or Neurofibrosarcoma		
Overall Rates (a)	19/250 (8%)	1/175 (1%)
Adjusted Rates (b)	9.1%	1.1%
Terminal Rates (c)	17/206 (8%)	0/36 (0%)
Week of First Observation	90	83
Life Table Tests (d)		P = 0.139N
Incidental Tumor Tests (d)		P = 0.026N
Fisher Exact Test (d)		P < 0.001N

TABLE B3c. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
Integumentary System or Salivary Gland: Sarcoma, Fibrosarcoma, or Neurofibrosarcoma		
Overall Rates (e)	12/250 (5%)	1/175 (1%)
Adjusted Rates (b)	5.8%	1.1%
Terminal Rates (c)	12/206 (6%)	0/36 (0%)
Week of First Observation	103	83
Life Table Tests (d)		P=0.331N
Incidental Tumor Tests (d)		P=0.187N
Fisher Exact Test (d)		P=0.009N
Integumentary System or Salivary Gland: Fibroma, Neurofibroma, Sarcoma, Fibrosarcoma, or Neurofibrosarcoma		
Overall Rates (e)	20/250 (8%)	1/175 (1%)
Adjusted Rates (b)	9.5%	1.1%
Terminal Rates (c)	18/206 (9%)	0/36 (0%)
Week of First Observation	90	83
Life Table Tests (d)		P=0.125N
Incidental Tumor Tests (d)		P=0.023N
Fisher Exact Test (d)		P<0.001N
Hematopoietic System: Leukemia		
Overall Rates (a)	83/250 (33%)	61/175 (35%)
Adjusted Rates (b)	38.3%	79.7%
Terminal Rates (c)	73/206 (35%)	23/36 (64%)
Week of First Observation	80	62
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P=0.400
Liver: Neoplastic Nodule		
Overall Rates (e)	10/250 (4%)	32/175 (18%)
Adjusted Rates (b)	4.9%	48.7%
Terminal Rates (c)	10/206 (5%)	11/36 (31%)
Week of First Observation	103	69
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P=0.
Liver: Hepatocellular Carcinoma		
Overall Rates (e)	0/250 (0%)	8/175 (5%)
Adjusted Rates (b)	0.0%	12.8%
Terminal Rates (c)	0/206 (0%)	2/36 (6%)
Week of First Observation		59
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.006
Fisher Exact Test (d)		P<0.001
Liver: Neoplastic Nodule or Hepatocellular Carcinoma		
Overall Rates (e)	10/250 (4%)	38/175 (22%)
Adjusted Rates (b)	4.9%	54.8%
Terminal Rates (c)	10/206 (5%)	13/36 (36%)
Week of First Observation	103	59
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001

TABLE B3b. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
Small Intestine: Adenocarcinoma		
Overall Rates (a)	0/250 (0%)	11/175 (6%)
Adjusted Rates (b)	0.0%	15.1%
Terminal Rates (c)	0/206 (0%)	3/36 (8%)
Week of First Observation		43
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.02
Fisher Exact Test (d)		P<0.001
Small Intestine: Signet Ring Carcinoma		
Overall Rates (e)	0/250 (0%)	8/175 (5%)
Adjusted Rates (b)	0.0%	7.8%
Terminal Rates (c)	0/206 (0%)	0/36 (0%)
Week of First Observation		62
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.137
Fisher Exact Test (d)		P<0.001
Small Intestine: Adenocarcinoma or Mucinous Cystadenocarcinoma		
Overall Rates (e)	1/250 (0%)	13/175 (7%)
Adjusted Rates (b)	0.5%	16.8%
Terminal Rates (c)	1/206 (0%)	3/36 (8%)
Week of First Observation	103	43
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.003
Fisher Exact Test (d)		P<0.001
Small Intestine: Adenomatous Polyp, Adenocarcinoma, Mucinous Cystadenocarcinoma, or Adenocarcinoma in Adenomatous Polyp		
Overall Rates (e)	2/250 (1%)	15/175 (9%)
Adjusted Rates (b)	1.0%	20.0%
Terminal Rates (c)	2/206 (1%)	4/36 (11%)
Week of First Observation	103	43
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Large Intestine: Signet Ring Carcinoma		
Overall Rates (e)	0/250 (0%)	8/175 (5%)
Adjusted Rates (b)	0.0%	7.8%
Terminal Rates (c)	0/206 (0%)	0/36 (0%)
Week of First Observation		62
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.137
Fisher Exact Test (d)		P<0.001
Large Intestine: Adenomatous Polyp		
Overall Rates (e)	0/250 (0%)	59/175 (34%)
Adjusted Rates (b)	0.0%	66.1%
Terminal Rates (c)	0/206 (0%)	15/36 (42%)
Week of First Observation		49
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001

TABLE B3c. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
Large Intestine: Adenocarcinoma		
Overall Rates (e)	0/250 (0%)	9/175 (5%)
Adjusted Rates (b)	0.0%	12.2%
Terminal Rates (c)	0/206 (0%)	2/36 (6%)
Week of First Observation		63
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.009
Fisher Exact Test (d)		P<0.001
Large Intestine: Mucinous Cystadenocarcinoma		
Overall Rates (e)	0/250 (0%)	7/175 (4%)
Adjusted Rates (b)	0.0%	5.7%
Terminal Rates (c)	0/206 (0%)	0/36 (0%)
Week of First Observation		60
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.199
Fisher Exact Test (d)		P=0.002
Large Intestine: Adenocarcinoma in Adenomatous Polyp		
Overall Rates (e)	0/250 (0%)	46/175 (26%)
Adjusted Rates (b)	0.0%	48.4%
Terminal Rates (c)	0/206 (0%)	7/36 (19%)
Week of First Observation		55
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Large Intestine: Adenocarcinoma, Mucinous Cystadenocarcinoma, or Adenocarcinoma in Adenomatous Polyp		
Overall Rates (e)	0/250 (0%)	59/175 (34%)
Adjusted Rates (b)	0.0%	56.7%
Terminal Rates (c)	0/206 (0%)	9/36 (25%)
Week of First Observation		55
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Large Intestine: Adenomatous Polyp, Adenocarcinoma, Mucinous Cystadenocarcinoma, or Adenocarcinoma in Adenomatous Polyp		
Overall Rates (e)	0/250 (0%)	96/175 (55%)
Adjusted Rates (b)	0.0%	81.8%
Terminal Rates (c)	0/206 (0%)	20/36 (56%)
Week of First Observation		49
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Kidney: Sarcoma		
Overall Rates (e)	1/250 (0%)	19/175 (11%)
Adjusted Rates (b)	0.5%	13.2%
Terminal Rates (c)	1/206 (0%)	0/36 (0%)
Week of First Observation	103	39
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.047
Fisher Exact Test (d)		P<0.001

TABLE B3c. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
Kidney: Malignant Mixed Tumor		
Overall Rates (e)	1/250 (0%)	35/175 (20%)
Adjusted Rates (b)	0.5%	34.0%
Terminal Rates (c)	0/206 (0%)	2/36 (6%)
Week of First Observation	101	54
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Kidney: Mixed Tumor Benign or Malignant		
Overall Rates (e)	2/250 (1%)	35/175 (20%)
Adjusted Rates (b)	1.0%	34.0%
Terminal Rates (c)	1/206 (0%)	2/36 (6%)
Week of First Observation	101	54
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Pituitary Gland: Adenoma		
Overall Rates (e)	107/249 (43%)	19/175 (11%)
Adjusted Rates (b)	49.4%	34.0%
Terminal Rates (c)	96/205 (47%)	8/36 (22%)
Week of First Observation	73	69
Life Table Tests (d)		P=0.335N
Incidental Tumor Tests (d)		P<0.001N
Fisher Exact Test (d)		P<0.001N
Pituitary Gland: Carcinoma		
Overall Rates (e)	11/249 (4%)	1/175 (1%)
Adjusted Rates (b)	5.1%	1.2%
Terminal Rates (c)	7/205 (3%)	0/36 (0%)
Week of First Observation	85	85
Life Table Tests (d)		P=0.310N
Incidental Tumor Tests (d)		P=0.010N
Fisher Exact Test (d)		P=0.015N
Pituitary Gland: Adenoma or Carcinoma		
Overall Rates (e)	118/249 (47%)	20/175 (11%)
Adjusted Rates (b)	53.5%	34.8%
Terminal Rates (c)	103/205 (50%)	8/36 (22%)
Week of First Observation	73	69
Life Table Tests (d)		P=0.231N
Incidental Tumor Tests (d)		P<0.001N
Fisher Exact Test (d)		P<0.001N
Adrenal Cortex: Cortical Adenoma		
Overall Rates (e)	13/249 (5%)	4/175 (2%)
Adjusted Rates (b)	6.3%	8.7%
Terminal Rates (c)	13/205 (6%)	2/36 (6%)
Week of First Observation	103	77
Life Table Tests (d)		P=0.299
Incidental Tumor Tests (d)		P=0.557
Fisher Exact Test (d)		P=0.101N
Adrenal Cortex: Cortical Adenoma or Carcinoma		
Overall Rates (e)	14/249 (6%)	4/175 (2%)
Adjusted Rates (b)	6.8%	8.7%
Terminal Rates (c)	14/205 (7%)	2/36 (6%)
Week of First Observation	103	77
Life Table Tests (d)		P=0.340
Incidental Tumor Tests (d)		P=0.594
Fisher Exact Test (d)		P=0.073N

TABLE B3c. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
Adrenal Medulla: Pheochromocytoma		
Overall Rates (e)	27/249 (11%)	3/175 (2%)
Adjusted Rates (b)	13.2%	6.1%
Terminal Rates (c)	27/205 (13%)	1/36 (3%)
Week of First Observation	103	82
Life Table Tests (d)		P=0.273N
Incidental Tumor Tests (d)		P=0.126N
Fisher Exact Test (d)		P<0.001N
Adrenal Medulla: Pheochromocytoma or Malignant Pheochromocytoma		
Overall Rates (e)	30/249 (12%)	4/175 (2%)
Adjusted Rates (b)	14.6%	8.8%
Terminal Rates (c)	30/205 (15%)	2/36 (6%)
Week of First Observation	103	82
Life Table Tests (d)		P=0.356N
Incidental Tumor Tests (d)		P=0.188N
Fisher Exact Test (d)		P<0.001N
Thyroid Gland: Follicular Cell Adenoma		
Overall Rates (e)	10/247 (4%)	6/174 (3%)
Adjusted Rates (b)	4.9%	10.5%
Terminal Rates (c)	10/204 (5%)	2/36 (6%)
Week of First Observation	103	83
Life Table Tests (d)		P=0.034
Incidental Tumor Tests (d)		P=0.303
Fisher Exact Test (d)		P=0.482N
Thyroid Gland: Follicular Cell Adenoma or Carcinoma		
Overall Rates (e)	13/247 (5%)	7/174 (4%)
Adjusted Rates (b)	6.4%	13.2%
Terminal Rates (c)	13/204 (6%)	3/36 (8%)
Week of First Observation	103	83
Life Table Tests (d)		P=0.028
Incidental Tumor Tests (d)		P=0.237
Fisher Exact Test (d)		P=0.365N
Thyroid Gland: C-Cell Adenoma		
Overall Rates (e)	37/247 (15%)	8/174 (5%)
Adjusted Rates (b)	18.0%	14.8%
Terminal Rates (c)	36/204 (18%)	3/36 (8%)
Week of First Observation	73	78
Life Table Tests (d)		P=0.489
Incidental Tumor Tests (d)		P=0.223N
Fisher Exact Test (d)		P<0.001N
Thyroid Gland: C-Cell Carcinoma		
Overall Rates (e)	29/247 (12%)	6/174 (3%)
Adjusted Rates (b)	14.0%	13.5%
Terminal Rates (c)	27/204 (13%)	3/36 (8%)
Week of First Observation	75	91
Life Table Tests (d)		P=0.518
Incidental Tumor Tests (d)		P=0.257N
Fisher Exact Test (d)		P<0.001N
Thyroid Gland: C-Cell Adenoma or Carcinoma		
Overall Rates (e)	65/247 (26%)	14/174 (8%)
Adjusted Rates (b)	31.3%	27.0%
Terminal Rates (c)	62/204 (30%)	6/36 (17%)
Week of First Observation	73	78
Life Table Tests (d)		P=0.414
Incidental Tumor Tests (d)		P=0.114N
Fisher Exact Test (d)		P<0.001N

TABLE B3b. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
Pancreatic Islets: Islet Cell Adenoma		
Overall Rates (e)	7/249 (3%)	2/175 (1%)
Adjusted Rates (b)	3.4%	5.2%
Terminal Rates (c)	7/205 (3%)	1/36 (3%)
Week of First Observation	103	102
Life Table Tests (d)		P=0.445
Incidental Tumor Tests (d)		P=0.617
Fisher Exact Test (d)		P=0.206N
Pancreatic Islets: Islet Cell Carcinoma		
Overall Rates (e)	7/249 (3%)	0/175 (0%)
Adjusted Rates (b)	3.4%	0.0%
Terminal Rates (c)	7/205 (3%)	0/36 (0%)
Week of First Observation	103	
Life Table Tests (d)		P=0.279N
Incidental Tumor Tests (d)		P=0.279N
Fisher Exact Test (d)		P=0.023N
Pancreatic Islets: Islet Cell Adenoma or Carcinoma		
Overall Rates (e)	14/249 (6%)	2/175 (1%)
Adjusted Rates (b)	6.8%	5.2%
Terminal Rates (c)	14/205 (7%)	1/36 (3%)
Week of First Observation	103	102
Life Table Tests (d)		P=0.529N
Incidental Tumor Tests (d)		P=0.397N
Fisher Exact Test (d)		P=0.013N
Mammary Gland: Adenoma		
Overall Rates (a)	14/250 (6%)	2/175 (1%)
Adjusted Rates (b)	6.6%	3.7%
Terminal Rates (c)	12/206 (6%)	0/36 (0%)
Week of First Observation	70	94
Life Table Tests (d)		P=0.397N
Incidental Tumor Tests (d)		P=0.066N
Fisher Exact Test (d)		P=0.013N
Mammary Gland: Fibroadenoma		
Overall Rates (a)	135/250 (54%)	18/175 (10%)
Adjusted Rates (b)	64.2%	38.8%
Terminal Rates (c)	131/206 (64%)	12/36 (33%)
Week of First Observation	70	77
Life Table Tests (d)		P=0.042N
Incidental Tumor Tests (d)		P<0.001N
Fisher Exact Test (d)		P<0.001N
Mammary Gland: Adenocarcinoma		
Overall Rates (a)	25/250 (10%)	1/175 (1%)
Adjusted Rates (b)	11.9%	1.2%
Terminal Rates (c)	23/206 (11%)	0/36 (0%)
Week of First Observation	85	84
Life Table Tests (d)		P=0.068N
Incidental Tumor Tests (d)		P=0.009N
Fisher Exact Test (d)		P<0.001N
Clitoral Gland: Carcinoma		
Overall Rates (e)	14/250 (6%)	3/175 (2%)
Adjusted Rates (b)	6.6%	8.3%
Terminal Rates (c)	12/206 (6%)	3/36 (8%)
Week of First Observation	69	103
Life Table Tests (d)		P=0.577
Incidental Tumor Tests (d)		P=0.446N
Fisher Exact Test (d)		P=0.035N

TABLE B3c. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
Clitoral Gland: Adenoma or Carcinoma		
Overall Rates (e)	15/250 (6%)	3/175 (2%)
Adjusted Rates (b)	7.1%	8.3%
Terminal Rates (c)	13/206 (6%)	3/36 (8%)
Week of First Observation	69	103
Life Table Tests (d)		P=0.613
Incidental Tumor Tests (d)		P=0.408N
Fisher Exact Test (d)		P=0.024N
Uterus: Endometrial Stromal Polyp		
Overall Rates (e)	31/250 (12%)	19/175 (11%)
Adjusted Rates (b)	14.5%	30.0%
Terminal Rates (c)	26/206 (13%)	7/36 (19%)
Week of First Observation	68	69
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.470
Fisher Exact Test (d)		P=0.372N
Brain: Glioma or Astrocytoma		
Overall Rates (e)	5/250 (2%)	0/175 (0%)
Adjusted Rates (b)	2.3%	0.0%
Terminal Rates (c)	2/206 (1%)	0/36 (0%)
Week of First Observation	82	
Life Table Tests (d)		P=0.320N
Incidental Tumor Tests (d)		P=0.020N
Fisher Exact Test (d)		P=0.069N
Ear Canal: Squamous Cell Papilloma or Carcinoma		
Overall Rates (e)	0/250 (0%)	4/175 (2%)
Adjusted Rates (b)	0.0%	7.3%
Terminal Rates (c)	0/206 (0%)	1/36 (3%)
Week of First Observation		82
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.071
Fisher Exact Test (d)		P=0.028
Zymbal Gland: Squamous Cell Papilloma		
Overall Rates (e)	3/250 (1%)	14/175 (8%)
Adjusted Rates (b)	1.5%	20.2%
Terminal Rates (c)	3/206 (1%)	4/36 (11%)
Week of First Observation	103	49
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.002
Fisher Exact Test (d)		P<0.001
Zymbal Gland: Carcinoma		
Overall Rates (e)	4/250 (2%)	23/175 (13%)
Adjusted Rates (b)	1.9%	23.5%
Terminal Rates (c)	4/206 (2%)	1/36 (3%)
Week of First Observation	103	49
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.007
Fisher Exact Test (d)		P<0.001
Zymbal Gland: Carcinoma or Squamous Cell Papilloma		
Overall Rates (e)	7/250 (3%)	37/175 (21%)
Adjusted Rates (b)	3.4%	39.2%
Terminal Rates (c)	7/206 (3%)	5/36 (14%)
Week of First Observation	103	49
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P<0.001
Fisher Exact Test (d)		P<0.001

TABLE B3c. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS: AMOSITE vs. AMOSITE + DIMETHYLHYDRAZINE (DMH) (Continued)

	1% Amosite	1% Amosite + DMH
All Sites: Benign Tumors		
Overall Rates (a)	213/250 (85%)	102/175 (58%)
Adjusted Rates (b)	93.8%	91.1%
Terminal Rates (c)	192/206 (93%)	28/36 (78%)
Week of First Observation	68	49
Life Table Tests (d)		P<0.001
Incidental Tumor Tests (d)		P=0.194N
Fisher Exact Test (d)		P<0.001N
All Sites: Malignant Tumors		
Overall Rates (a)	166/250 (66%)	164/175 (94%)
Adjusted Rates (b)	71.2%	98.1%
Terminal Rates (c)	139/206 (67%)	33/36 (92%)
Week of First Observation	69	39
Life Table Test (d)		P<0.001
Incidental Tumor Test (d)		P<0.001
Fisher Exact Test (d)		P<0.001
All Sites: All Tumors		
Overall Rates (a)	240/250 (96%)	175/175 (100%)
Adjusted Rates (b)	98.4%	100.0%
Terminal Rates (c)	202/206 (98%)	36/36 (100%)
Week of First Observation	68	39
Life Table Test (d)		P<0.001
Incidental Tumor Test (d)		P<0.001
Fisher Exact Test (d)		P=0.005

(a) Number of tumor-bearing animals/number of animals examined grossly at the site

(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality

(c) Observed tumor incidence in animals killed at the end of the study

(d) Beneath the 1% amosite + DMH group incidence are the P values corresponding to pairwise comparisons between that dosed group and the 1% amosite group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in a dosed group than in controls is indicated by (N).

(e) Number of tumor-bearing animals/number of animals examined microscopically at the site

TABLE B4a. INCIDENCE OF EPITHELIAL TUMORS OF THE LARGE INTESTINE IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Incidence	Diagnosis
SR Chrysotile	0/87 (0%)	Adenomatous polyp, NOS Mucinous cystadenocarcinoma
IR Chrysotile	0/87 (0%)	
Tremolite	1/118 (1%)	
Crocidolite	1/118 (1%)	
Amosite	0/117 (0%)	
TOTAL	2/527 (0.4%)	
SD (b)	0.46%	

(a) Standard deviation

TABLE B4b. INCIDENCE OF EPITHELIAL TUMORS OF THE SMALL INTESTINE IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Incidence	Diagnosis
SR Chrysotile	1/87 (1%)	Adenomatous polyp
IR Chrysotile	0/87 (0%)	
Tremolite	0/118 (0%)	Adenomatous polyp
Crocidolite	0/118 (0%)	
Amosite	1/117 (1%)	
TOTAL	2/527 (0.4%)	
SD (a)	0.56%	

(a) Standard deviation

TABLE B4c. INCIDENCE OF LEUKEMIA IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Incidence
SR Chrysotile	28/88 (32%)
IR Chrysotile	34/88 (39%)
Tremolite	56/118 (47%)
Crocidolite	43/118 (36%)
Amosite	40/117 (34%)
TOTAL	201/529 (38.0%)
SD (a)	6.01%

(a) Standard deviation

TABLE B4d. INCIDENCE OF PITUITARY GLAND TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Adenoma	Carcinoma	Adenoma or Carcinoma
SR Chrysotile	39/87 (45%)	6/87 (7%)	45/87 (52%)
IR Chrysotile	49/87 (56%)	4/87 (5%)	53/87 (61%)
Tremolite	51/117 (44%)	5/117 (4%)	56/117 (48%)
Crocidolite	42/116 (36%)	9/116 (8%)	51/116 (44%)
Amosite	50/117 (43%)	2/117 (2%)	52/117 (44%)
TOTAL	231/524 (44.1%)	26/524 (5.0%)	257/524 (49.0%)
SD (a)	7.29%	2.38%	6.96%

(a) Standard deviation

TABLE B4e. INCIDENCE OF THYROID GLAND FOLLICULAR CELL TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Adenoma	Carcinoma	Adenoma or Carcinoma
SR Chrysotile	1/87 (1%)	4/87 (5%)	5/87 (6%)
IR Chrysotile	6/87 (7%)	1/87 (1%)	7/87 (8%)
Tremolite	3/118 (3%)	5/118 (4%)	7/118 (6%)
Crocidolite	8/117 (7%)	3/117 (3%)	11/117 (9%)
Amosite	2/116 (2%)	7/116 (6%)	9/116 (8%)
TOTAL	20/525 (3.8%)	20/525 (3.8%)	39/525 (7.4%)
SD (a)	2.82%	1.89%	1.54%

(a) Standard deviation

TABLE B4f. INCIDENCE OF LIVER TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Neoplastic Nodule	Hepatocellular Carcinoma	Neoplastic Nodule or Hepatocellular Carcinoma
SR Chrysotile	3/87 (3%)	0/87 (0%)	3/87 (3%)
IR Chrysotile	3/87 (3%)	1/87 (1%)	4/87 (5%)
Tremolite	2/118 (3%)	0/118 (0%)	2/118 (2%)
Crocidolite	3/118 (3%)	0/118 (0%)	3/118 (3%)
Amosite	4/117 (3%)	1/117 (1%)	5/117 (4%)
TOTAL	15/527 (2.8%)	2/527 (0.4%)	17/527 (3.2%)
SD (a)	0.78%	0.56%	1.20%

(a) Standard deviation

TABLE B4g. INCIDENCE OF KIDNEY SARCOMAS AND MIXED TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

0/526

TABLE B4h. INCIDENCE OF CLITORAL GLAND TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Adenoma	Carcinoma	Adenoma or Carcinoma
SR Chrysotile	1/88 (1%)	2/88 (2%)	3/88 (3%)
IR Chrysotile	0/88 (0%)	1/88 (1%)	1/88 (1%)
Tremolite	0/118 (0%)	6/118 (5%)	6/118 (5%)
Crocidolite	1/118 (1%)	4/118 (4%)	5/118 (4%)
Amosite	0/117 (0%)	6/117 (5%)	6/117 (5%)
TOTAL	2/529 (0.4%)	19/529 (3.6%)	21/529 (4.0%)
SD (a)	0.55%	1.75%	1.65%

(a) Standard deviation

TABLE B4i. INCIDENCE OF ZYMBALE GLAND TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Incidence
SR Chrysotile	3/88 (3%)
IR Chrysotile	1/88 (1%)
Tremolite	3/118 (3%)
Crocidolite	0/118 (0%)
Amosite	3/117 (3%)
TOTAL	10/529 (1.9%)
SD (a)	1.35%

(a) Standard deviation

TABLE B5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (a)

	Untreated Control	DMH	1% Amosite
Animals initially in study	117	125	250
Animals necropsied	117	125	250
Animals examined histopathologically	117	124	250
INTEGUMENTARY SYSTEM			
*Skin	(117)	(125)	(250)
Epidermal inclusion cyst	1 (1%)		3 (1%)
Abscess, NOS		1 (1%)	2 (1%)
Inflammation, chronic focal	1 (1%)		2 (1%)
Necrosis, focal			1 (0%)
Hyperkeratosis	1 (1%)		4 (2%)
Acanthosis			2 (1%)
*Subcut tissue	(117)	(125)	(250)
Inflammation, chronic		1 (1%)	
RESPIRATORY SYSTEM			
*Nasal turbinate	(117)	(125)	(250)
Inflammation, acute			1 (0%)
Inflammation, chronic	1 (1%)		
Inflammation, chronic focal			1 (0%)
#Trachea	(116)	(122)	(249)
Inflammation, chronic	1 (1%)		
#Lung/bronchus	(116)	(124)	(250)
Bronchiectasis			1 (0%)
Inflammation, chronic	1 (1%)		
#Lung/bronchiole	(116)	(124)	(250)
Foreign body, NOS			1 (0%)
#Lung	(116)	(124)	(250)
Congestion, NOS	1 (1%)		11 (4%)
Edema, NOS	1 (1%)		1 (0%)
Hemorrhage	3 (3%)	2 (2%)	7 (3%)
Inflammation, interstitial	1 (1%)		4 (2%)
Inflammation, acute		1 (1%)	
Inflammation, acute focal	1 (1%)		
Inflammation, chronic	02 (88%)	89 (71%)	30 (92%)
Granuloma, NOS			1 (0%)
Pigmentation, NOS	4 (3%)	2 (2%)	4 (2%)
Hyperplasia, alveolar epithelium		1 (1%)	6 (2%)
#Lung/alveoli	(116)	(124)	(250)
Histiocytosis	4 (3%)		6 (2%)
HEMATOPOIETIC SYSTEM			
#Bone marrow	(116)	(124)	(250)
Hypoplasia, NOS	3 (3%)		4 (2%)
Hyperplasia, NOS	1 (1%)		
Histiocytosis			1 (0%)
Myelofibrosis	1 (1%)		
#Spleen	(117)	(124)	(249)
Hemorrhage	1 (1%)	1 (1%)	1 (0%)
Fibrosis, focal	1 (1%)		6 (2%)
Fibrosis, multifocal	1 (1%)		3 (1%)
Fibrosis, diffuse			1 (0%)
Necrosis, NOS	1 (1%)	1 (1%)	2 (1%)
Necrosis, focal			2 (1%)
Pigmentation, NOS			1 (0%)
Hemosiderosis	15 (13%)	4 (3%)	81 (33%)
Atrophy, NOS		1 (1%)	1 (0%)
Hyperplasia, reticulum cell	1 (1%)		1 (0%)

TABLE B5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
HEMATOPOIETIC SYSTEM			
#Spleen (Continued)	(117)	(124)	(249)
Hematopoiesis	33 (28%)	20 (16%)	46 (18%)
Myelopoiesis		1 (1%)	
#Splenic capsule	(117)	(124)	(249)
Hemorrhage		1 (1%)	
#Splenic follicles	(117)	(124)	(249)
Atrophy, NOS	5 (4%)		7 (3%)
#Mandibular l. node	(117)	(124)	(250)
Congestion, NOS			1 (0%)
Hemorrhage		3 (2%)	5 (2%)
Abscess, NOS			1 (0%)
Pigmentation, NOS			1 (0%)
Hyperplasia, lymphoid	30 (26%)	12 (10%)	31 (12%)
#Cervical lymph node	(117)	(124)	(250)
Hemorrhage			2 (1%)
Erythrophagocytosis	1 (1%)		
Hyperplasia, reticulum cell	1 (1%)		
Hyperplasia, lymphoid	1 (1%)		2 (1%)
#Mediastinal l. node	(117)	(124)	(250)
Congestion, NOS	1 (1%)		
Hemorrhage	2 (2%)	4 (3%)	10 (4%)
Pigmentation, NOS	11 (9%)	3 (2%)	34 (14%)
Hemosiderosis			2 (1%)
Erythrophagocytosis	4 (3%)		4 (2%)
Hyperplasia, reticulum cell	2 (2%)		3 (1%)
Hyperplasia, lymphoid		4 (3%)	5 (2%)
Hematopoiesis	1 (1%)		
#Pancreatic lymph node	(117)	(124)	(250)
Hemorrhage		2 (2%)	
Pigmentation, NOS		2 (2%)	13 (5%)
Atrophy, NOS			1 (0%)
Hyperplasia, reticulum cell	5 (4%)	1 (1%)	5 (2%)
Hyperplasia, lymphoid	1 (1%)	1 (1%)	1 (0%)
#Mesenteric lymph node	(117)	(124)	(250)
Hemorrhage	2 (2%)	1 (1%)	5 (2%)
Inflammation, chronic			1 (0%)
Amyloidosis	1 (1%)		
Pigmentation, NOS	5 (4%)	3 (2%)	25 (10%)
Atrophy, NOS			2 (1%)
Erythrophagocytosis		1 (1%)	4 (2%)
Hyperplasia, reticulum cell	55 (47%)	16 (13%)	20 (48%)
Hyperplasia, lymphoid			9 (4%)
#Ileocolic lymph node	(117)	(124)	(250)
Atrophy, NOS			1 (0%)
Hyperplasia, reticulum cell	1 (1%)		
Hyperplasia, lymphoid		1 (1%)	
#Renal lymph node	(117)	(124)	(250)
Hemorrhage	1 (1%)		1 (0%)
Pigmentation, NOS	1 (1%)	1 (1%)	3 (1%)
Erythrophagocytosis	1 (1%)		
Hyperplasia, reticulum cell	1 (1%)		1 (0%)
Hyperplasia, lymphoid	1 (1%)		
#Liver	(117)	(124)	(250)
Leukocytosis, NOS	1 (1%)	1 (1%)	5 (2%)
Hematopoiesis	1 (1%)		1 (0%)
#Bile duct	(117)	(124)	(250)
Hyperplasia, lymphoid	1 (1%)		
#Peyer's patch	(117)	(124)	(249)
Hyperplasia, lymphoid		1 (1%)	1 (0%)

TABLE B5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
HEMATOPOIETIC SYSTEM (Continued)			
#Perirenal tissue	(117)	(124)	(250)
Hematopoiesis			1 (0%)
#Thymus	(79)	(95)	(210)
Cyst, NOS		1 (1%)	1 (0%)
Multilocular cyst			1 (0%)
Hemorrhage	1 (1%)	2 (2%)	
Hyperplasia, epithelial			1 (0%)
Hematopoiesis	1 (1%)		
CIRCULATORY SYSTEM			
#Mediastinal l. node	(117)	(124)	(250)
Lymphangiectasis	1 (1%)		1 (0%)
#Mesenteric lymph node	(117)	(124)	(250)
Lymphangiectasis	1 (1%)		4 (2%)
#Ileocolic lymph node	(117)	(124)	(250)
Lymphangiectasis		1 (1%)	4 (2%)
#Renal lymph node	(117)	(124)	(250)
Lymphangiectasis	4 (3%)	2 (2%)	1 (0%)
#Lung	(116)	(124)	(250)
Thrombosis, NOS		1 (1%)	
Thrombus, fibrin	1 (1%)		
#Heart/atrium	(116)	(122)	(250)
Thrombosis, NOS	4 (3%)		4 (2%)
#Myocardium	(116)	(122)	(250)
Mineralization			1 (0%)
Inflammation, chronic	1 (1%)		1 (0%)
Inflammation, chronic focal	37 (32%)	8 (7%)	96 (38%)
Inflammation, chronic diffuse	25 (22%)	2 (2%)	46 (18%)
Fibrosis, focal	4 (3%)	2 (2%)	2 (1%)
Fibrosis, diffuse			1 (0%)
Degeneration, NOS			1 (0%)
#Cardiac valve	(116)	(122)	(250)
Inflammation, chronic	1 (1%)		
Inflammation, chronic focal	1 (1%)		
*Aorta	(117)	(125)	(250)
Mineralization			1 (0%)
*Coronary artery	(117)	(125)	(250)
Mineralization			1 (0%)
*Mesenteric artery	(117)	(125)	(250)
Thrombosis, NOS	1 (1%)		
Inflammation, acute/chronic	1 (1%)		
Necrosis, NOS	1 (1%)		
#Liver	(117)	(124)	(250)
Thrombosis, NOS	2 (2%)	1 (1%)	
#Pancreas	(116)	(124)	(249)
Periarteritis	1 (1%)		
#Uterus	(117)	(124)	(250)
Thrombosis, NOS	1 (1%)		
#Uterus/endometrium	(117)	(124)	(250)
Thrombosis, NOS	1 (1%)		
#Adrenal	(117)	(124)	(249)
Thrombosis, NOS	2 (2%)		

TABLE B5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
DIGESTIVE SYSTEM			
*Hard palate	(117)	(125)	(250)
Foreign body, NOS			1 (0%)
Inflammation, chronic focal			1 (0%)
Necrosis, focal			1 (0%)
*Tongue	(117)	(125)	(250)
Hyperkeratosis			1 (0%)
Acanthosis			3 (1%)
#Salivary gland	(116)	(123)	(246)
Edema, NOS	1 (1%)		
Inflammation, chronic	1 (1%)		
Inflammation, chronic focal	1 (1%)		1 (0%)
Fibrosis, focal			1 (0%)
#Parotid gland	(116)	(124)	(246)
Atrophy, focal			2 (1%)
#Liver	(117)	(124)	(250)
Congestion, NOS	1 (1%)		4 (2%)
Hemorrhage		2 (2%)	6 (2%)
Inflammation, chronic			5 (2%)
Granuloma, NOS	31 (26%)	15 (12%)	65 (26%)
Fibrosis, focal		1 (1%)	
Fibrosis, multifocal			1 (0%)
Hepatitis, toxic	12 (10%)	30 (24%)	28 (11%)
Degeneration, NOS			1 (0%)
Necrosis, NOS	1 (1%)		
Necrosis, focal	14 (12%)	22 (18%)	39 (16%)
Metamorphosis fatty	44 (38%)	37 (30%)	76 (30%)
Pigmentation, NOS	16 (14%)	7 (6%)	61 (24%)
Mitotic alteration			1 (0%)
Focal cellular change	55 (47%)	65 (52%)	29 (52%)
Angiectasis		4 (3%)	13 (5%)
#Liver/kupffer cell	(117)	(124)	(250)
Hyperplasia, NOS			1 (0%)
#Bile duct	(117)	(124)	(250)
Cyst, NOS	1 (1%)	7 (6%)	
Multilocular cyst		2 (2%)	
Cystic ducts			2 (1%)
Inflammation, chronic	7 (6%)	3 (2%)	10 (4%)
Fibrosis	5 (4%)	2 (2%)	1 (0%)
Hyperplasia, NOS	15 (13%)	16 (13%)	15 (6%)
Hyperplasia, focal	1 (1%)		1 (0%)
#Pancreas	(116)	(124)	(249)
Ectopia	8 (7%)	4 (3%)	11 (4%)
Inflammation, acute diffuse			1 (0%)
Inflammation, chronic		1 (1%)	
Inflammation, chronic focal		2 (2%)	1 (0%)
Atrophy, NOS		1 (1%)	
Atrophy, focal	8 (7%)	3 (2%)	28 (11%)
Atrophy, diffuse			3 (1%)
#Pancreatic acinus	(116)	(124)	(249)
Hyperplasia, focal	1 (1%)		2 (1%)
#Esophagus	(117)	(119)	(246)
Inflammation, chronic diffuse	1 (1%)		
Parasitism			1 (0%)
Necrosis, NOS	1 (1%)		
Hyperkeratosis	7 (6%)	3 (3%)	7 (3%)
#Stomach	(117)	(124)	(250)
Mineralization	3 (3%)		2 (1%)
Cyst, NOS	1 (1%)		1 (0%)

TABLE B5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
DIGESTIVE SYSTEM			
#Stomach (Continued)	(117)	(124)	(250)
Edema, NOS	1 (1%)		
Hemorrhage	1 (1%)		
Ulcer, NOS		1 (1%)	
Inflammation, acute focal			1 (0%)
Inflammation, chronic	4 (3%)	7 (6%)	4 (2%)
Inflammation, chronic focal	7 (6%)		20 (8%)
Inflammation, chronic diffuse	11 (9%)	3 (2%)	35 (14%)
Ulcer, perforated	4 (3%)		30 (12%)
Necrosis, NOS	1 (1%)		
Necrosis, focal	13 (11%)	10 (8%)	37 (15%)
Necrosis, diffuse			3 (1%)
Hyperkeratosis	24 (21%)	5 (4%)	56 (22%)
Acanthosis	26 (22%)	14 (11%)	72 (29%)
#Gastric mucosa	(117)	(124)	(250)
Hyperplasia, focal			2 (1%)
#Gastric submucosa	(117)	(124)	(250)
Edema, NOS	1 (1%)		1 (0%)
#Gastric muscularis	(117)	(124)	(250)
Degeneration, NOS	2 (2%)		3 (1%)
#Gastric fundus	(117)	(124)	(250)
Hyperplasia, diffuse	2 (2%)		1 (0%)
#Small intestine	(117)	(124)	(249)
Inflammation, chronic focal			1 (0%)
Necrosis, focal			2 (1%)
#Duodenum	(117)	(124)	(249)
Hemorrhage			1 (0%)
Necrosis, focal	1 (1%)		
#Jejunum	(117)	(124)	(249)
Hyperplasia, epithelial		1 (1%)	
#Large intestine	(117)	(124)	(250)
Parasitism	1 (1%)		
#Colon	(117)	(124)	(250)
Mineralization			1 (0%)
Inflammation, chronic focal	1 (1%)		
Parasitism	2 (2%)	3 (2%)	6 (2%)
Necrosis, focal			1 (0%)
Hyperplasia, epithelial			2 (1%)
Hyperplasia, focal		1 (1%)	
#Colonic muscularis propria	(117)	(124)	(250)
Degeneration, NOS			1 (0%)
#Cecum	(117)	(124)	(250)
Inflammation, acute diffuse			1 (0%)
Inflammation, chronic			1 (0%)
Inflammation, chronic focal		2 (2%)	1 (0%)
Inflammation, chronic diffuse		1 (1%)	1 (0%)
Parasitism	1 (1%)		2 (1%)
Necrosis, focal		1 (1%)	1 (0%)
Necrosis, diffuse			1 (0%)
#Ascending colon	(117)	(124)	(250)
Necrosis, focal		1 (1%)	
#Descending colon	(117)	(124)	(250)
Inflammation, chronic focal		1 (1%)	
Hyperplasia, epithelial		1 (1%)	

TABLE B5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
URINARY SYSTEM			
#Kidney	(117)	(124)	(250)
Mineralization	69 (59%)	5 (4%)	76 (70%)
Hydronephrosis	1 (1%)	1 (1%)	1 (0%)
Congestion, NOS			1 (0%)
Hemorrhage			1 (0%)
Inflammation, acute focal	1 (1%)		
Inflammation, chronic	07 (91%)	68 (54%)	29 (92%)
Inflammation, chronic focal			1 (0%)
Inflammation, chronic diffuse		1 (1%)	1 (0%)
Fibrosis, diffuse	1 (1%)		1 (0%)
Infarct, NOS		1 (1%)	
Calcification, NOS	2 (2%)	20 (16%)	
Pigmentation, NOS			1 (0%)
Atrophy, NOS			1 (0%)
Angiectasis			1 (0%)
#Kidney/cortex	(117)	(124)	(250)
Cyst, NOS	4 (3%)		2 (1%)
Abscess, NOS	1 (1%)		
#Kidney/tubule	(117)	(124)	(250)
Mineralization			2 (1%)
Inflammation, chronic	1 (1%)		
Metamorphosis fatty			1 (0%)
Pigmentation, NOS	70 (60%)	29 (23%)	79 (72%)
Nuclear enlargement	1 (1%)		
Cytoplasmic vacuolization			1 (0%)
*Ureter	(117)	(125)	(250)
Dilatation, NOS			1 (0%)
Hemorrhage			1 (0%)
#Urinary bladder	(117)	(121)	(248)
Calculus, unkn gross or micro			1 (0%)
Hemorrhage			1 (0%)
Inflammation, chronic	1 (1%)		
Inflammation, chronic focal			1 (0%)
Pigmentation, NOS			1 (0%)
Hyperplasia, epithelial	2 (2%)		1 (0%)
Hyperplasia, papillary	2 (2%)		
Acanthosis			1 (0%)
ENDOCRINE SYSTEM			
#Pituitary	(117)	(123)	(249)
Cyst, NOS	9 (8%)	3 (2%)	13 (5%)
Hemorrhage	1 (1%)	1 (1%)	1 (0%)
Hemorrhagic cyst			4 (2%)
Pigmentation, NOS			4 (2%)
Hyperplasia, NOS	1 (1%)		
Hyperplasia, focal	9 (8%)	13 (10%)	18 (7%)
Angiectasis	20 (17%)	2 (2%)	41 (16%)
#Adrenal	(117)	(124)	(249)
Ectopia	1 (1%)		
Cyst, NOS			1 (0%)
Congestion, NOS			1 (0%)
Hemorrhage	1 (1%)		
Necrosis, focal	1 (1%)		
Metamorphosis fatty	2 (2%)	2 (2%)	2 (1%)
Hyperplasia, focal	1 (1%)		2 (1%)
Angiectasis			4 (2%)
Metaplasia, osseous			1 (0%)

TABLE B5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
ENDOCRINE SYSTEM (Continued)			
#Adrenal cortex	(117)	(124)	(249)
Hemorrhage		1 (1%)	1 (0%)
Degeneration, NOS	1 (1%)		1 (0%)
Necrosis, NOS		1 (1%)	
Metamorphosis fatty	49 (42%)	5 (4%)	14 (46%)
Pigmentation, NOS			2 (1%)
Hyperplasia, NOS			1 (0%)
Hyperplasia, focal	8 (7%)	1 (1%)	14 (6%)
Angiectasis			4 (2%)
#Adrenal medulla	(117)	(124)	(249)
Hyperplasia, NOS	1 (1%)		2 (1%)
Hyperplasia, focal	18 (15%)	9 (7%)	50 (20%)
Hyperplasia, diffuse		1 (1%)	
#Periadrenal tissue	(117)	(124)	(249)
Hemorrhage	1 (1%)		
#Thyroid	(116)	(123)	(247)
Follicular cyst, NOS	2 (2%)	3 (2%)	17 (7%)
Pigmentation, NOS	1 (1%)		
Hyperplasia, C-cell	22 (19%)	17 (14%)	71 (29%)
Hyperplasia, follicular cell	1 (1%)		
#Parathyroid	(109)	(118)	(240)
Hyperplasia, NOS	7 (6%)		18 (8%)
Hyperplasia, focal			1 (0%)
Angiectasis			1 (0%)
#Pancreatic islets	(116)	(124)	(249)
Hyperplasia, focal			1 (0%)
REPRODUCTIVE SYSTEM			
*Mammary gland	(117)	(125)	(250)
Galactocele	18 (15%)		36 (14%)
Cyst, NOS		1 (1%)	2 (1%)
Cystic ducts	40 (34%)	4 (3%)	14 (46%)
Inflammation, diffuse			1 (0%)
Abscess, NOS	1 (1%)		
Fibrosis, focal			1 (0%)
Hyperplasia, NOS	17 (15%)	5 (4%)	33 (13%)
Hyperplasia, focal			2 (1%)
Hyperplasia, diffuse	3 (3%)		13 (5%)
*Preputial gland	(117)	(125)	(250)
Cyst, NOS	1 (1%)		
Cystic ducts	2 (2%)		9 (4%)
Inflammation, acute	1 (1%)		
Abscess, NOS			1 (0%)
Hyperplasia, NOS	1 (1%)		1 (0%)
Hyperplasia, diffuse	1 (1%)		2 (1%)
Hyperkeratosis			2 (1%)
*Vagina	(117)	(125)	(250)
Inflammation, acute			1 (0%)
Acanthosis		1 (1%)	
#Uterus	(117)	(124)	(250)
Hydrometra	5 (4%)	5 (4%)	12 (5%)
Hemorrhage	3 (3%)		
Pyometra		1 (1%)	
Abscess, NOS	1 (1%)		
Inflammation, chronic	1 (1%)	1 (1%)	
Inflammation, chronic focal			2 (1%)
Fibrosis			1 (0%)
Pigmentation, NOS			1 (0%)

TABLE B5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
REPRODUCTIVE SYSTEM (Continued)			
#Cervix uteri	(117)	(124)	(250)
Cyst, NOS			2 (1%)
Abscess, NOS			2 (1%)
Inflammation, chronic	1 (1%)		1 (0%)
Inflammation, chronic focal			1 (0%)
Fibrosis	1 (1%)	2 (2%)	2 (1%)
Fibrosis, diffuse			1 (0%)
Necrosis, focal			1 (0%)
Hyperkeratosis	2 (2%)		3 (1%)
Acanthosis	3 (3%)		4 (2%)
#Uterus/endometrium	(117)	(124)	(250)
Cyst, NOS	2 (2%)	5 (4%)	7 (3%)
Hyperplasia, NOS		1 (1%)	1 (0%)
Hyperplasia, papillary			1 (0%)
#Endometrial gland	(117)	(124)	(250)
Cyst, NOS		2 (2%)	
#Ovary	(117)	(124)	(250)
Cyst, NOS	7 (6%)	5 (4%)	8 (3%)
Follicular cyst, NOS	2 (2%)		2 (1%)
Parovarian cyst	3 (3%)	7 (6%)	9 (4%)
Hyperplasia, papillary	2 (2%)		
NERVOUS SYSTEM			
#Cerebrum	(117)	(124)	(250)
Hydrocephalus, NOS		1 (1%)	
Hemorrhage			2 (1%)
Inflammation, chronic focal	1 (1%)		
Necrosis, NOS		1 (1%)	
Necrosis, focal			2 (1%)
#Cerebellum	(117)	(124)	(250)
Hemorrhage			3 (1%)
Gliosis		1 (1%)	
SPECIAL SENSE ORGANS			
*Eye	(117)	(125)	(250)
Hemorrhage	8 (7%)		9 (4%)
Inflammation, chronic	1 (1%)		
Inflammation, chronic focal	2 (2%)		1 (0%)
Synechia, anterior		1 (1%)	1 (0%)
Synechia, posterior	2 (2%)		2 (1%)
Degeneration, NOS	1 (1%)		
Cataract	15 (13%)	3 (2%)	26 (10%)
Phthisis bulbi	1 (1%)	1 (1%)	1 (0%)
*Eye anterior chamber	(117)	(125)	(250)
Empyema			2 (1%)
*Eye/cornea	(117)	(125)	(250)
Inflammation, necrotizing			1 (0%)
Inflammation, chronic		2 (2%)	
Inflammation, chronic focal			4 (2%)
Inflammation, chronic diffuse	2 (2%)		3 (1%)
*Eye/retina	(117)	(125)	(250)
Degeneration, NOS	30 (26%)	5 (4%)	78 (31%)
*Eye/crystalline lens	(117)	(125)	(250)
Rupture	1 (1%)		1 (0%)
*Nasolacrimal duct	(117)	(125)	(250)
Inflammation, acute			1 (0%)
Hyperkeratosis			1 (0%)

TABLE B5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
SPECIAL SENSE ORGANS (Continued)			
*Harderian gland	(117)	(125)	(250)
Hyperplasia, focal			1 (0%)
*Ear	(117)	(125)	(250)
Abscess, NOS		1 (1%)	
*Ear canal	(117)	(125)	(250)
Hyperkeratosis		1 (1%)	
*Zymbal gland	(117)	(125)	(250)
Cystic ducts	15 (13%)	1 (1%)	22 (9%)
Abscess, NOS	1 (1%)		
Hyperplasia, NOS			1 (0%)
Hyperplasia, focal			1 (0%)
MUSCULOSKELETAL SYSTEM			
*Skull	(117)	(125)	(250)
Osteopetrosis	6 (5%)	1 (1%)	13 (5%)
Exostosis		1 (1%)	
*Sternum	(117)	(125)	(250)
Osteopetrosis	9 (8%)		13 (5%)
Exostosis		1 (1%)	
*Rib	(117)	(125)	(250)
Degeneration, NOS			8 (3%)
*Intercostal muscle	(117)	(125)	(250)
Inflammation, chronic			1 (0%)
BODY CAVITIES			
*Mediastinum	(117)	(125)	(250)
Inflammation, chronic		1 (1%)	
Inflammation, chronic focal			1 (0%)
*Abdominal cavity	(117)	(125)	(250)
Steatitis		2 (2%)	1 (0%)
Necrosis, NOS	1 (1%)		
Necrosis, fat	4 (3%)	3 (2%)	8 (3%)
*Mesentery	(117)	(125)	(250)
Inflammation, acute/chronic			1 (0%)
Inflammation, chronic focal	2 (2%)		13 (5%)

TABLE B5a. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: UNTREATED CONTROL, DMH, 1% AMOSITE (Continued)

	Untreated Control	DMH	1% Amosite
ALL OTHER SYSTEMS			
Multiple sites			
Inflammation, chronic	1		
*Multiple organs	(117)	(125)	(250)
Mineralization	1 (1%)		1 (0%)
Inflammation, chronic	6 (5%)		11 (4%)
Necrosis, NOS	1 (1%)		
Pigmentation, NOS	1 (1%)		1 (0%)
Head			
Abscess, NOS		1	
Diaphragm			
Hernia, NOS	1	2	5
Inflammation, acute focal	1		
Inflammation, acute diffuse			1
Adipose tissue			
Hemorrhage			1
SPECIAL MORPHOLOGY SUMMARY			
Auto/necropsy/histo perf		1	

(a) DMH indicates a group receiving five doses of 15 mg/kg 1,2-dimethylhydrazine dihydrochloride by gavage in pH 5 acetate buffer.

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

Number of animals examined microscopically at this site

TABLE B5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (a)

	1% Amosite + PW	1% Amosite + DMH
Animals initially in study	100	175
Animals necropsied	100	175
Animals examined histopathologically	100	175
INTEGUMENTARY SYSTEM		
*Skin	(100)	(175)
Epidermal inclusion cyst	1 (1%)	2 (1%)
Abscess, NOS	1 (1%)	1 (1%)
Acanthosis		1 (1%)
*Subcut tissue	(100)	(175)
Abscess, NOS	1 (1%)	2 (1%)
Necrosis, fat		1 (1%)
RESPIRATORY SYSTEM		
#Lung	(100)	(175)
Congestion, NOS	4 (4%)	2 (1%)
Hemorrhage		1 (1%)
Inflammation, interstitial	2 (2%)	
Pneumonia, aspiration	1 (1%)	
Inflammation, acute focal	1 (1%)	
Inflammation, acute diffuse	1 (1%)	
Inflammation, chronic	88 (88%)	57 (90%)
Granuloma, NOS	4 (4%)	
Necrosis, focal		1 (1%)
Necrosis, diffuse	1 (1%)	
Pigmentation, NOS	1 (1%)	
Hyperplasia, alveolar epithelium	3 (3%)	1 (1%)
Metaplasia, squamous	2 (2%)	
#Lung/alveoli	(100)	(175)
Histiocytosis	2 (2%)	
HEMATOPOIETIC SYSTEM		
#Brain	(100)	(175)
Hematopoiesis		1 (1%)
#Bone marrow	(100)	(174)
Osteopetrosis		1 (1%)
Hypoplasia, NOS	1 (1%)	1 (1%)
Hyperplasia, NOS	1 (1%)	
Myelofibrosis	1 (1%)	
#Spleen	(100)	(175)
Ectopia	1 (1%)	
Congestion, NOS		1 (1%)
Hemorrhage	1 (1%)	2 (1%)
Fibrosis		1 (1%)
Fibrosis, focal	6 (6%)	
Fibrosis, diffuse	2 (2%)	
Hepatitis, toxic		1 (1%)
Necrosis, focal		3 (2%)
Pigmentation, NOS	2 (2%)	4 (2%)
Hemosiderosis	32 (32%)	13 (7%)
Hematopoiesis	27 (27%)	48 (27%)
Myelopoiesis		1 (1%)
#Splenic follicles	(100)	(175)
Atrophy, NOS	5 (5%)	2 (1%)
#Mandibular l. node	(100)	(175)
Hemorrhage		3 (2%)
Hyperplasia, lymphoid	16 (16%)	30 (17%)

TABLE B5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
HEMATOPOIETIC SYSTEM (Continued)		
#Thoracic lymph node	(100)	(175)
Hemorrhage		1 (1%)
#Mediastinal l. node	(100)	(175)
Congestion, NOS	1 (1%)	
Hemorrhage	4 (4%)	21 (12%)
Inflammation, chronic		1 (1%)
Pigmentation, NOS	19 (19%)	26 (15%)
Atrophy, NOS		1 (1%)
Hyperplasia, reticulum cell		2 (1%)
Hyperplasia, lymphoid	1 (1%)	4 (2%)
Mastocytosis		1 (1%)
#Pancreatic lymph node	(100)	(175)
Pigmentation, NOS	4 (4%)	7 (4%)
Hyperplasia, reticulum cell	3 (3%)	5 (3%)
#Mesenteric lymph node	(100)	(175)
Hemorrhage	1 (1%)	
Pigmentation, NOS	6 (6%)	10 (6%)
Erythrophagocytosis	1 (1%)	
Hyperplasia, reticulum cell	49 (49%)	55 (31%)
Hyperplasia, lymphoid	3 (3%)	4 (2%)
#Ileocolic lymph node	(100)	(175)
Abscess, NOS		1 (1%)
#Renal lymph node	(100)	(175)
Hemorrhage		1 (1%)
Hyperplasia, reticulum cell		1 (1%)
#Liver	(100)	(175)
Leukocytosis, NOS		1 (1%)
Hyperplasia, reticulum cell		1 (1%)
Hematopoiesis		1 (1%)
#Hepatic sinusoid	(100)	(175)
Leukocytosis, NOS		1 (1%)
#Adrenal	(100)	(175)
Hematopoiesis		2 (1%)
#Thymus	(81)	(139)
Atrophy, NOS	1 (1%)	
Hyperplasia, epithelial	3 (4%)	
Hyperplasia, reticulum cell	1 (1%)	
CIRCULATORY SYSTEM		
#Mandibular l. node	(100)	(175)
Lymphangiectasis	1 (1%)	2 (1%)
#Mediastinal l. node	(100)	(175)
Lymphangiectasis	1 (1%)	1 (1%)
#Mesenteric lymph node	(100)	(175)
Lymphangiectasis	2 (2%)	2 (1%)
#Ileocolic lymph node	(100)	(175)
Lymphangiectasis		5 (3%)
#Heart	(100)	(175)
Inflammation, chronic diffuse		1 (1%)
#Myocardium	(100)	(175)
Inflammation, chronic focal	48 (48%)	36 (21%)
Inflammation, chronic diffuse	23 (23%)	27 (15%)
Fibrosis, focal		3 (2%)
Fibrosis, multifocal		2 (1%)
Degeneration, NOS	2 (2%)	1 (1%)
#Cardiac valve	(100)	(175)
Inflammation, chronic		1 (1%)
Inflammation, chronic focal		2 (1%)

TABLE B5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
CIRCULATORY SYSTEM (Continued)		
*Pulmonary artery	(100)	(175)
Granuloma, NOS		1 (1%)
*Mesentery	(100)	(175)
Periarteritis	1 (1%)	
#Kidney	(100)	(175)
Thrombosis, NOS		1 (1%)
Thrombus, organized		1 (1%)
#Uterus	(100)	(175)
Thrombosis, NOS	1 (1%)	
Thrombus, organized		1 (1%)
#Adrenal	(100)	(175)
Thrombosis, NOS		1 (1%)
DIGESTIVE SYSTEM		
*Hard palate	(100)	(175)
Acanthosis	1 (1%)	
*Tongue	(100)	(175)
Hyperkeratosis		1 (1%)
Acanthosis		1 (1%)
#Salivary gland	(100)	(174)
Inflammation, chronic		1 (1%)
Inflammation, chronic diffuse		1 (1%)
Atrophy, diffuse		1 (1%)
#Parotid gland	(100)	(174)
Hyperplasia, focal	1 (1%)	
#Liver	(100)	(175)
Congestion, NOS	3 (3%)	
Hemorrhage	1 (1%)	1 (1%)
Inflammation, acute focal	1 (1%)	
Inflammation, chronic focal		1 (1%)
Granuloma, NOS	32 (32%)	25 (14%)
Hepatitis, toxic	9 (9%)	33 (19%)
Degeneration, NOS	1 (1%)	
Necrosis, focal	12 (12%)	19 (11%)
Infarct, NOS	1 (1%)	
Metamorphosis fatty	28 (28%)	32 (18%)
Pigmentation, NOS	24 (24%)	8 (5%)
Focal cellular change	47 (47%)	13 (65%)
Angiectasis	1 (1%)	6 (3%)
#Hepatic capsule	(100)	(175)
Granuloma, foreign body	1 (1%)	
#Bile duct	(100)	(175)
Cyst, NOS		31 (18%)
Multiple cysts		3 (2%)
Inflammation, chronic	10 (10%)	28 (16%)
Fibrosis	1 (1%)	2 (1%)
Hyperplasia, NOS	11 (11%)	35 (20%)
Hyperplasia, focal		1 (1%)
#Pancreas	(100)	(175)
Ectopia	5 (5%)	3 (2%)
Inflammation, chronic		1 (1%)
Inflammation, chronic focal		3 (2%)
Atrophy, focal	7 (7%)	7 (4%)
Atrophy, diffuse	3 (3%)	1 (1%)
#Esophagus	(100)	(175)
Hyperkeratosis	6 (6%)	6 (3%)

TABLE B5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
DIGESTIVE SYSTEM (Continued)		
#Stomach	(100)	(175)
Embryonal rest	1 (1%)	
Edema, NOS	1 (1%)	
Inflammation, acute focal		1 (1%)
Inflammation, chronic	1 (1%)	5 (3%)
Inflammation, chronic focal	9 (9%)	2 (1%)
Inflammation, chronic diffuse	8 (8%)	2 (1%)
Ulcer, perforated	10 (10%)	
Necrosis, NOS	1 (1%)	
Necrosis, focal	11 (11%)	9 (5%)
Hyperkeratosis	17 (17%)	12 (7%)
Acanthosis	23 (23%)	18 (10%)
#Small intestine	(100)	(175)
Parasitism		1 (1%)
#Peyer's patch	(100)	(175)
Hyperplasia, NOS		1 (1%)
#Ileum	(100)	(175)
Hyperplasia, diffuse		1 (1%)
#Colon	(100)	(175)
Cyst, NOS		1 (1%)
Inflammation, acute focal	1 (1%)	
Inflammation, chronic diffuse		1 (1%)
Fibrosis, focal	1 (1%)	
Parasitism	8 (8%)	7 (4%)
Necrosis, focal	1 (1%)	
Hyperplasia, focal		6 (3%)
#Colonic submucosa	(100)	(175)
Fibrosis, focal	1 (1%)	
#Cecum	(100)	(175)
Hemorrhage	2 (2%)	
Inflammation, chronic diffuse		1 (1%)
Parasitism	1 (1%)	
Necrosis, focal	1 (1%)	2 (1%)
#Ascending colon	(100)	(175)
Parasitism		1 (1%)
Necrosis, focal		1 (1%)
#Transverse colon	(100)	(175)
Hemorrhage		1 (1%)
Parasitism		1 (1%)
Necrosis, focal		1 (1%)
Hyperplasia, focal		1 (1%)
#Descending colon	(100)	(175)
Parasitism		1 (1%)
*Rectum	(100)	(175)
Abscess, NOS		1 (1%)
URINARY SYSTEM		
#Kidney	(100)	(175)
Mineralization	81 (81%)	58 (33%)
Hydronephrosis		1 (1%)
Congestion, NOS	3 (3%)	
Inflammation, chronic	96 (96%)	13 (65%)
Fibrosis, focal		1 (1%)
Fibrosis, diffuse	1 (1%)	
Calcification, NOS	1 (1%)	
Pigmentation, NOS		2 (1%)
Hyperplasia, tubular cell	1 (1%)	

TABLE B5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
URINARY SYSTEM (Continued)		
#Kidney/cortex	(100)	(175)
Cyst, NOS	4 (4%)	
#Kidney/tubule	(100)	(175)
Pigmentation, NOS	85 (85%)	73 (42%)
#Urinary bladder	(99)	(173)
Calculus, unkn gross or micro		1 (1%)
Hemorrhage		1 (1%)
Inflammation, chronic		1 (1%)
Hyperplasia, epithelial		1 (1%)
Hyperplasia, papillary	1 (1%)	1 (1%)
ENDOCRINE SYSTEM		
#Pituitary	(100)	(175)
Cyst, NOS	4 (4%)	7 (4%)
Hemorrhage	4 (4%)	
Hemorrhagic cyst	3 (3%)	1 (1%)
Necrosis, focal	1 (1%)	
Pigmentation, NOS	3 (3%)	1 (1%)
Hyperplasia, focal	6 (6%)	4 (2%)
Angiectasis	28 (28%)	17 (10%)
#Adrenal	(100)	(175)
Cyst, NOS	1 (1%)	
Congestion, NOS		1 (1%)
Hemorrhage	1 (1%)	2 (1%)
Necrosis, NOS		1 (1%)
Atrophy, NOS		1 (1%)
Angiectasis		2 (1%)
#Adrenal cortex	(100)	(175)
Congestion, NOS		1 (1%)
Hemorrhage		1 (1%)
Degeneration, NOS		2 (1%)
Necrosis, NOS	1 (1%)	3 (2%)
Necrosis, focal		3 (2%)
Metamorphosis fatty	46 (46%)	28 (16%)
Hyperplasia, focal	12 (12%)	2 (1%)
Angiectasis		1 (1%)
#Adrenal medulla	(100)	(175)
Hyperplasia, focal	13 (13%)	10 (6%)
#Thyroid	(100)	(174)
Cystic follicles	1 (1%)	
Follicular cyst, NOS	2 (2%)	8 (5%)
Hyperplasia, C-cell	26 (26%)	24 (14%)
#Parathyroid	(96)	(172)
Ectopia	1 (1%)	
Hyperplasia, NOS	7 (7%)	
REPRODUCTIVE SYSTEM		
*Mammary gland	(100)	(175)
Galactocele	15 (15%)	
Cystic ducts	63 (63%)	21 (12%)
Abscess, NOS	1 (1%)	
Hyperplasia, NOS	7 (7%)	4 (2%)
Hyperplasia, focal	1 (1%)	
Hyperplasia, diffuse	9 (9%)	

TABLE B5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
REPRODUCTIVE SYSTEM (Continued)		
*Preputial gland	(100)	(175)
Cystic ducts	2 (2%)	
Abscess, NOS	2 (2%)	
Necrosis, focal	1 (1%)	
Hyperkeratosis	1 (1%)	
*Vagina	(100)	(175)
Inflammation, acute	1 (1%)	
Abscess, NOS	1 (1%)	
Hyperkeratosis		1 (1%)
Acanthosis		2 (1%)
#Uterus	(100)	(175)
Hydrometra	6 (6%)	10 (6%)
Inflammation, acute		1 (1%)
Pigmentation, NOS	2 (2%)	
#Uterine serosa	(100)	(175)
Abscess, NOS	1 (1%)	
#Cervix uteri	(100)	(175)
Cyst, NOS	3 (3%)	
Inflammation, acute focal	1 (1%)	
Fibrosis	2 (2%)	3 (2%)
Hyperkeratosis	3 (3%)	
Acanthosis	3 (3%)	
#Uterus/endometrium	(100)	(175)
Cyst, NOS	5 (5%)	13 (7%)
Hyperplasia, NOS		3 (2%)
Hyperplasia, focal		3 (2%)
Hyperplasia, papillary	1 (1%)	
#Ovary	(99)	(175)
Cyst, NOS	5 (5%)	
Follicular cyst, NOS	1 (1%)	3 (2%)
Parovarian cyst		12 (7%)
NERVOUS SYSTEM		
#Cerebrum	(100)	(175)
Hydrocephalus, NOS		2 (1%)
Hemorrhage	3 (3%)	
Abscess, NOS	1 (1%)	1 (1%)
Gliosis		2 (1%)
#Cerebellum	(100)	(175)
Hemorrhage	1 (1%)	
Necrosis, focal	1 (1%)	
#Medulla oblongata	(100)	(175)
Hemorrhage		1 (1%)
SPECIAL SENSE ORGANS		
*Eye	(100)	(175)
Synechia, anterior		1 (1%)
Cataract	9 (9%)	6 (3%)
Phthisis bulbi		1 (1%)
*Eye anterior chamber	(100)	(175)
Empyema	1 (1%)	1 (1%)
*Eye/cornea	(100)	(175)
Inflammation, acute		1 (1%)
Inflammation, chronic		1 (1%)
Inflammation, chronic focal	1 (1%)	
Inflammation, chronic diffuse	1 (1%)	
Necrosis, NOS		1 (1%)
Necrosis, focal	1 (1%)	

TABLE B5b. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND DMH: 1% AMOSITE + PW, 1% AMOSITE + DMH (Continued)

	1% Amosite + PW	1% Amosite + DMH
SPECIAL SENSE ORGANS (Continued)		
*Eye/retina	(100)	(175)
Degeneration, NOS	28 (28%)	9 (5%)
*Eyelid	(100)	(175)
Abscess, NOS	1 (1%)	
*Zymbal gland	(100)	(175)
Cystic ducts	6 (6%)	2 (1%)
Abscess, NOS		2 (1%)
Hyperplasia, NOS		2 (1%)
Hyperkeratosis		1 (1%)
MUSCULOSKELETAL SYSTEM		
*Skull	(100)	(175)
Osteopetrosis	4 (4%)	5 (3%)
*Sternum	(100)	(175)
Osteopetrosis	4 (4%)	3 (2%)
BODY CAVITIES		
*Mediastinum	(100)	(175)
Congenital malformation, NOS	1 (1%)	
*Abdominal cavity	(100)	(175)
Steatitis		1 (1%)
Inflammation, chronic focal		1 (1%)
Necrosis, fat		2 (1%)
*Mesentery	(100)	(175)
Hemorrhage		1 (1%)
Inflammation, chronic focal	1 (1%)	
ALL OTHER SYSTEMS		
*Multiple organs	(100)	(175)
Hemorrhage	1 (1%)	
Inflammation, chronic	1 (1%)	5 (3%)
Pigmentation, NOS	1 (1%)	1 (1%)
Diaphragm		
Hernia, NOS	2	7
Necrosis, focal	1	
Pigmentation, NOS	1	
SPECIAL MORPHOLOGY SUMMARY		
None		

(a) DMH indicates a group receiving five doses of 15 mg/kg 1,2-dimethylhydrazine dihydrochloride by gavage in pH 5 acetate buffer.

PW indicates a group administered 0.47 mg/g chrysotile asbestos daily by gavage for 3 weeks beginning at birth.

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

Number of animals examined microscopically at this site

APPENDIX C

PATHOGEN BURDEN SURVEY

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TABLE C1. INITIAL MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F₀ RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Animal/Specimen Number (a)	Micro-organisms Identified (b)
181/3812	None
182/3813	None
183/3814	1 + Coliform; 1 + <i>Proteus vulgaris</i>
184/3815	3 + Coliform; 2 + <i>Proteus vulgaris</i>
185/3816	1 + Coliform
186/3817	1 + Coliform; 1 + <i>Proteus vulgaris</i>
187/3818	None
188/3819	3 + Coliform
189/3820	1 + Coliform; 1 + <i>Proteus vulgaris</i>
190/3821	2 + Coliform; 1 + <i>Proteus vulgaris</i>
191/3822	1 + Coliform
192/3823	3 + Coliform; 2 + <i>Proteus vulgaris</i>
193/3824	1 + Coliform; 1 + <i>Proteus vulgaris</i>
194/3825	2 + Coliform
195/3826	2 + Coliform; 3 + <i>Proteus vulgaris</i>
196/3827	3 + Coliform; 3 + <i>Proteus vulgaris</i>

(a) Date of specimen: 12/18/77

(b) Lung, spleen, feces, and tracheal wash were examined for each specimen; no growth observed in the spleen or lungs; no mycoplasma isolated from tracheal washings.

TABLE C2. MURINE VIRUS ANTIBODY DETERMINATION IN F₀ RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Sample Number	Complement Fixation	
	Sendai	LCM
3812	--	--
3813	--	--
3814	--	--
3815	--	--
3816	--	--
3817	--	--
3818	--	--
3819	--	--
3820	--	--
3821	--	--
3822	--	--
3823	--	--
3824	--	--
3825	--	--
3826	--	--
Significant titer	10	10

TABLE C3. REPEATED MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F₀ RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Animal/Specimen Number (a)	Micro-organisms Identified (b)
297/4031	4+ Group D <i>Streptococcus</i> ; 1+ <i>Micrococcus</i> sp.; 1+ Coliform
298/4032	4+ Group D <i>Streptococcus</i> ; 3+ <i>Micrococcus</i> sp.; 2+ <i>Pseudomonas aeruginosa</i>
299/4033	4+ Group D <i>Streptococcus</i> ; 2+ Coliform; 2+ <i>Pseudomonas aeruginosa</i>
300/4034	4+ Group D <i>Streptococcus</i> ; 2+ Coliform; 2+ <i>Pseudomonas aeruginosa</i> ; 2+ <i>Proteus vulgaris</i>
301/4035	4+ Group D <i>Streptococcus</i>
302/4036	4+ Group D <i>Streptococcus</i> ; 2+ <i>Micrococcus</i> sp.; 1+ Coliform;
303/4037	4+ Group D <i>Streptococcus</i> ; 2+ <i>Micrococcus</i> sp.; 2+ Coliform; 1+ <i>Candida brumptii</i>
304/4038	4+ Group D <i>Streptococcus</i> ; 2+ Coliform; 3+ <i>Proteus vulgaris</i>
305/4039	4+ Group D <i>Streptococcus</i> ; 2+ <i>Micrococcus</i> sp.; 2+ Coliform; 1+ <i>Pseudomonas aeruginosa</i>

(a) Date of specimen: 6/14/78

(b) Lung, spleen, feces, and tracheal wash were examined for each specimen; no growth observed in the spleen or lung; no mycoplasma isolated from tracheal washings.

TABLE C4. REPEATED MURINE VIRUS ANTIBODY DETERMINATION IN F₀ RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Sample Number	Complement Fixation	
	Sendai	LCM
4031	320	—
4032	160	—
4033	40	—
4034	40	—
4035	40	—
4036	80	—
4037	40	—
4038	320	—
4039	80	—
Significant titer	10	10

Pathogen Burden Summary (F₀ Initial)

The tissues evaluated were remarkably free of spontaneous disease. The mild peribronchial accumulation of lymphocytes frequently seen was within normal limits for non-germfree rats. The extramedullary hematopoiesis is also normally present.

Pathogen Burden Summary (F₀ Repeated)

Sections of brain, heart, lung, spleen, liver, kidney, small intestine, large intestine, salivary gland, urinary bladder, harderian gland, skin, anus, and larynx or trachea were examined from nine rats in the parental generation killed for pathology burden. These consisted of two rats of each sex in Group 1 (control) and three males and two females in Group 2 (DMH).

Evidence of early spontaneous respiratory disease was noted in all rats. This was characterized by minimal-to-moderate peribronchial lymphoid hyperplasia in all rats and minimal perivascular lymphoid hyperplasia in two Group 2 males. Agonal hemorrhage was noted in the lungs of a single Group 1 male.

Minimal focal nonsuppurative myocarditis was noted in two Group 2 males. Minimal focal chronic interstitial nephritis was noted in three males. Focal mineralization was noted at the corticomedullary junction in all four females and foci of regenerative tubule epithelium were noted in one female.

Congestion occurred in the large intestine of one Group 1 female. Presumptive infection with sialadenitis virus was noted in three rats by the presence of chronic nonsuppurative inflammation in the salivary gland and/or harderian gland.

TABLE C5. REPEATED INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F₀ RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Site/Lesion	Animal Number:	Group 1 (Control)				Group 2 (Amosite Asbestos)			
		Male		Female		Male		Female	
		2	2	3	3	2	3	3	3
		9	9	0	0	9	0	0	0
		7	8	2	3	9	0	1	4
Brain		X	X	X	X	X	X	X	X
Heart		X	X	X	X	X			X
Focal nonsuppurative myocarditis							1	1	
Lung									
Peribronchial lymphoid hyperplasia		2	2	2	2	1	2	3	1
Perivascular lymphoid hyperplasia						1	1		3
Angonal hemorrhage		P							
Spleen		X	O	X	X	X	X	X	X
Liver		X	O	X	X	X	X	X	X
Kidney						X		X	O
Chronic interstitial nephritis		1					1	1	
Focal mineralization				P	P				P
Foci of regenerative epithelium					P				P
Small intestine		X	X	X	X	X	X	X	X
Large intestine		X	X	X		X	X	O	X
Congestion					P				
Salivary gland			O	X	X	X	X	O	X
Nonsuppurative sialoadenitis		P							P
Urinary bladder		X	O	X	O	X	X	X	X
Harderian gland		O	O		O	X	X	X	X
Chronic inflammation				P					P
Skin		X	X	X	X	X	X	X	X
Anus		O	O	X	X	X	X	X	X
Larynx-Trachea		X	X	X	X	X	O	X	X

Type of Finding:

- O = Tissue absent
- X = Tissue examined and not remarkable
- P = Finding present

Degree of Finding:

- 1 = Minimal
- 2 = Slight
- 3 = Moderate
- 4 = Moderately severe

Pathogen Burden Summary (F₁ Initial)

Sections of brain, heart, lung, spleen, liver, kidney, small intestine, salivary gland, urinary bladder, eye, skin, anus, and cecum were examined from 16 rats in the F₁ generation killed for pathology burden. These consisted of one Group 1 (control) male, seven Group 2 (DMH) males, three Group 1 females, and five Group 2 females.

Evidence of respiratory disease was noted in all rats. This was characterized by minimal-to-moderate peribronchial lymphoid hyperplasia in all rats, focal hyperplasia of the bronchiolar epithelium in 6 rats, accumulation of mucous exudate and inflammatory cells (mostly macrophages) within the tracheo-bronchial tree in 10 rats and focal pneumonitis in 1 rat. Accumulated mucus and scattered inflammatory cells were noted in the trachea of one male. Aspirated blood was noted in one rat, and agonal hemorrhage occurred in two. The consistent evidence of bronchiolitis with a hyperplastic response in affected bronchiolar epithelium is characteristic of Sendai virus infection, and this conclusion was supported serologically. The disease is usually mild and self-limiting in rats.

In sections of liver, foci of mononuclear cells were noted in two rats and focal pleocellular infiltrate occurred in one.

In sections of kidney, foci of regenerative tubules were noted in three rats, foci of mineralization in five rats (four were females), and focal accumulation of mononuclear cells in one male.

Focal hemorrhage within the tips of the villi in the duodenum in one male was noted as an apparent agonal change.

TABLE C6. INITIAL INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F₁ RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Site/Lesion	Group 1 (Control)				Group 2 (Control and DMH)											
	Animal Number:	Male		Female		Male					Female					
		2	2	2	2	2	2	2	2	2	2	2	2	2	2	
	6	6	7	7	6	6	6	6	6	6	6	7	7	7	7	
	1	9	0	1	2	3	4	5	6	7	8	2	3	4	5	6
Brain	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Heart	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Lung																
Peribronchial lymphoid hyperplasia	1	3	2	1	3	3	2	2	2	2	3	1	2	3	1	2
Focal pneumonitis							P									
Focal hyperplasia of bronchiolar epithelium	P				P	P		P		P				P		
Exudate	P	P	P	P	P	P		P	P	P						
Inflammatory cells (bronchial tree)		P	P	P	P	P			P	P		P		P		
Aspirated blood		P														
Agonal hemorrhage								P								P
Spleen	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Liver	X			X	X	X	X	X	X	X	X		X	X	X	X
Mononuclear cells		P	P													
Pleocellular infiltrate												P				
Kidney				X	X	X			X	X	X	X	X	X		
Foci of regenerative tubules	P			P				P								
Mononuclear cells	P															
Foci of mineralization		P	P				P								P	P
Small intestine	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Focal hemorrhage		P														
Salivary gland	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
Lymphoid hyperplasia (cervical lymph node)							P									
Urinary bladder	X	X	X	X	X	X	X	X	X	X	X	O	X	X	X	X
Harderian gland	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
Harderian gland porphyrins							P									
Skin	X	O	X	X	X	X	X	X	X	X	X	X	X	X	X	O
Anus	X	X	X	X	X	X	O	X	X	X	X	X	X	X	X	X
Cecum	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Trachea																
Foci of mucus with inflammatory cells occurring just over the epithelium	P															

Type of Finding:

- O = Tissue absent
- X = Tissue examined and not remarkable
- P = Finding present

Degree of Finding:

- 1 = Minimal
- 2 = Slight
- 3 = Moderate
- 4 = Moderately severe
- 5 = Severe

TABLE C7. MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F₁ RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Animal/Specimen Number (a)	Micro-organisms Identified (b)
261/3983	4+ Group D <i>Streptococcus</i> ; 3+ <i>Staphylococcus aureus</i> ; 3+ Coliform
262/3984	4+ Group D <i>Streptococcus</i> ; 1+ Coliform; 2+ <i>Micrococcus</i> sp.; 1+ <i>Proteus vulgaris</i>
263/3985	4+ Group D <i>Streptococcus</i> ; 2+ <i>Micrococcus</i> sp.; 3+ <i>Proteus vulgaris</i>
264/3986	4+ Group D <i>Streptococcus</i> ; 1+ Coliform; 1+ <i>Pseudomonas aeruginosa</i>
265/3987	4+ Group D <i>Streptococcus</i> ; 3+ <i>Micrococcus</i> sp.; 3+ Coliform
266/3988	4+ Group D <i>Streptococcus</i> ; 3+ Coliform; 3+ <i>Proteus morgani</i>
267/3989	4+ Group D <i>Streptococcus</i> ; 2+ Coliform; 1+ <i>Micrococcus</i> sp.
268/3990	3+ Group D <i>Streptococcus</i> ; 4+ <i>Proteus vulgaris</i>
269/3991	4+ Group D <i>Streptococcus</i> ; 3+ <i>Micrococcus</i> sp.; 4+ <i>Proteus vulgaris</i>
270/3992	4+ Group D <i>Streptococcus</i> ; 4+ Coliform; 1+ <i>Pseudomonas aeruginosa</i>
271/3993	4+ Group D <i>Streptococcus</i> ; 4+ Coliform
272/3994	4+ Group D <i>Streptococcus</i> ; 3+ Coliform; 2+ <i>Micrococcus</i> sp.
273/3995	4+ Group D <i>Streptococcus</i> ; 2+ Coliform; 1+ <i>Pseudomonas aeruginosa</i> ; 4+ <i>Staphylococcus aureus</i>
274/3996	3+ Group D <i>Streptococcus</i>
275/3997	3+ Group D <i>Streptococcus</i> ; 3+ Coliform; 3+ <i>Pseudomonas aeruginosa</i>
276/3998	3+ Group D <i>Streptococcus</i> ; 2+ Coliform; 3+ <i>Micrococcus</i> sp.; 2+ <i>Proteus vulgaris</i>

(a) Date of specimen: 5/11/78

(b) Lung, spleen, feces, and tracheal wash were examined for each specimen; no growth observed in the spleen or lung; no mycoplasma isolated from tracheal washings.

TABLE C8. INITIAL MURINE VIRUS ANTIBODY DETERMINATION IN F₁ RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Sample Number	Complement Fixation	
	Sendai	LCM
261	≥ 1280	—
262	160	—
263	80	—
264	—	—
265	—	—
266	—	—
267	80	—
268	80	—
269	160	—
270	40	—
272	640	—
276	—	—
Significant titer	10	10

Pathogen Burden Summary (F₁ Repeated)

Accumulation of porphyrins within the harderian gland occurred in two rats. This was accompanied by hyperplasia of the cervical lymph nodes in one rat.

Sections of the liver and lung were examined from 12 rats in the F₁ generation killed for pathogen burden determination. These consisted of three males and three females in Group 1 (control) and three males and three females in Group 2 (DMH).

Evidence of early spontaneous respiratory disease was noted in all animals. This lesion consisted of minimal-to-moderate peribronchial lymphoid hyperplasia in all rats and minimal-to-slight perivascular lymphoid hyperplasia in two Group 1 males. These two males also had focal areas of pneumonitis, and one of them also had a fibrinous exudate in the areas of pneumonitis.

Minimal nonsuppurative pericholangitis was noted in single male and female rats in Group 1.

TABLE C9. REPEATED INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F₁ RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Site/Lesion	Animal Number:	Group 1 (Control)						Group 2 (DMH)					
		Male			Female			Male			Female		
		3	3	3	3	3	3	3	3	3	3	3	3
		0	0	0	1	1	1	0	1	1	1	1	1
		6	7	8	2	3	4	9	0	1	5	6	7
Lung													
Peribronchial lymphoid hyperplasia		2	2	2	2	2	1	2	2	3	1	2	2
Perivascular lymphoid hyperplasia		1		2									
Focal pneumonitis		P		P									
Fibrinous exudate				P									
Liver													
Nonsuppurative pericholangitis		X	X			X	X	X	X	X	X	X	X
				1	1								

Type of Finding:

O = Tissue absent
X = Tissue examined and not remarkable
P = Finding present

Degree of Finding:

1 = Minimal
2 = Slight
3 = Moderate
4 = Moderately severe

TABLE C10. REPEATED MURINE VIRUS ANTIBODY DETERMINATION IN F₁ RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

Sample Number	Complement Fixation Sendai
47	10
48	20
49	40
50	40
51	40
52	10
53	40
54	40
55	10
56	40
57	40
58	40
Significant titer	10

APPENDIX D

ANALYSIS OF BEDDING SAMPLES IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

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TABLE D1. ANALYSIS OF BEDDING SAMPLES AT HAZLETON LABORATORIES

Collection Date	Desired Level (ppm)	Determined Level of	
		Pentachlorophenol (ppm)	Polychlorinated Biphenyls (ppm)
07/78	<1.0	6.0	<0.5
08/78	<1.0	<0.5	<0.5
08/79	<1.0	<0.2	<0.5
01/80	<1.0	<0.2	<0.5
08/80	<1.0	<0.2	<0.5

TABLE D2. ANALYSIS OF BEDDING SAMPLES AT ILLINOIS INSTITUTE OF TECHNOLOGY RESEARCH INSTITUTE

Collection Date	Fiber Concentration	
	Total (a)	Asbestos (a)
03/77	110/g	ND
03/79	90/g	ND
02/80	130/g	ND
08/80	40/g	ND

(a) ND = less than detection limit (~ 25,000 fibers per liter or 25 fibers per gram)

APPENDIX E

WATER ANALYSIS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

APPENDIX E. WATER ANALYSIS

Samples of drinking water were submitted to the Water Supply Research Laboratory, U.S. Environmental Protection Agency, Cincinnati, OH, for baseline asbestos determinations. The samples were collected on November 8, 1976, and November 11, 1980.

The results of the first analysis determined the concentration of chrysotile asbestos and amphibole asbestos to be below detectable limits of 10,000 fibers per liter.

The second analysis detected one chrysotile asbestos fiber, equivalent to 50,000 fibers per liter, but a count based on a single fiber is not statistically significant. The chrysotile asbestos fiber was probably a contaminant from the study diet.

APPENDIX F

AIR ANALYSIS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

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APPENDIX F. ANALYSIS OF AIR SAMPLES

Results of air sample analyses are presented in Table F1.

Initially, 6-hour samplings of air were taken for baseline asbestos determinations from clean and dirty corridors and two rooms. Samples were sent for analysis to the Illinois Institute of Technology Research Institute (IITRI). Additional 6-hour air samplings of rooms and corridors were taken when each asbestos diet was introduced into a room and thereafter approximately every 6 months.

Air samples were obtained with a portable pump Model G (part no. 456058) from Mining Safety Appliances Co. (Pittsburgh, PA), which was connected by Tygon tubing to a Millipore Filter Field Monitor (pore size, 5 μ).

TABLE F1. RESULTS OF ANALYSES OF AIR SAMPLES IN LIFETIME FEED STUDIES OF AMOSITE ASBESTOS IN RATS (a)

Date	Room No. 32 (next to return hall door)	Service Hall (outside room no. 30)	Room No. 35 (next to service hall door)	Return Hall Intersection of Nos. 45 and 44	Room No. 36 (next to return hall door)
Total Fiber Concentration (no./cc of air)					
6/78	0.06	0	0	0	0
1/79	0.17	0.04	0.04		0.30
2/80	0.095		0.048		
7/80	0.11	0.09	0.03		0
Asbestos Fiber Concentration (no./cc of air)					
6/78	0.06	0	0	0	0
1/79	0.13	0.04	0.00		0.17
2/80	0.095		0.048		
7/80	0.03	0.03	0.03		
>5 μm (no./cc of air)					
6/78	0	0		0	0
1/79	0	0	0		0
2/80	0		0		
7/80	0	0	0		0
>1 μm (no./cc of air)					
6/78	0	0		0	0
1/79	0.13	0	0		0.14
2/80	0		0		
7/80	0	0	0.03		0

Date	Service Hall Intersection of Nos. 29 and 55	Room No. 33 (next to return hall door)	Return Hall (No. 20) Outside of Women's Locker Room	Room No. 30 (next to return hall door)	Service Hall
Total Fiber Concentration (no./cc of air)					
6/78	0.12	(b)0	0	0	
1/79		0.11		0.04	0.04
2/80		0.00			
7/80		0.11		0.34	
Asbestos Fiber Concentration (no./cc of air)					
6/78	0.06	(b)0	0	0	
1/79		0.04		0.04	0
2/80		0.00			
7/80		0.03		0.23	
>5 μm (no./cc of air)					
6/78	0	(b)0	0	0	
1/79		0		0	0
2/80		0			
7/80		0		0	
>1 μm (no./cc of air)					
6/78	0	(b)0	0	0	
1/79		0		0	0
2/80		0			
7/80		0.03		0.11	

TABLE F1. RESULTS OF ANALYSES OF AIR SAMPLES IN LIFETIME FEED STUDIES OF AMOSITE ASBESTOS IN RATS (Continued)

Date	Return Hall	Service Hall (halls 55 and 56)	Room 31	Room 34	Blank
Total Fiber Concentration (no./cc of air)					
6/78			0.13	0.17	0.04
1/79	0.07		0.048	0.24	
2/80	0.048	0.048	0.03	0.20	0.03
7/80		0.26			
Asbestos Fiber Concentration (no./cc of air)					
6/78			0.04	0.04	0
1/79	0.04		0.00	0.14	
2/80	0.048	0.048	0.03	0.09	0
7/80		0.20			
>5 μm (no./cc of air)					
6/78			0	0	0
1/79	0		0	0	
2/80	0	0	0	0	0
7/80		0.06	0	0	0
>1 μm (no./cc of air)					
6/78			0	0.04	0
1/79	0		0	0.05	
2/80	0	0	0	0.06	0
7/80		0.14	0		

Date	Service Hall	Wash Area Room 48	Change Area	Room 56
Total Fiber Concentration (no./cc of air)				
6/78				
1/79	0			
2/80		0.06	0.11	0.09
7/80				
Asbestos Fiber Concentration (no./cc of air)				
6/78				
1/79	0			
2/80		0	0.03	0.09
7/80				
>5 μm (no./cc of air)				
6/78				
1/79	0			
2/80		0	0	0
7/80				
>1 μm (no./cc of air)				
6/78				
1/79	0			
2/80		0	0.03	0.09
7/80				

(a) Samples analyzed by IITRI; the computations are based on a 1 liter/min sample rate and a 6-h sample period = 360 min.
 (b) Sample holder was damaged.

APPENDIX G

SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS PRIOR TO MORIBUND KILL IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

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TABLE G1. SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS: UNTREATED CONTROL (a)

	<u>Weeks 71-76</u>		<u>Weeks 77-81</u>		<u>Weeks 82-86</u>		<u>Weeks 87-91</u>	
	Male	Female	Male	Female	Male	Female	Male	Female
Number of animals killed in moribund condition	2	3	1	1	1	1	3	3
Pale							2	1
Thin				1	1		2	
Head tilt		1						
Eye small and opaque		1						
Pale eyes			1					1
Eyes dark					1			
Depressed							1	1
Labored respiration					1		1	
Rapid respiration							1	
Tissue mass (abscessed)--right ear, axilla, head, neck, chest, inguinal	1	2	1		1	1	2	
Wheezing				1				
Palpable mass in abdomen					1			3
Hunched				1				
Cold to touch								1
Anal nodule	1							
Loss of righting reflex							1	
Muscle tone flaccid							1	
Circling				1				
			<u>Weeks 92-96</u>		<u>Weeks 97-101</u>			
			Male	Female	Male	Female		
Number of animals killed in moribund condition			3	3	3	2		
Pale			2	2	2	1		
Thin			2		1			
Depressed					1	1		
Tissue mass (abscessed)--right ear, axilla, head, neck, chest, inguinal			2		1	1		
Malocclusion			1					
Palpable mass in abdomen			1	3	2			
Abdomen firm and dark			1					
Abdomen distended			1					
Loss of equilibrium						1		
Red discharge from vagina				1				

(a) The intervals were arbitrarily selected based on weeks when a large percentage of moribund kills occurred. Clinical signs observed after the last interval selected were believed not to be readily discernible from signs of aging.

TABLE G4. SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS: 1% AMOSITE + DMH (a)

	<u>Weeks 71-76</u>		<u>Weeks 77-81</u>		<u>Weeks 82-86</u>		<u>Weeks 87-91</u>	
	Male	Female	Male	Female	Male	Female	Male	Female
Number of animals killed in moribund condition	33	17	17	24	11	6	8	12
Pale		1	2	1	1	1	1	3
Thin			1	2	1	1	2	1
Hunched				1		2		
Head tilt			1	1	1			
Pale eyes		1	4	3	1	1		2
Eye(s) squinted						1	1	
Unkempt or rough hair coat					1		1	
Salivating						1		
Labored respiration			1					1
Rapid respiration		2		1				1
Wheezing			2		1		2	1
Lacking movement or inactive			2			1		
Depressed			1		1		1	4
Yellowish appearance of extremities								1
Cold to touch			1			1		
Tissue mass (abscessed)--lower midline, cervical, anus, neck, inguinal, axilla, side of head, ear, tail								
<1.0 cm	1		5					
1.0-5.0 cm	8	3	2	2			1	1
5.0-10.0 cm			1					2
Abdomen dark							2	
Abdomen bloated or distended				1			2	2
Palpable mass					1			
Palpable mass in abdomen	2	3	3	10	3	3	2	6
Dark red or red discharge from ear	1			1				
Dark red, red discharge, or discharge from anus	3		5	4	5	1	3	2
Red stains around anus	1				1			
Dark crust perineal region		1						
Soft (watery) feces	4		2	2	1		1	
Anal nodule		1	1	7	4	1	1	3
Muscle tone flaccid			1					
Loss of equilibrium		1						
Loss of righting reflex						1		1
Circling				1				
Fecal stains							1	
Yellow crust around nose							1	
Malocclusion			1					
Twitching						1		
Alopecia					1		1	
Ear--green cheesy material		1						
Dark crust inner left ear		1						
Protruding eye					1			
Nodule	1				1		1	

TABLE G4. SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS: 1% AMOSITE + DMH (Continued)

	<u>Weeks 92-96</u>		<u>Weeks 97-101</u>		<u>Weeks 102-106</u>	
	Male	Female	Male	Female	Male	Female
Number of animals killed in moribund condition	6	17	15	10	9	13
Pale	2	9	4	3	4	8
Thin	2	4	4		2	6
Hunched		1				
Head tilt	1					
Pale eyes	1	2	1			
Lacrimating eye(s)		2				
Unkempt or rough hair coat	1		1			
Labored respiration			2			1
Rapid respiration		1				
Wheezing		1				
Depressed	1	4	4	1	1	4
Yellowish appearance of extremities		2				
Cold to touch		1	1			
Tissue mass (abscessed)--lower midline, cervical, anus, neck, inguinal, axilla, side of head, ear, tail						
<1.0 cm	3	1	2		1	
1.0-5.0 cm		2	2	3		3
5.0-10.0 cm		2				
Abdomen dark			1			
Abdomen firm			1			
Abdomen bloated or distended			1			
Palpable mass in abdomen	1	10	7	6	4	7
Dark red, red discharge, or discharge from anus	2		2		1	
Soft (watery) feces		1				
Anal nodule	2	3	2	4		2
Muscle tone flaccid		2				
Loss of equilibrium					1	1
Circling	1					
Malocclusion	1	1	1		1	
Paralysis in hindlegs			1			
Red discharge from vagina		1				
Nodule			1			
Animal prostrate in cage					1	

(a) The intervals were arbitrarily selected based on weeks when a large percentage of moribund kills occurred. Clinical signs observed after the last interval selected were believed not to be readily discernible from signs of aging.

TABLE G5. SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS: 1% AMOSITE + PW (a)

	<u>Weeks 71-76</u>		<u>Weeks 77-81</u>		<u>Weeks 82-86</u>		<u>Weeks 87-91</u>	
	Male	Female	Male	Female	Male	Female	Male	Female
Number of animals killed in moribund condition	1		4		3		1	
Pale			1					
Thin			3		2		1	
Hunched					1			
Head tilt			1		1			
Pale eyes							1	
Wheezing			2		1			
Depressed			1				1	
Abdomen distended (with firm mass)	1							
Palpable mass in abdomen			1		1			
Tissue mass (abscessed)--cervical, shoulder, mouth, axilla, head, neck, chest, back, inguinal, perineal								
1.0-5.0 cm			2				1	
5.0-10.0 cm					1			
Red discharge from anus					1			
	<u>Weeks 92-96</u>		<u>Weeks 97-101</u>		<u>Weeks 102-106</u>		<u>Weeks 107-111</u>	
	Male	Female	Male	Female	Male	Female	Male	Female
Number of animals killed in moribund condition	2	2	5	4	4	3	13	9
Pale		1	1	2	3	1	4	2
Thin			1	1	1	1	3	5
Hunched								1
Pale eyes	1		1				1	
Rapid respiration								1
Labored respiration	1						2	1
Wheezing			1	1			1	
Unkempt			1					1
Depressed	2	1	1	2	2	1	2	1
Cyanotic	1		1			1	1	
Inactive		1						1
Abdomen distended (with firm mass)			1					
Palpable mass in abdomen	1	2	1	2	3		4	3
Palpable mass in chest								1
Tissue mass--cervical, shoulder, mouth, axilla, head, neck, chest, back, inguinal, perineal								
1.0-5.0 cm			1	1		1	2	2
5.0-10.0 cm					1	1	3	3
Cold to touch	1							
Loss of equilibrium	1			1			3	1
Yellowish appearance of extremities		1		1				
Prostrate in cage				1				
Dark stains on urogenitals								1

(a) The intervals were arbitrarily selected based on weeks when a large percentage of moribund kills occurred. Clinical signs observed after the last interval selected were believed not to be readily discernible from signs of aging.

APPENDIX H

FEED AND COMPOUND CONSUMPTION BY RATS IN THE LIFETIME FEED STUDIES OF AMOSITE ASBESTOS

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TABLE H1. FEED AND COMPOUND CONSUMPTION BY MALE RATS FOR REPRESENTATIVE WEEKS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS

Week	Control		1% Amosite			1% Amosite + PW		
	Grams Feed/Day (a)	Body Weight (grams)	Grams Feed/Day (a)	Body Weight (grams)	Dose/Day (b)	Grams Feed/Day (a)	Body Weight (grams)	Dose/Day (b)
17	16	303	17	259	656	18	279	645
27	16	369	17	318	535	18	338	533
37	18	403	18	356	506	19	376	505
48	19	425	17	375	453	18	390	462
57	17	450	17	393	433	17	416	409
67	18	471	18	411	438	17	438	388
77	17	477	17	429	396	17	443	384
87	16	475	17	424	401	18	439	410
97	17	471	18	417	432	17	440	386
107	16	459	17	410	415	19	420	452
117	16	423	17	390	436	18	391	460
127	17	393	18	358	503	19	370	514
137	17	340	16	334	479	17	327	520
Mean	16.9	420	17.2	375	468	17.8	390	467
SD (c)	1.0		0.6		70.6	0.8		75.9
CV (d)	5.6		3.5		15.1	4.5		16.3

(a) Average grams of feed removed from feeder per animal per day; not corrected for scatter.

(b) Estimated milligrams of amosite consumed per day per kilogram of body weight

(c) Standard deviation

(d) Coefficient of variation = (standard deviation/mean) × 100

TABLE H2. FEED AND COMPOUND CONSUMPTION BY MALE RATS FOR REPRESENTATIVE WEEKS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH)

Week	Control		DMH		1% Amosite + DMH		
	Grams Feed/Day (a)	Body Weight (grams)	Grams Feed/Day (a)	Body Weight (grams)	Grams Feed/Day (a)	Body Weight (grams)	Dose/Day (b)
17	16	303	16	306	17	254	669
27	16	369	17	372	17	322	528
37	18	403	17	394	18	354	508
48	19	425	18	417	18	370	486
57	17	450	18	444	18	396	455
67	18	471	17	459	17	417	408
77	17	477	16	464	17	425	400
87	16	475	17	457	17	424	401
97	17	471	15	432	18	402	448
107	16	459	20	419	19	397	479
Mean	17.0	430	17.1	416	17.6	376	478
SD (c)	1.1		1.4		0.7		80.5
CV (d)	6.2		8.0		4.0		16.8

(a) Average grams of feed removed from feeder per animal per day; not corrected for scatter.

(b) Estimated milligrams of amosite consumed per day per kilogram of body weight

(c) Standard deviation

(d) Coefficient of variation = (standard deviation/mean) × 100

TABLE H3. FEED AND COMPOUND CONSUMPTION BY FEMALE RATS FOR REPRESENTATIVE WEEKS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS

Week	Control		1% Amosite			1% Amosite + PW		
	Grams Feed/Day (a)	Body Weight (grams)	Grams Feed/Day (a)	Body Weight (grams)	Dose/Day (b)	Grams Feed/Day (a)	Body Weight (grams)	Dose/Day (b)
17	11	185	12	168	714	13	176	739
27	11	212	12	192	625	13	198	657
37	12	222	13	204	637	13	211	616
48	13	241	13	221	588	12	224	536
57	12	260	14	241	581	14	247	567
67	13	295	13	271	480	13	275	473
77	13	321	13	294	442	14	294	476
87	13	334	13	298	436	14	296	473
97	14	336	14	300	467	16	303	528
107	14	340	15	306	490	19	305	623
117	15	331	14	293	478	14	287	488
127	16	326	15	282	532	16	278	576
137	14	294	13	250	520	15	269	558
Mean	13.2	284	13.4	255	538	14.3	259	562
SD (c)	1.5		1.0		85.1	1.8		80.5
CV (d)	11.1		7.2		15.8	12.9		14.3

- (a) Average grams of feed removed from feeder per animal per day; not corrected for scatter.
 (b) Estimated milligrams of amosite consumed per day per kilogram of body weight
 (c) Standard deviation
 (d) Coefficient of variation = (standard deviation/mean) × 100

TABLE H4. FEED AND COMPOUND CONSUMPTION BY FEMALE RATS FOR REPRESENTATIVE WEEKS IN THE LIFETIME FEED STUDY OF AMOSITE ASBESTOS AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH)

Week	Control		DMH		1% Amosite + DMH		
	Grams Feed/Day (a)	Body Weight (grams)	Grams Feed/Day (a)	Body Weight (grams)	Grams Feed/Day (a)	Body Weight (grams)	Dose/Day (b)
17	11	185	12	181	12	162	741
27	11	212	11	209	13	195	667
37	12	222	12	217	13	200	650
48	13	241	12	239	13	217	599
57	12	260	13	260	15	236	636
67	13	295	13	281	13	260	500
77	13	321	14	300	13	281	463
87	13	334	13	294	14	281	498
97	14	336	12	293	14	284	493
Mean	12.4	267	12.4	253	13.3	235	583
SD (c)	1.0		0.9		0.9		97.6
CV (d)	8.1		7.1		6.5		16.7

- (a) Average grams of feed removed from feeder per animal per day; not corrected for scatter.
 (b) Estimated milligrams of amosite consumed per day per kilogram of body weight
 (c) Standard deviation
 (d) Coefficient of variation = (standard deviation/mean) × 100