NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 280

TOXICOLOGY AND CARCINOGENESIS STUDIES OF CROCIDOLITE ASBESTOS

(CAS NO. 12001-28-4)

IN F344/N RATS

(FEED STUDIES)

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

NATIONAL TOXICOLOGY PROGRAM

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

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

Special Note: This Technical Report was peer reviewed in public session and approved by the NTP Board of Scientific Counselers' Technical Reports Review Subcommittee on February 28, 1983 [see page 8]. 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. [A summary of the data audit is presented in Appendix I.] Consequently, printing and distribution of this Technical Report have been delayed, and 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 CROCIDOLITE ASBESTOS

(CAS NO. 12001-28-4)

IN F344/N RATS

(FEED STUDIES)

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NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
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Public Health Service
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NOTE TO THE READER

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.

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

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CAS No. 12001-28-4

$Na_2O \cdot Fe_2O_3 \cdot 3FeO \cdot 8SiO_2 \cdot H_2O$

ABSTRACT

Carcinogenesis studies of crocidolite asbestos were conducted with male and female F344/N rats. This form of asbestos was administered at a concentration of 1% in pelleted diet for the lifetime of the rats, starting with the dams of the study animals. The studies were started in January 1978 and ended in December 1980. Group sizes were 118 for male and female controls and 250 for male and female crocidolite asbestos-exposed rats.

The offspring from mothers exposed to crocidolite asbestos and the controls were similar in size at birth but were slightly smaller at weaning and remained so throughout their life. Feed consumption and survival were comparable in the exposed and control groups. No overt toxicity was observed in the crocidolite asbestos-exposed animals. There was an elevated ($P < 0.05$) incidence of thyroid gland C-cell adenomas (control, 4/117, 3%, vs. exposed, 23/250, 9%) and of thyroid gland C-cell carcinomas (12/117, 10%, vs. 46/250, 18%) in crocidolite asbestos-exposed female rats relative to concurrent controls. Because these control incidences were low relative to control incidences observed in other contemporary studies at this laboratory (21% for thyroid gland C-cell tumors), this slight increase was not regarded as being biologically important.

The data, documents, and pathology materials from the lifetime studies of crocidolite asbestos have been audited. The audit findings show that the conduct of these studies is documented adequately and support the data and results presented in this Technical Report.

Conclusions: Under the conditions of these feed studies, crocidolite asbestos was not overtly toxic and did not cause a carcinogenic response when ingested at a concentration of 1% in the diet by male and female F344/N rats for their lifetime.

CONTRIBUTORS

The NTP Technical Report on the Toxicology and Carcinogenesis Studies of Crocidolite Asbestos is based on the lifetime studies that began in January 1978 and ended in December 1980 at Hazleton Laboratories America, Inc. (Vienna, Virginia).

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The members of the Peer Review Panel who evaluated the draft Technical Report on crocidolite asbestos on February 28, 1983, 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 CROCIDOLITE ASBESTOS

On February 28, 1983, the draft Technical Report on the toxicology and carcinogenesis studies of crocidolite 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, North Carolina.

Dr. E.E. McConnell, NIEHS, introduced the studies by reviewing the experimental design, results, and proposed conclusions (crocidolite asbestos was not overtly toxic and did not cause a carcinogenic response when ingested at a concentration of 1% in the diet by male and female F344/N rats for their lifetime).

Dr. Harper, a principal reviewer, agreed with the conclusions as written. He said that offspring of asbestos-fed mothers were slightly smaller at weaning than were offspring of control mothers and that this fact should be emphasized.

A second principal reviewer, Dr. Elashoff, agreed with the conclusions. He noted that the justifiable use of historical control data on the incidences of thyroid gland C-cell adenomas and carcinomas in male rats likely averted a probable false positive finding in this study. He expressed interest and concern as to the design considerations and tradeoffs that led to use of a single dose group, the stated concentration, and the stated sample size. Dr. McConnell described the rationale for the design of these and other asbestos studies in the series. Because of the high dietary exposure (1%) and the lifetime duration of the studies, the design committee decided to recommend larger but fewer exposure groups.

As a third principal reviewer, Dr. Davis said that the thyroid gland tumors were a carcinogenic response but that because of the control incidences in the other lifetime asbestos studies, the results might not be important. She commented that additional data on tumor incidences in recent control groups, data on feed contaminants for both experimental and control groups, and data from 24-month rat studies would provide valuable information for further interpretation of the results from the current studies. Dr. Davis noted that by incorporating bulk rather than fractionated asbestos into the feed, a majority of the fibers were much longer than fibers to which humans are usually exposed in drinking water and that there is an inverse correlation between fiber length and toxicity and biologic translocation. She expressed concern that there were no specifications in the report of engineering and safety practices regarding production of the asbestos and preparation of the pellets used in the diet. She recommended that environmental and occupational monitoring be done of firms preparing test substances. She said that the increased longevity and decreased body weights in crocidolite asbestos-exposed animals merited more emphasis and speculated that the decreased weight might have been due in part to more rapid gastrointestinal transit time produced by the high fiber diet. Dr. Davis urged that due consideration be given to new studies using smaller fibers that are fractionated by size and, further, that exposure of animals should be through drinking water.

There was considerable discussion among panel members and NTP staff concerning the aspect ratio for the fibers used in the studies which was greater than the optimal aspect ratios for biologic translocation and carcinogenicity. With regard to diet formulation and route of exposure, Dr. McConnell said that had ground or fractionated fibers been used, there could have been a potential safety hazard as well as some undesired inhalation exposure. Administration in water would have been more hazardous to laboratory personnel, and because of settling of fibers, the dosage would have been uncertain. In terms of fiber size, he stated that fibers of the size range used were potent carcinogens for the

pleural cavity. He said that NTP could do an ashing study on tissues such as liver, kidney, and lymph nodes to see if fibers were present. Dr. Scala opined that useful information could be gained by grinding up or dissolving some of the asbestos pellets and examining the fiber composition. Dr. Moore said that data were available which characterize the proportion of fibers by length and width by electron microscopic examination. Dr. Swenberg asked for the incidences of thyroid gland C-cell tumors in recent lifetime studies. Dr. Haseman replied that in four recent lifetime studies carried out at this laboratory, these incidences were 20%, 21%, 21%, and 24%,which, taken together, were similar to the 27% incidence in the crocidolite asbestos-exposed animals. Dr. Davis requested that the wording of the last sentence of the second paragraph of the abstract be changed to say that "this slight increase [in tumor incidence] was not regarded as being biologically important," with "important" replacing "significant."

Dr. Davis then moved that the Technical Report on crocidolite asbestos be accepted with the additions and revisions discussed. Dr. Harper seconded the motion, which was approved unanimously.

I. INTRODUCTION

CROCIDOLITE ASBESTOS

CAS No. 12001-28-4

$Na_2O \cdot Fe_2O_3 \cdot 3FeO \cdot 8SiO_2 \cdot H_2O$

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. Chrysotile is the most abundant and widely used of the various types of asbestos. The essential characteristic of asbestos minerals is their fibrous nature.

Studies conducted during the past 25 years have established a clear association between occupational exposure to asbestos and increased risk of cancer. Excellent reviews of public health effects associated with past heavy asbestos exposure, primarily occupational exposure via the inhalation route, 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 causal association between occupational inhalation exposure to chrysotile, amosite, crocidolite, and anthophyllite asbestos and an increased risk of lung cancer as well as mesothelioma. The latter form of cancer is perhaps unique in its association with these fibrous minerals and is particularly associated with exposure to crocidolite asbestos (Wagner et al., 1960). A noteworthy review of the pathology associated with inhalation exposure to asbestos is that by Craighead et al. (1982).

Large portions of the population ingest asbestos through consumption of food and water (NAS, 1977). Analysis of water samples from 359 cities found that 65% of the samples had detectable levels of various types of asbestos (Millette et al., 1983). The water supplies of 41 cities have had asbestos concentrations in water which exceeded 10 million fibers per liter, but the length of the vast majority of fibers is under 5 μm. Asbestos or asbestos-like fibers may enter water supplies as a result of mining (e.g., operations at Lake Superior). Natural serpentine or amphibole deposits have been detected in watersheds (Seattle, Washington, and San Francisco, California); under certain conditions, the presence of asbestos may have resulted from the use of chrysotile asbestos-cement pipe for municipal water supplies (USEPA, 1980). In the latter instance, erosion of the pipe (and release of fibers) is associated with the "aggressiveness" of the water, a term representing a mathematical expression of alkalinity and calcium content. Approximately 69% of the water systems in the United States have aggressive water that has the potential to erode asbestos-cement pipe.

Several studies have provided evidence that ingestion of asbestos in either food or water can result in the migration of asbestos through the gastrointestinal mucosa and to distant organ sites in humans (Carter and Taylor, 1980), in rats (Cunningham et al., 1977; Sebastien et al., 1980), and in 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) did not detect an association between the use of asbestos-cement pipe for municipal water supplies and the incidence of gastrointestinal cancer. Statistically significant trends for the incidence of several cancer types, including stomach, gallbladder, esophageal, and peritoneal cancer, were found when census tracts were analyzed on a gradient of low to high asbestos content in municipal water in the San Francisco Bay area (Cooper et al., 1979). The association between asbestos concentration in San Francisco Bay area drinking water and cancer was confirmed in subsequent studies (Kanarek, 1983; Conforti, 1983).

Inhalation of asbestos by laboratory animals produces lung carcinoma and mesothelioma in the pleural cavity (Wagner et al., 1974). Intrapleural, intratracheal, and intraperitoneal injection of asbestos will also produce neoplasia in

several species of laboratory animals (Wagner, 1962; Stanton and Wrench, 1972; Levine, 1978; Stanton et al., 1981).

Asbestos (chrysotile, amosite, and crocidolite) has been shown to be cytotoxic in vitro to human embryonic intestinal cells, mouse epithelial-like colon-derived cells, and rat liver epithelial cells (Reiss et al., 1979). Chrysotile asbestos was far more toxic than were the amphibole fibers, and the effects were more pronounced in the intestine-derived cells than in those from the liver. Chrysotile asbestos also was found to be cytotoxic to Syrian hamster (Bey and Harrington, 1971) and mouse (Wright et al., 1983) peritoneal macrophages and to rabbit alveolar macrophages (Desai and Richards, 1983). Chrysotile, amosite, and crocidolite asbestos were not mutagenic in *Salmonella typhimurium* or *Escherichia coli* (Chamberlain and Tarmy, 1977) or at the HGPRT locus in mammalian cells (Reiss et al., 1982; Oshimura et al., 1984).

In November 1973, the National Institute of Environmental Health Sciences and the EPA cosponsored a symposium on the possible biologic effects of ingested asbestos (EHP, 1974). The participants at this conference concluded that the data concerning the effects of ingested asbestos were inadequate 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 subsequently reviewed existing data and prepared a draft research protocol that the Committee felt was responsive to the major public health consensus. On the basis of comments received, a revised protocol was developed by the NTP for long-term animal toxicology and carcinogenesis studies. The forms of asbestos included chrysotile tested in Syrian golden hamsters (NTP, 1988a) and in F344/N rats (NTP, 1985a), amosite in Syrian golden hamsters (NTP, 1985b) and in F344/N rats (NTP, 1988b), crocidolite in F344/N rats (this report), and a nonfibrous tremolite, which contained low levels of asbestiform fibers, in F344/N rats (NTP, 1988c). All studies encompassed the lifetime of the animal, including exposure of the dams from which the study animals were derived. A single concentration of 1% in the diet was chosen because it represented the highest concentration thought to be reasonable from a biologic standpoint and that could be tolerated in a lifetime study.

This Technical Report presents the results of those studies undertaken to determine the effects of crocidolite asbestos fed to male and female F344/N rats in the diet.

II. MATERIALS AND METHODS

STUDY MATERIAL
STUDY DIETS
SOURCE AND SPECIFICATIONS OF STUDY ANIMALS
ANIMAL MAINTENANCE
SAFETY PRECAUTIONS
CLINICAL EXAMINATIONS AND PATHOLOGY
STATISTICAL METHODS

II. MATERIALS AND METHODS

STUDY MATERIAL

The crodicolite asbestos used in these studies was purchased by the U.S. Bureau of Mines from Certain-Teed Co. The 6,000-pound sample was identified as ML-6. Air jet milling was selected because this type of pulverizer would be the least damaging to the amphibole crystalline structure. The sample was passed through the mill twice to reduce the number of very long fibers in the final material. The crocidolite asbestos was bagged in 100-pound silicone-treated Dacron® filter bags.

To homogenize the sample, lots of six 100-pound bags were manually blended on a 5-foot × 8-foot blending table. After final blending, 1,200 pounds of crocidolite asbestos was packaged in 20-pound lots in virgin fiberboard containers. These drums were shipped to a special warehouse at Research Triangle Park, North Carolina. Each drum received a color marking unique to the mineral type. Homogeneity of the samples was verified by fluorescent X-ray spectrography from samples collected from six randomly selected drums. No significant differences were detected for samples from the various containers.

The homogeneity of the samples and the physical and chemical properties of the material have been extensively characterized (Bureau of Mines, 1980; IITRI). [Copies of these reports are available on request from the National Toxicology Program (Public Information Office, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709).] Selected chemical and physical properties of crocidolite are presented in Tables 1 and 2 (Bureau of Mines (1980). In an analysis of mineralogic composition, crocidolite ($Na_2O \cdot Fe_2O_3 \cdot 3FeO \cdot 8SiO_2 \cdot H_2O$) was detected at a volume percent abundance of 99%; trace amounts (less than 1% total) of biotite, quartz, opaques, feldspar, and glass were found.

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

Fiber characteristics			
Surface area (m^2/g)	9.8 ± 1.0		
Density (g/cm^3)	3.32 ± 0.08		
Mean length (μm) by electron micropscopy	10		
Mean width (μm) by electron micropscopy	0.27		
Chemical instrumental analysis (expressed as weight percent)			
Al_2O_3	0.07	TiO_2	0.07
CaO	1.04	MnO	0.08
FeO	18.32	Cr_2O_3	0.02
Fe_2O_3	18.62	CO_2	2.18
MgO	3.81	H_2O^-	0.45
K_2O	0.07	H_2O^+	2.10
SiO_2	48.73	Benzene-extracted organics	0.041
Na_2O	4.43		

TABLE 2. PARTICLE SIZE DISTRIBUTION OF CROCIDOLITE ASBESTOS BY PARTICLE NUMBER (a)

	Length Interval (μm)							
	8-8.99	9-9.99	10-19.99	20-39.99	40-59.99	60-79.99	80-99.99	>100
Crocidolite asbestos mean width (μm)	0.31	0.29	0.28	0.35	0.40	0.33	0.44	0.64
Crocidolite asbestos particles per interval	29	39	125	72	25	12	1	10
Percent of total crocidolite asbestos particles	2.8	3.8	12.0	6.8	2.4	1.1	0.1	1.0
Cumulative percent crocidolite asbestos	72.8	76.6	88.6	95.4	97.8	98.9	99.0	100
Volume percent crocidolite asbestos (b)	1.6	1.8	7.4	18.9	12.4	7.3	1.0	39.4
Cumulative volume percent crocidolite asbestos	11.8	13.6	21.0	39.9	52.3	59.6	60.6	100
Number of other particles	0	0	0	0	0	0	0	0
Crocidolite asbestos particles per length interval, percent, by aspect ratio								
1:1-2.9:1	0	0	0	0	0	0	0	0
3:1-4.9:1	0	0	0	0	0	0	0	0
5:1-9.9:1	7	0	0	0	0	0	0	0
10:1-19.9:1	0	3	1	1	0	0	0	0
20:1-49.9:1	83	89	48	5	0	0	0	0
50:1-99.9:1	10	8	45	53	16	16	0	0
100:1-199:1	0	0	6	39	64	42	0	50
200:1-499:1	0	0	0	2	20	42	100	50

(a) By electron micropscopy; total particles = 1,050; total crocidolite asbestos = 1,040; total others = 10.
(b) Calculated from particle number data, assuming a rectangular cross-section with third dimension equal to one-third measured width

STUDY DIETS

The feed used was NIH 31 Rat and Mouse Ration. Crocidolite asbestos was incorporated to a concentration of 1% by weight into the study diet. Pilot studies determined that homogeneous mixing of crocidolite asbestos and feed would occur in a blender loaded by alternate layering of feed and crocidolite asbestos. Results of analyses for crocidolite asbestos in feed are given in Table 3. Each lot of blended feed was analyzed for crocidolite asbestos concentration, pesticide contamination, and nutrient content. Further details are given in Table 4.

SOURCE AND SPECIFICATIONS OF STUDY ANIMALS

Parental Generation (F_0): 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 F_0 generation and were received November 15, 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 at random, 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 (Appendix C, 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 randomly on January 27, 1978, into two groups (control and crocidolite asbestos) according to tables of random numbers.

TABLE 3. RESULTS OF ANALYSIS OF FORMULATED DIETS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

Date Mixed	Determined Concentration in Feed for Target Concentration of 10,000 ppm (1%) (a)
11/21/77	11,100 ± 900
12/07/77	11,000 ± 500
02/01/78	9,100 ± 240
03/22/78	10,500 ± 30
05/22/78	11,800 ± 30
07/11/78	9,500 ± 20
09/14/78	11,600 ± 120
10/30/78	9,500 ± 60
12/15/78	9,300 ± 40
02/15/79	9,200 ± 40
04/02/79	10,900 ± 60
05/09/79	11,300 ± 60
06/26/79	10,700 ± 30
08/28/79	10,000 ± 100
10/16/79	10,000 ± 130
12/03/79	9,600 ± 430
01/10/80	9,500 ± 260
02/27/80	8,900 ± 170
04/18/80	8,900 ± 90
05/29/80	13,200 ± 290
07/18/80	10,500 ± 160
08/26/80	9,400 ± 40
10/13/80	9,600 ± 150
	Mean = 10,200 ± 210

(a) Average of five samples

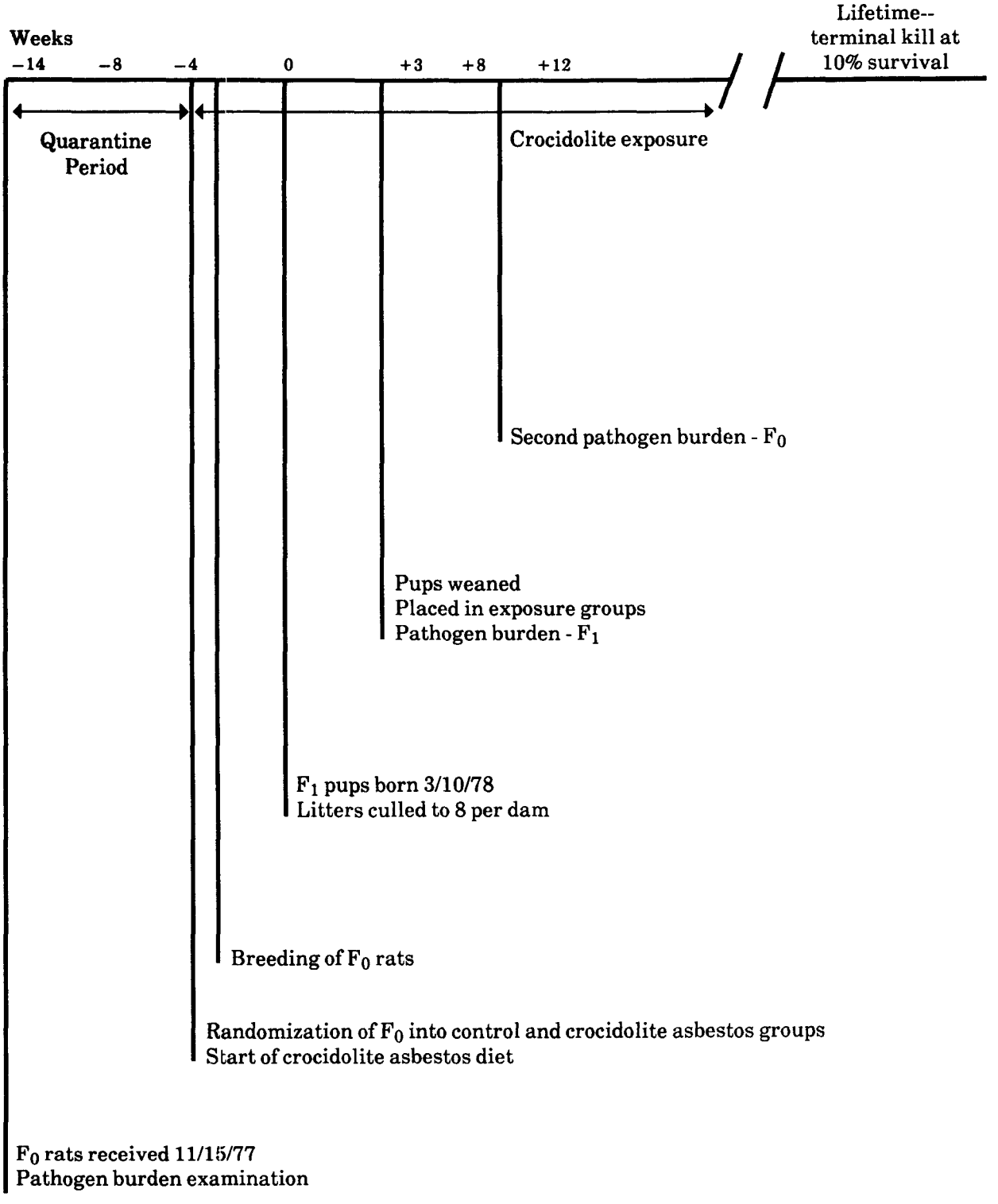

FIGURE 1. SCHEDULE OF MAJOR EVENTS IN RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

TABLE 4. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

EXPERIMENTAL DESIGN	
Size of Study Groups	F_0--control: male, 25; female, 50; dosed: male, 75; female, 150; F_1--control: 118; crocidolite asbestos: 250 rats of each sex
Doses	0% or 1% (10,000 ppm) crocidolite asbestos in feed
Date of First Dose	F_0--obtained 11/15/77, bred starting 2/17/78; F_1--date of weaning 4/1/78
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 Examination	Necropsy performed on all animals. Tissues examined histologically: adrenal glands; bone marrow (sternum); brain; bronchial, celiac, cervical, iliac, iliocolonic, mandibular, mesenteric, pancreatic, and renal lymph nodes; cecum; colon (carpet rolled); duodenum; esophagus; heart; ileum; jejunum; kidneys; larynx; liver; lungs and bronchi; mammary gland; pancreas; parathyroids; pituitary gland; prostate/testes or ovaries/uterus; salivary glands; small intestine; spleen; stomach; thigh muscle; 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	F_1--male: 142 wk; female: 145 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	
Lot Numbers Used	N/A
Supplier	Certain-Teed (Ambler, PA); obtained from a mine in South Africa located near the Kalahari Desert in the Kuruman Hills

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

FORMULATED DIETS	
Preparation	20 lb crocidolite asbestos/ton of feed mixed in a 55-ft^3 Patterson-Kelly® V-blender with intensifier bar; oval, 3/8-inch × 3/4-inch pellets prepared with Sprout-Waldron pellet mill. Pelleted feed packaged in 25-pound aliquots in standard paper feed bags that were color coded
Storage Conditions	Not available

After at least 7 days' exposure to the designated diets, the rats (16-17 weeks old) were placed in breeding cages (one male to two females) on February 3, 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, 10 rats (5 rats of each sex) were selected from the F_0 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 (F_1): The F_0 females were allowed to deliver their F_1 litters naturally, and these were culled to groups of no more than eight pups (four per sex if possible) per litter. No particular system was used in reducing the number of pups to eight (other than four per sex).

At birth, the litters from the F_0 dams within the control and dosed groups were assigned randomly to the corresponding lifetime feeding phase groups (control and dosed) such that birth dates were equally distributed. Twenty-one days after birth, the pups were weaned, given a temporary number, and then assigned, according to a table of random numbers, to groups for the lifetime feed study. Litters in which only one sex was present were excluded from those animals to be selected. At this time, 16 rats (8 rats per sex) were selected for pathogen burden determinations (Tables C7-C9).

ANIMAL MAINTENANCE

The control and crocidolite 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. 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.

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 asbestos concentrations. Additional samples were collected approximately every 6 months for analysis to assure personnel safety (Appendix F).

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 they were excessively autolyzed or cannibalized. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study in each group. 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 crocidolite 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, Illinois, or Diabutal®, Diamond Laboratories, Inc., Des Moines, Iowa). Final body weights were recorded, and necropsies were performed which 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.

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 and Tarone's (1975) life table test for a dose-related trend. When significant survival differences were detected, additional analyses using these procedures were carried out to determine the time point at which significant differences in the survival curves were first detected. 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/Cochran-Armitage trend analyses. Tests of significance include pairwise comparisons of high dose and low dose groups with controls and tests for overall dose-response trends. For studies in which administration of the test 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 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) and of Tarone (1975). The underlying variable considered by this analysis is time to death due to tumor. If the tumor is rapidly lethal, then time to death due to tumor closely approximates time to tumor onset. In this case, the life table test also provides a comparison of the time-specific tumor incidences.

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

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

Historical Control Data: Although the concurrent control group is always the first and most appropriate control group used for evaluation, there are certain instances in which historical control data can be helpful in the overall assessment of tumor incidence. Consequently, control tumor incidences from the NTP historical control data base (Haseman et al., 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

ESTABLISHMENT OF STUDY GROUPS

The studies were designed to evaluate the effects of ingested crocidolite asbestos during the entire life of the animal, starting from the time the rats were able to eat solid food. For this reason, the mated female rats had been on the study diets for approximately 14 weeks when the first litters were born. 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.

Litter size and survival of offspring were unaffected by the presence of crocidolite asbestos in the diet. The average number of live fetuses born to crocidolite asbestos-exposed dams was 7.7 vs. 7.4 for the control groups. The average weight at birth of the crocidolite asbestos-exposed pups, determined by dividing the weight of each litter by the number of live pups, was 4.8 g vs. 5.0 g for the controls. The crocidolite asbestos-exposed offspring were smaller at weaning than were controls (22.2 g vs. 27.5 g).

A summary of groups, number of animals, diets for the parental (F_0) animals, as well as the distribution of and diets for the filial (F_1) animals is presented in Figure 1 and Table 4.

PATHOGEN BURDEN

The tissues of the F_0 animals evaluated for pathogen burden revealed evidence of early spontaneous respiratory disease present in the lungs of all but one of the rats examined (Appendix C). The lesions consisted of minimal to slight peribronchial lymphoid hyperplasia and minimal perivascular lymphoid hyperplasia in three of these rats. In the repeated pathogen burden examination of the F_0 animals, evidence of respiratory disease was noted in all animals. This disease was characterized by moderate peribronchial lymphoid hyperplasia in all rats with an accompanying bronchial exudate in six males. The respiratory disease was slightly more pronounced than that observed at the earlier kill.

In the lungs of all F_1 rats examined, evidence of early spontaneous respiratory disease was present, characterized by minimal to slight peribronchial lymphoid hyperplasia.

No serologic evidence of Sendai virus was present in either F_0 or F_1 animals (Appendix C).

CLINICAL SIGNS

A summary of clinical signs from weeks 83 to 112 is presented in Appendix G. This time period was chosen for illustration because few signs were noted before week 83 and age-related signs complicated the observations after week 112.

The incidence of clinical signs occurred at essentially comparable frequencies in the crocidolite asbestos-exposed and control rats throughout the studies. The following representative findings were observed at generally comparable frequencies in all groups: soft feces; urine stains; pale, thin and/or hunched appearance; depression; localized alopecia or sores on head or body; rough haircoats; 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.

BODY WEIGHTS AND FEED CONSUMPTION

Mean body weights of rats in the lifetime feed studies, body weights relative to controls, and survival are presented in Table 5; mean body weights are also shown in Figure 2.

Mean body weights were statistically analyzed at selected intervals: birth and weeks 3, 8, 10, 14, 23, 34, 58, 86, and 112 for the males and birth and weeks 3, 8, 11, 16, 27, 48, 60, 86, and 112 for the females. The birth weights of pups from exposed and control dams were approximately the same but the crocidolite asbestos-exposed pups weighed 19% less than did the controls at weaning. The depression in body weight gain in the crocidolite asbestos-exposed rats was greatest at 7 weeks of age (male, 32%; female, 23%), after which time weight gain was parallel to that in the controls for the remainder of the studies, with mean body weights remaining lower at all time points.

A summary of average weekly feed consumption per rat and ratios for dosed vs. control groups is given in Appendix H. The average weekly feed consumption by the crocidolite asbestos-exposed males and females was 95% that by the controls. These differences may have contributed to some degree to the depressed body weight gain in the crocidolite asbestos-exposed rats.

TABLE 5. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

Weeks on Study (from birth)	Control		1% Crocidolite		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors
MALE					
7	165	118	112	68	250
17	312	118	244	78	250
27	359	118	317	88	249
37	408	118	351	86	249
47	411	118	366	89	248
57	443	118	392	88	248
67	466	117	413	89	247
77	471	114	427	91	246
87	471	109	429	103	240
97	464	102	424	91	230
107	460	89	419	91	206
117	424	65	399	94	167
127	401	45	373	93	112
137	361	19	332	92	52
FEMALE					
7	126	118	97	77	250
17	188	118	163	87	250
27	203	118	186	92	250
37	224	118	200	89	250
47	228	118	220	96	249
57	251	118	235	94	248
67	282	117	259	92	244
77	303	115	280	92	239
87	317	109	292	92	232
97	328	94	294	90	228
107	334	81	302	90	202
117	324	70	295	91	160
127	314	51	275	88	111
137	295	28	253	86	66

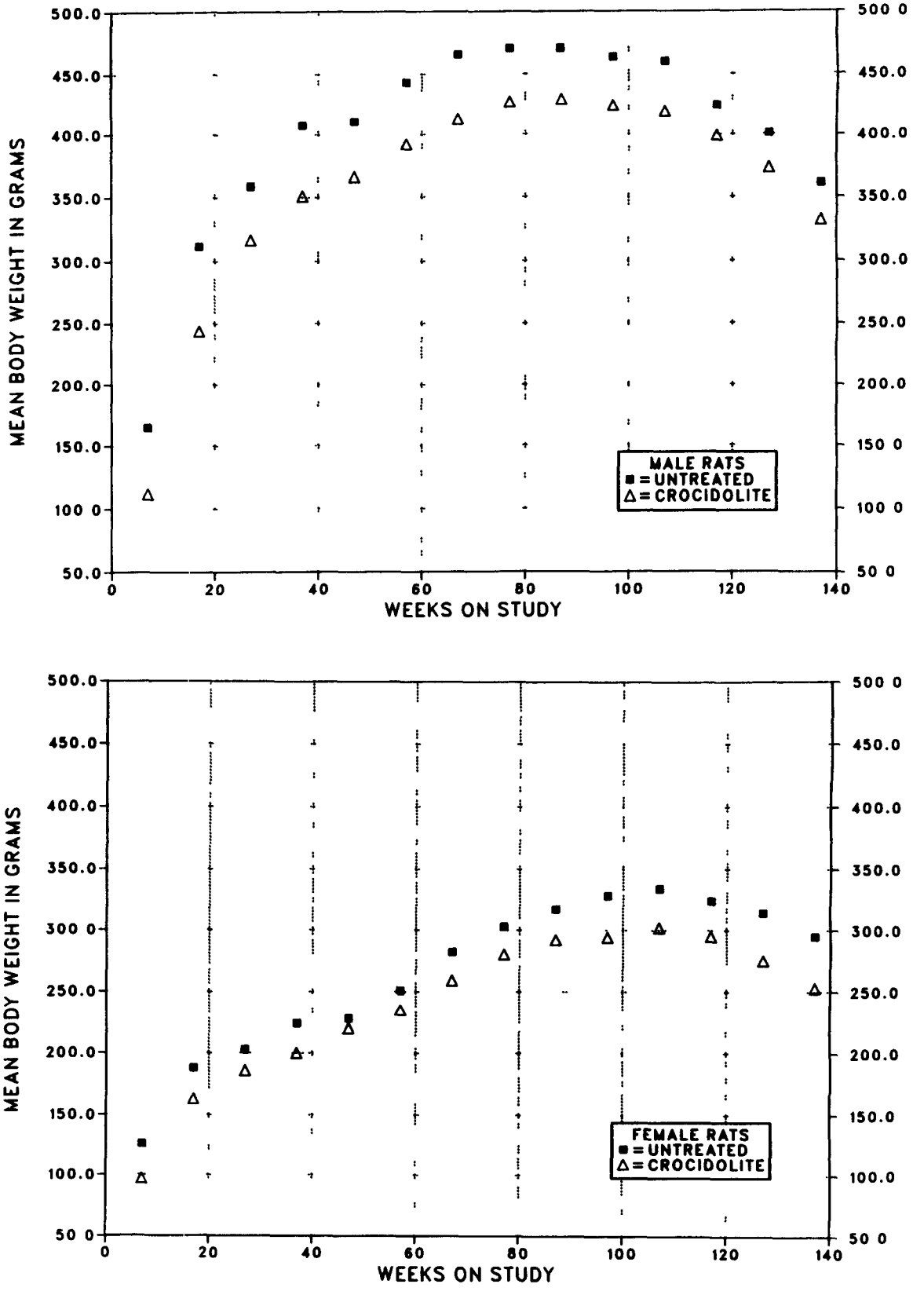

FIGURE 1. GROWTH CURVES FOR RATS IN THE LIFTETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

SURVIVAL

Estimates of the probabilities of survival for male and female rats fed diets containing crocidolite asbestos and for the controls are shown in Table 6 and in the Kaplan and Meier curves in Figure 3. No significant differences in survival between the dosed and control groups were observed, although a greater percentage of crocidolite asbestos-exposed rats were alive during most of the studies. Survival of males and females was approximately equal until week 112, after which a greater proportion of the females survived.

PATHOLOGY AND STATISTICAL ANALYSES OF RESULTS

This section describes the significant or 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 control rat because of autolysis.

Lesions in male rats are summarized in Appendix A. Histopathologic findings on neoplasms are summarized in Table A1. Table A2 gives the survival and tumor status for individual male rats. Table A3 contains the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups. The statistical analyses used are discussed in Chapter II (Statistical Methods) and Table A3 (footnotes). Historical incidences of tumors in control male rats are listed in Table A4. Findings on nonneoplastic lesions are summarized in Table A5.

Lesions in female rats are summarized in Appendix B. Histopathologic findings on neoplasms are summarized in Table B1. Table B2 gives the survival and tumor status for individual female rats. Table B3 contains the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups. The statistical analyses used are discussed in Chapter II (Statistical Methods) and Table B3 (footnotes). Historical incidences of tumors in control female rats are listed in Table B4. Findings on nonneoplastic lesions are summarized in Table B5.

TABLE 6. SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS AT VARIOUS TIME POINTS AFTER WEEK 112

		Male		Female	
Group	Week	Number Alive/ Total Number	Percent Survival	Number Alive/ Total Number	Percent Survival
Control	112	78/118	66	75/118	64
	120	56/118	47	62/118	53
	134	20/118	17	32/118	27
	144	--	--	15/118	13
***Crocidolite* asbestos**	112	179/250	72	172/250	69
	120	149/250	60	143/250	57
	134	64/250	26	73/250	29
	144	--	--	29/250	12

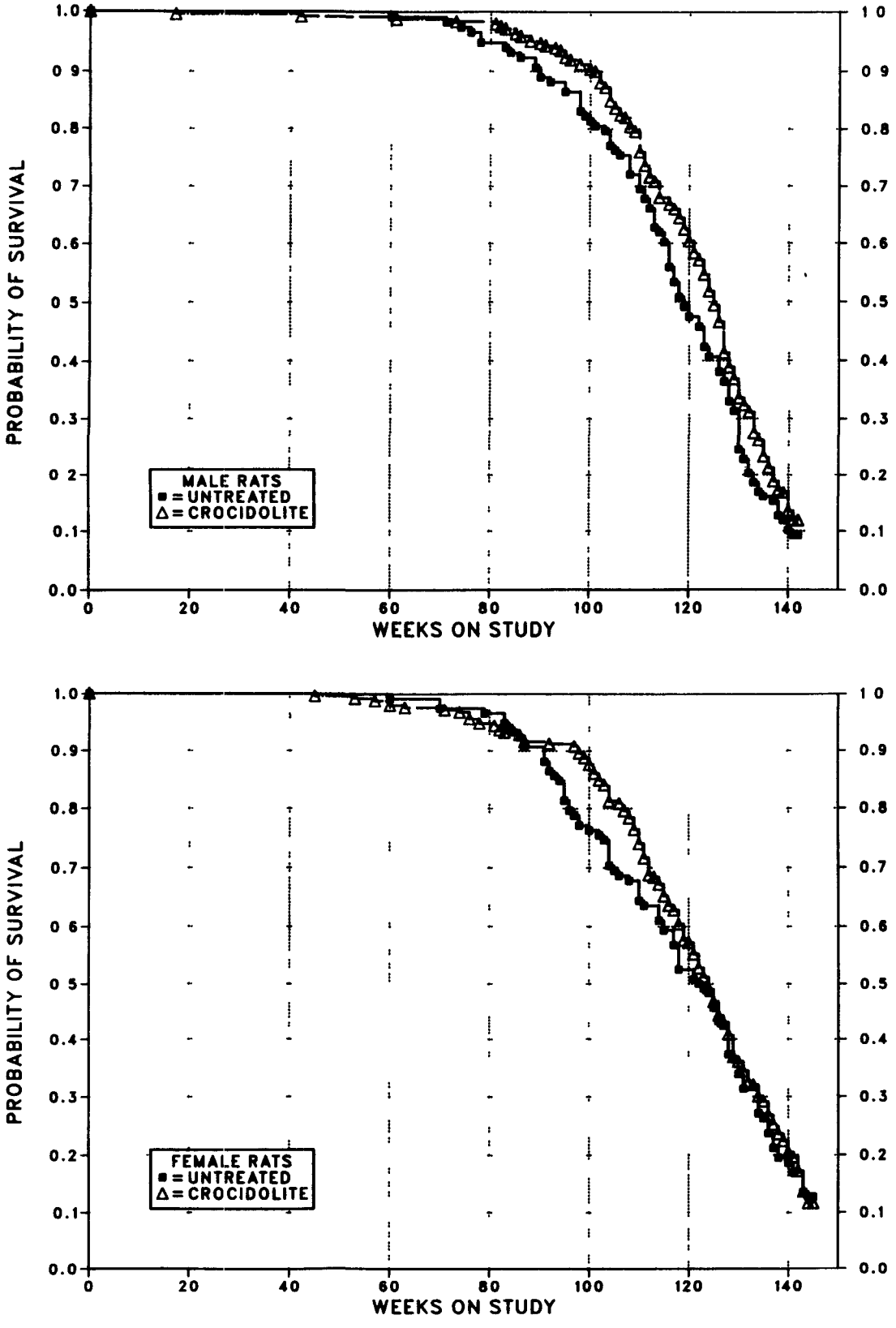

FIGURE 2. KAPLAN-MEIER SURVIVAL CURVES FOR RATS IN THE LIFTETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

A variety of neoplasms was found in the control and crocidolite asbestos-exposed groups, including monocytic (mononuclear cell) leukemia, endocrine tumors, testicular interstitial cell tumors, and mammary gland neoplasms (Table 7).

Stomach Neoplasms: Squamous cell papillomas occurred in the forestomach (nonglandular) and appeared as exophytic growths of thickened epithelium resting on a proliferative connective tissue stalk. Squamous cell carcinomas also occurred in the forestomach and were composed of proliferating small basophilic squamous cells that were growing down into the lamina propria and occasionally formed keratin pearls.

Intestinal Tract Neoplasms:

The primary epithelial neoplasms in the crocidolite asbestos studies were divided by the original pathologist into three major types, based on morphology and biologic behavior: adenomatous polyps, adenocarcinomas arising in an adenomatous polyp, and carcinomatas.

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 accompanied by an inflammatory response. Invasion of the pedicle was not observed. These polyps often occurred as multiple neoplasms in the large intestine.

Adenocarcinomas arising in adenomatous polyps--These neoplasms were exophytic lesions of the mucosa composed of proliferating deeply basophilic hypertrophic epithelial cells similar to those described above. 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.

Carcinomatas--This classification includes signet ring cell carcinomas, adenocarcinomas, mucinous cystadenocarcinomas, and carcinomas. Biologically, all were similar and were usually characterized by transmural growth that penetrated the muscular tunics and serosa and spread throughout 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 clear oval cells with eccentric nuclei. 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

TABLE 7. INCIDENCE OF PRIMARY NEOPLASMS IN RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

	Male		Female	
	Control	1% Crocidolite	Control	1% Crocidolite
No. of animals examined	118	250	118	250
Total animals with primary tumors	118 (100%)	248 (99%)	115 (97%)	242 (97%)
Total primary tumors	(a) 395 (3.3)	(a) 831 (3.4)	(a) 291 (2.5)	(a) 661 (2.7)
Total animals with benign tumors	117 (99%)	242 (97%)	91 (77%)	190 (76%)
Total benign tumors	(a) 251 (2.1)	(a) 498 (2.1)	(a) 166 (1.8)	(a) 378 (2.0)
Total animals with malignant tumors	97 (82%)	209 (84%)	80 (68%)	187 (75%)
Total malignant tumors	(a) 134 (1.4)	(a) 315 (1.5)	(a) 120 (1.5)	(a) 273 (1.5)

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

same tumor, suggesting that the above morphologic types probably have the same histogenesis.

A few mesenchymal neoplasms of connective tissue or smooth muscle origin also were observed in the gastrointestinal tract. The incidences of these and of epithelial neoplasms are shown in Table 8. No statistically significant differences between the control and crocidolite asbestos-exposed groups were observed.

Evaluation of the incidence of the various categories of epithelial intestinal neoplasia by site and week of occurrence within the gastrointestinal tract does not indicate any significant ($P<0.05$) compound-related effect (Table 9). In addition, the incidences of nonneoplastic lesions of the gastrointestinal tract, such as enteritis, ulceration, and inflammation, were generally comparable in the control and crocidolite asbestos-exposed rats (Table 10).

TABLE 8. INCIDENCE OF GASTROINTESTINAL TRACT NEOPLASMS IN RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

	Male		Female	
	Control	1% Crocidolite	Control	1% Crocidolite
No. of animals examined	117	249	118	250
Total animals with neoplasms	5 (4.3%)	15 (6.0%)	3 (2.5%)	5 (2.0%
Total animals with epithelial neoplasms	3 (2.6%)	9 (3.6%)	1 (0.8%)	5 (2.0%)
Total animals with mesenchymal neoplasms	2 (1.7%)	6 (2.4%)	2 (1.7%)	0 (0.0%)

TABLE 9. WEEK OF OCCURRENCE FOR EACH RAT WITH GASTROINTESTINAL TRACT EPITHELIAL NEOPLASMS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

	Male		Female	
Site/Neoplasm	Control	1% Crocidolite	Control	1% Crocidolite
Stomach (forestomach)				
Squamous cell papilloma	--	108	--	71
Squamous cell carcinoma	--	142	--	86
Basal cell carcinoma	--	133	--	--
Stomach (fundus)				
Carcinoma, NOS	(a) 83	136	--	143
Adenomatous polyp	--	--	--	118
Jejunum				
Mucinous cystadenocarcinoma	--	121	126	--
Malignant carcinoid tumor	--	--	--	53
Ileum				
Adenocarcinoma	78	--	--	--
Cecum				
Adenomatous polyp	(b) 130	--	--	--
Colon (ascending)				
Adenomatous polyp	--	132	--	--
Colon (descending)				
Adenomatous polyp	--	104, 116, 142	--	--
Colon (transverse)				
Carcinoma	(b) 130	--	--	--

(a) Carcinoma in situ
(b) A carcinoma of the transverse colon and an adenomatous polyp of the cecum occurred in the same animal.

TABLE 10. INCIDENCE OF NONNEOPLASTIC LESIONS IN THE ALIMENTARY TRACT IN RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

	Male		Female	
	Control	1% Crocidolite	Control	1% Crocidolite
Tongue	118	250	118	250
Inflammation	0 (0%)	2 (1%)	0 (0%)	0 (0%)
Hyperkeratosis	0 (0%)	2 (1%)	0 (0%)	0 (0%)
Acanthosis	0 (0%)	1 (<1%)	0 (0%)	1 (<1%)
Esophagus	115	247	116	239
Inflammation	0 (0%)	0 (0%)	1 (1%)	0 (0%)
Necrosis	0 (0%)	0 (0%)	1 (1%)	0 (0%)
Hyperkeratosis	8 (7%)	17 (7%)	5 (4%)	3 (1%)
Acanthosis	1 (1%)	0 (0%)	0 (0%)	0 (0%)
Stomach (nonglandular)	116	249	118	250
Mineralization	4 (3%)	3 (1%)	1 (1%)	0 (0%)
Inflammation, chronic	25 (22%)	38 (15%)	21 (18%)	46 (18%)
Ulcer, perforated	10 (9%)	21 (8%)	9 (8%)	17 (7%)
Necrosis, focal	19 (16%)	47 (19%)	23 (19%)	36 (14%)
Hyperplasia	4 (3%)	2 (1%)	1 (1%)	1 (<1%)
Hyperkeratosis	17 (15%)	47 (19%)	31 (26%)	28 (11%)
Acanthosis	28 (24%)	60 (24%)	28 (24%)	50 (20%)
Stomach (glandular)	116	249	118	250
Hyperplasia	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Small intestine	117	249	118	250
Inflammation	1 (1%)	1 (<1%)	0 (0%)	3 (1%)
Necrosis	1 (1%)	1 (<1%)	0 (0%)	2 (1%)
Ulcer, perforated	0 (0%)	1 (<1%)	0 (0%)	1 (<1%)
Colon	117	249	118	250
Parasitism	5 (4%)	9 (4%)	9 (8%)	9 (4%)
Inflammation	1 (1%)	3 (1%)	0 (0%)	0 (0%)
Necrosis	2 (2%)	3 (1%)	1 (1%)	0 (0%)
Hyperplasia	0 (0%)	1 (<1%)	0 (0%)	0 (0%)
Cecum	117	249	118	250
Parasitism	0 (0%)	1 (<1%)	0 (0%)	0 (0%)
Inflammation	1 (1%)	2 (1%)	0 (0%)	6 (2%)
Necrosis	1 (1%)	3 (1%)	1 (1%)	2 (1%)
Hyperplasia	0 (0%)	0 (0%)	0 (0%)	2 (1%)

Miscellaneous Neoplasms: Occasionally, a somewhat higher or lower incidence of commonly occurring neoplasms was observed in dosed groups, but most of these were without statistical significance (Table 11). The only neoplasms showing a statistically significant increase were leukemia (Table 12) and tumors of the thyroid gland (Tables 13 and 14) and clitoral gland (referred to as preputial gland in Appendix B) (Table 15).

The incidence of leukemia (mononuclear cell leukemia or monocytic leukemia) was significantly increased ($P<0.05$) in female crocidolite asbestos-exposed rats compared with that in the control group (Table 12). However, statistical significance was absent ($P=0.15$) when the incidence was examined by life table analysis.

The incidence of follicular cell carcinomas of the thyroid gland showed significant increases ($P<0.05$) in male rats exposed to crocidolite asbestos (Table 13). The incidences of follicular cell adenomas and adenomas or carcinomas (combined) were not significantly increased in male rats, whereas the combination was significantly decreased ($P<0.05$) in females.

TABLE 11. INCIDENCE OF PRIMARY NEOPLASMS IN RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS (a)

	Male		Female	
	Control	1% Crocidolite	Control	1% Crocidolite
Skin	118	250	118	250
Squamous cell papilloma	1 (1%)	6 (2%)	0 (0%)	1 (<1%)
Squamous cell carcinoma	2 (2%)	3 (1%)	1 (1%)	1 (<1%)
Basal cell carcinoma	2 (2%)	10 (4%)	1 (1%)	0 (0%)
Keratoacanthoma	4 (3%)	11 (4%)	0 (0%)	1 (<1%)
Subcutaneous tissue or skin	118	250	118	250
Fibroma	18 (15%)	27 (11%)	6 (5%)	9 (4%)
Fibrosarcoma	8 (7%)	7 (3%)	3 (3%)	5 (2%)
Neurofibroma	3 (3%)	9 (4%)	0 (0%)	1 (<1%)
Neurofibrosarcoma	0 (0%)	4 (2%)	0 (0%)	1 (<1%)
Lung	117	250	118	250
Alveolar/bronchiolar adenoma	1 (1%)	2 (1%)	0 (0%)	1 (<1%)
Alveolar/bronchiolar carcinoma	2 (2%)	2 (1%)	1 (1%)	2 (1%)
Hematopoietic system	118	250	118	250
Leukemia (monocytic or mononuclear cell)	43 (36%)	113 (45%)	43 (36%)	(b) 118 (47%)
Lymphoma	1 (1%)	5 (2%)	0 (0%)	1 (<1%)
Circulatory system	118	250	118	250
Hemangiosarcoma	3 (3%)	4 (2%)	0 (0%)	0 (0%)
Liver	117	250	118	250
Neoplastic nodule	8 (7%)	16 (6%)	3 (3%)	6 (2%)
Hepatocellular carcinoma	4 (3%)	3 (1%)	0 (0%)	1 (<1%)
Pancreas	118	249	118	249
Acinar cell adenoma	8 (7%)	15 (6%)	2 (2%)	5 (2%)
Acinar cell carcinoma	0 (0%)	2 (1%)	0 (0%)	1 (<1%)
Kidney	117	250	117	250
Tubular cell adenoma	0 (0%)	2 (1%)	2 (2%)	0 (0%)
Tubular cell adenocarcinoma	0 (0%)	5 (2%)	1 (1%)	0 (0%)
Pituitary gland	117	245	116	247
Adenoma	15 (13%)	41 (17%)	42 (36%)	101 (41%)
Carcinoma	3 (3%)	4 (2%)	9 (8%)	8 (3%)
Adrenal gland	117	250	118	250
Cortical adenoma	2 (2%)	8 (3%)	4 (3%)	18 (7%)
Cortical carcinoma	0 (0%)	0 (0%)	2 (2%)	1 (<1%)
Pheochromocytoma, benign	33 (28%)	54 (22%)	17 (14%)	39 (16%)
Pheochromocytoma, malignant	2 (2%)	8 (3%)	2 (2%)	3 (1%)
Thyroid gland	116	249	117	250
Follicular cell adenoma	7 (6%)	15 (6%)	8 (7%)	8 (3%)
Follicular cell carcinoma	3 (3%)	(b) 22 (9%)	3 (3%)	2 (1%)
C-cell adenoma	13 (11%)	34 (14%)	4 (3%)	(c) 23 (9%)
C-cell carcinoma	19 (16%)	48 (19%)	12 (10%)	(b) 46 (18%)
Pancreatic islets	117	249	118	249
Islet cell adenoma	2 (2%)	0 (0%)	2 (2%)	5 (2%)
Islet cell carcinoma	11 (9%)	(d) 11 (4%)	3 (3%)	6 (2%)
Mammary gland	118	250	118	250
Adenoma	0 (0%)	1 (<1%)	2 (2%)	1 (<1%)
Adenocarcinoma	1 (1%)	4 (2%)	16 (14%)	23 (9%)
Fibroadenoma	18 (15%)	(d) 18 (7%)	48 (41%)	112 (45%)

TABLE 11. INCIDENCE OF PRIMARY NEOPLASMS IN RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS (Continued)

	Male		Female	
	Control	1% Crocidolite	Control	1% Crocidolite
Preputial/clitoral gland	118	250	118	250
Adenoma	0 (0%)	0 (0%)	1 (1%)	2 (1%)
Carcinoma or squamous cell carcinoma	3 (3%)	16 (6%)	4 (3%)	(c) 23 (9%)
Testis	118	249		
Interstitial cell tumor	116 (98%)	237 (95%)		
Uterus			116	248
Endometrial stromal polyp			19 (16%)	38 (15%)
Endometrial stromal sarcoma			1 (1%)	3 (1%)
Ovary			116	248
Granulosa cell tumor			1 (1%)	4 (2%)
Granulosa cell carcinoma			1 (1%)	1 (<1%)
Zymbal gland	118	250	118	250
Squamous cell papilloma	0 (0%)	0 (0%)	0 (0%)	1 (<1%)
Squamous cell carcinoma	4 (3%)	5 (2%)	0 (0%)	4 (2%)
Tunica vaginalis	118	250		
Mesothelioma	4 (3%)	5 (2%)		

(a) Incidence of all neoplasms (other than those in the alimentary tract) that occurred at an incidence of 2% or more in at least one group
(b) $P<0.05$ (increase) relative to controls (incidental tumor and the Fisher exact tests)
(c) $P<0.05$ (increase) relative to controls
(d) $P<0.01$ (decrease) relative to controls

TABLE 12. ANALYSIS OF MONOCYTIC OR MONUCLEAR CELL LEUKEMIA IN RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS (a)

	Male (b)		Female (c)	
	Control	1% Crocidolite	Control	1% Crocidolite
Overall Rates	43/118 (36%)	113/250 (45%)	43/118 (36%)	118/250 (47%)
Adjusted Rates	77.7%	81.2%	66.7%	74.9%
Terminal Rates	4/11 (36%)	15/29 (52%)	3/15 (20%)	8/29 (28%)
Week of First Observation	71	83	60	76
Life Table Test		P=0.452		P=0.152
Incidental Tumor Test		P=0.082		P=0.032
Fisher Exact Test		P=0.070		P=0.033

(a) The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix A, Table A3 (footnotes).
(b) Historical incidence in untreated male controls in lifetime NTP studies (mean ± SD): 192/529 (36% ± 3%)
(c) Historical incidence in untreated female controls in lifetime NTP studies (mean ± SD): 201/529 (38% ± 6%)

TABLE 13. ANALYSIS OF FOLLICULAR CELL TUMORS OF THE THYROID GLAND IN RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

	Male		Female	
	Control	1% Crocidolite	Control	1% Crocidolite
Adenoma				
Overall Rates	7/116 (6%)	15/249 (6%)	8/117 (7%)	8/250 (3%)
Adjusted Rates	15.5%	14.2%	18.8%	13.5%
Terminal Rates	0/11 (0%)	0/29 (0%)	1/15 (7%)	2/29 (7%)
Week of First Observation	108	88	92	118
Life Table Test		P=0.443N		P=0.092N
Incidental Tumor Test		P=0.562N		P=0.084N
Fisher Exact Test		P=0.582N		P=0.097N
Carcinoma				
Overall Rates	3/116 (3%)	22/249 (9%)	3/117 (3%)	2/250 (1%)
Adjusted Rates	9.0%	31.7%	11.0%	2.0%
Terminal Rates	0/11 (0%)	6/29 (21%)	1/15 (7%)	0/29 (0%)
Week of First Observation	100	110	121	118
Life Table Test		P=0.061		P=0.175N
Incidental Tumor Test		P=0.034		P=0.161N
Fisher Exact Test		P=0.019		P=0.188N
Adenoma or Carcinoma (a,b)				
Overall Rates	10/116 (9%)	37/249 (15%)	11/117 (9%)	10/250 (4%)
Adjusted Rates	23.1%	41.5%	28.2%	15.2%
Terminal Rates	0/11 (0%)	6/29 (21%)	2/15 (13%)	2/29 (7%)
Week of First Observation	100	88	92	118
Life Table Test		P=0.196		P=0.032N
Incidental Tumor Test		P=0.095		P=0.025N
Fisher Exact Test		P=0.065		P=0.037N

(a) Historical incidence in untreated male controls in lifetime NTP studies (mean ± SD): 44/520 (9% ± 1%)
(b) Historical incidence in untreated female controls in lifetime NTP studies (mean ± SD): 39/525 (7% ± 2%)

TABLE 14. ANALYSIS OF C-CELL TUMORS OF THE THYROID GLAND IN RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

	Male		Female	
	Control	1% Crocidolite	Control	1% Crocidolite
Adenoma				
Overall Rates	13/116 (11%)	34/249 (14%)	4/117 (3%)	23/250 (9%)
Adjusted Rates	34.8%	31.2%	17.1%	34.3%
Terminal Rates	2/11 (18%)	3/29 (10%)	2/15 (13%)	5/29 (17%)
Week of First Observation	78	88	122	107
Life Table Test		P=0.518		P=0.046
Incidental Tumor Test		P=0.321		P=0.038
Fisher Exact Test		P=0.319		P=0.034
Carcinoma				
Overall Rates	19/116 (16%)	48/249 (19%)	12/117 (10%)	46/250 (18%)
Adjusted Rates	62.5%	57.8%	39.9%	53.4%
Terminal Rates	5/11 (45%)	10/29 (34%)	3/15 (20%)	6/29 (21%)
Week of First Observation	98	95	114	99
Life Table Test		P=0.497N		P=0.054
Incidental Tumor Test		P=0.436		P=0.041
Fisher Exact Test		P=0.304		P=0.030
Adenoma or Carcinoma (a)				
Overall Rates	32/116 (28%)	79/249 (32%)	16/117 (14%)	68/250 (27%)
Adjusted Rates	80.1%	71.6%	52.2%	71.2%
Terminal Rates	7/11 (64%)	13/29 (45%)	5/15 (33%)	11/29 (38%)
Week of First Observation	78	88	114	99
Life Table Test		P=0.458N		P=0.008
Incidental Tumor Test		P=0.353		P=0.003
Fisher Exact Test		P=0.250		P=0.002

(a) Historical incidence in untreated female controls in lifetime NTP studies (mean ± SD): 103/525 (20% ± 4%)

C-Cell adenomas and C-cell carcinomas showed statistically significant increases ($P<0.05$) in exposed female but not male rats (Table 14). The increases were statistically significant by all three tests.

The incidence of clitoral gland tumors was significantly increased ($P<0.05$) in female crocidolite asbestos-exposed rats compared with that in the controls (Table 15). However, there was no evidence of an increase in neoplasms in the male counterpart (preputial gland) of this tissue.

Nonneoplastic Findings

A plethora of incidental lesions of aging was found in all groups. Although the incidence of a few specific lesions in exposed rats was statistically different ($P<0.05$) from that in controls, none of these lesions was thought to be compound related. Histopathologic findings are summarized in Appendixes A and B. Nonneoplastic lesions that were observed in more than 5% of the rats in any of the study groups are shown in Table 16.

TABLE 15. INCIDENCE OF FEMALE RATS WITH TUMORS OF THE CLITORAL GLAND IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

	Control	1% Crocidolite
Squamous Cell Carcinoma		
Overall Rates	4/118 (3%)	22/250 (9%)
Adjusted Rates	20.6%	31.6%
Terminal Rates	2/15 (13%)	5/29 (17%)
Week of First Observation	137	109
Life Table Test		P=0.058
Incidental Tumor Test		P=0.053
Fisher Exact Test		P=0.042
Carcinoma or Squamous Cell Carcinoma		
Overall Rates	4/118 (3%)	23/250 (9%)
Adjusted Rates	20.6%	32.2%
Terminal Rates	2/15 (13%)	5/29 (17%)
Week of First Observation	137	109
Life Table Test		P=0.047
Incidental Tumor Test		P=0.043
Fisher Exact Test		P=0.032
Adenoma, Carcinoma, or Squamous Cell Carcinoma (a)		
Overall Rates	5/118 (4%)	25/250 (10%)
Adjusted Rates	22.2%	33.1%
Terminal Rates	2/15 (13%)	5/29 (17%)
Week of First Observation	127	109
Life Table Test		P=0.060
Incidental Tumor Test		P=0.056
Fisher Exact Test		P=0.041

(a) Historical incidence in untreated female controls in lifetime NTP studies (mean ± SD): 21/529 (4% ± 2%)

TABLE 16. NONNEOPLASTIC LESIONS OBSERVED IN MORE THAN 5% OF RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

Lung: chronic inflammation, congestion, hemorrhage, histiocytosis
Spleen: fibrosis, hemosiderosis, hematopoiesis, necrosis
Lymph nodes (various): lymphoid or reticulum cell hyperplasia, pigmentation, hemorrhage, erythrophagocytosis
Heart: chronic inflammation
Liver: degeneration, necrosis, fatty metamorphosis, toxic hepatitis, granulomas, pigmentation, focal cellular change
Bile duct (extrahepatic) chronic inflammation, hyperplasia
Pancreas (exocrine)· atrophy, hyperplasia, ectopia
Kidney: chronic inflammation, cysts, pigmentation, mineralization
Pituitary gland: cysts, angiectasis, hyperplasia
Adrenal gland (cortex) fatty metamorphosis, hyperplasia, degeneration, angiectasis
Adrenal gland (medulla) hyperplasia
Thyroid gland: follicular cysts, C-cell hyperplasia
Parathyroid: hyperplasia
Testis: degeneration, interstitial cell hyperplasia
Prostate: abscess, chronic inflammation, hyperplasia
Ovary· cysts
Uterus. endometrial cysts
Mammary gland· cystic ducts, galactocele, hyperplasia
Abdominal cavity: fat necrosis
Eye: cataract, inflammation, retinal degeneration
Zymbal gland: cystic ducts
Bone: osteopetrosis
Esophagus: hyperkeratosis
Stomach: hyperkeratosis, chronic inflammation, necrosis, acanthosis, ulcers

IV. DISCUSSION AND CONCLUSIONS

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Crocidolite asbestos was administered at a concentration of 1% in feed to male and female F344/N rats for their lifetime, beginning with exposure of the dams before and during gestation. The clinicopathologic results showed that the ingestion of crocidolite asbestos did not adversely affect the fertility of the mothers or the litter size of the F_1 animals. However, the average weight of the offspring at weaning from mothers exposed to crocidolite asbestos during gestation and lactation was 19% lower than that of the offspring of nonexposed mothers. This result was not due to gestational effects of crocidolite asbestos, since birth weights of the exposed pups were comparable to those of concurrent controls. Body weight gain differences became more apparent by 8 weeks of age (male, 32%; female, 23%), after which body weight gains of the crocidolite asbestos-exposed rats paralleled those of the control rats, even though the exposed rats remained smaller throughout their lives. Lower body weight of offspring of asbestos-exposed mothers has been a consistent finding in NTP oral asbestos studies, having been observed in both the amosite asbestos (NTP, 1988b) and the tremolite asbestos (NTP, 1988c) studies. The decreased body weight gain was not related to a decrease in feed consumption, and the reason for this effect is not known. Although feed consumption by both groups was similar, the total caloric intake was slightly lower in the crocidolite asbestos group because its diet contained 1% asbestos. The differential in weight gain was not considered a toxic effect because the lifespan was not altered and no compound-related lesions were observed.

No clinical signs were observed which could be attributed to the ingestion of crocidolite asbestos. The ingestion of 1% crocidolite asbestos in feed for the lifespan of the rats appeared to enhance the survival of both males and females. The most plausible explanation for the increased survival of the crocidolite asbestos-exposed rats is their lower weight throughout the studies. Yu et al. (1982) showed that F344 rats with lower body weights resulting from restricted caloric intake lived longer than rats that were given feed ad libitum.

Survival of the rats (control and exposed) in the current studies compares favorably with that in other long-term NTP studies; at 112 weeks of age, the proportions of rats still alive in these studies were as follows: male control, 66%; exposed male, 72%; control female, 64%; exposed female, 69%. In reviewing 25 NTP feed studies, Haseman (1983) reported that an average of 66% of control males and 73% of control females were alive at 112 weeks of age.

In the crocidolite asbestos studies, the survival of males was similar to that of females at 112 weeks of age. However, after 134 weeks, better survival was observed for both control and exposed females. In most 2-year studies involving rats, females usually have better survival than males. It is possible that the rats in these studies could have tolerated a higher level of exposure, although a dietary concentration of 1% for the entire life of the animal is substantial.

Ingestion of crocidolite asbestos over the lifetime of these rats did not cause any biologically significant increase in neoplasms at any particular anatomic site compared with the concurrent controls. Since the gastrointestinal tract was considered a target organ, based on epidemiologic studies in humans (Cooper et al., 1979) and because the study material was administered in feed, the incidence of gastrointestinal neoplasms in the control and exposed groups was examined in particular detail. Overall, the incidence was low, and no significant ($P<0.05$) differences in the total number of gastrointestinal neoplasms or neoplasms for any anatomic site within the gastrointestinal tract were observed between the exposed and control groups. Additionally, time to observation of the tumors was not affected by the ingestion of crocidolite asbestos. Most of these neoplasms were observed in rats over 112 weeks of age, the time when standard 2-year carcinogenesis studies are normally terminated.

Crocidolite asbestos did not cause an increase in any type of nonneoplastic disease in the gastrointestinal tract. In summary, the ingestion of this form of asbestos did not cause any adverse effects on the gastrointestinal tract of either male or female F344/N rats.

Statistically significant ($P<0.05$) increased incidences of mononuclear cell leukemia (monocytic

leukemia, Fischer rat leukemia) were observed in exposed female rats. However, this is readily explained because the exposed group of rats lived longer than the concurrent control group and the increased tumor incidence is not significant ($P=0.15$) when survival differences are taken into account by a life table test. The historical incidence of mononuclear cell leukemia in 2-year feed studies is 33% for male rats and 19% for females; in lifetime studies, the incidence is 36% for males (Table A4a) and 38% for females (Table B4a), compared with 36% for both sexes in the current studies (see Table 12). Based on these data, it is apparent that the incidence of this type of neoplasm increases after 112 weeks of age.

There was a statistically significant ($P<0.05$) increase in the number of follicular cell carcinomas in the thyroid gland of exposed male rats and a decrease in the incidence of follicular cell adenomas in exposed female rats. Since the progression of this neoplastic lesion is a continuum from benign to malignant and differentiation between the two is somewhat arbitrary, the combined incidence of tumors is more appropriate for comparative purposes when effects on the thyroid gland are evaluated. When the totals are compared, the differences for males disappear, whereas the incidences for females show a significant decrease ($P<0.05$). The reason for this decrease is unknown, but Haseman (1983) has observed that certain endocrine neoplasms and hormonally related neoplasms (e.g., mammary gland) commonly are decreased in exposed rats that weigh less than their respective control groups.

C-cell neoplasms (adenomas and carcinomas) in the thyroid gland were significantly ($P<0.05$) increased in crocidolite asbestos-exposed female rats. Benign and malignant lesions of this tissue should be combined for the same reasons noted above. The analysis of combined C-cell neoplasms strengthens the significant ($P<0.01$) difference between the exposed and control groups. The most plausible explanation for this observation is that the incidence in the control group may be abnormally low. In the corollary asbestos studies (Table B4c), the combined incidence of C-cell neoplasms in the female control groups were amosite, 21%, tremolite, 21%, long-range chrysotile, 24%, and short-range chrysotile, 20%, compared with 14% in control and 27% in exposed rats in the current studies (see Table 14). When the incidence in the crocidolite asbestos-exposed group is compared with that in any of these other control groups, the statistical significance disappears. Another reason for discounting the relationship between C-cell neoplasms and crocidolite asbestos is that it is difficult to envision an increase in these neoplasms in the absence of lesions in the target tissues. For these reasons, the increase in C-cell neoplasms was not considered biologically important. The increased incidence of clitoral gland tumors (see Table 15) was discounted because there was no increase in neoplasms in the male counterpart to this organ, i.e., the preputial gland, and because this site was not a primary target for distribution of the asbestos fibers.

A large variety of nonneoplastic lesions, primarily age related, was observed in all groups. There was no obvious correlation between exposure and specific lesions. Therefore, crocidolite asbestos at a concentration of 1% in feed did not appear to be toxic in this sense. The decrease in body weight may or may not be considered an asbestos-related toxic effect.

Other studies on the effects of long-term ingestion of crocidolite asbestos are not available. However, Stanton et al. (1981) showed that the intrapleural inoculation of several different samples of South African crocidolite asbestos caused a high incidence of pleural sarcoma in Osborne Mendel rats. Also, crocidolite asbestos is considered to be the most "dangerous" form of asbestos in humans because of its strong association with mesothelioma (Craighead et al., 1982).

Few studies have dealt with the long-term ingestion of other types of asbestos. In a companion study to this investigation, F344/N rats were exposed to short-range or intermediate-range chrysotile asbestos at a concentration of 1% in the diet for their lifespan (NTP, 1985a). Neither type of fiber affected fertility, litter size, body weight, or survival. Adenomatous polyps of the large intestine in male rats exposed to intermediate-range chrysotile asbestos fibers were considered some evidence of carcinogenicity; no other asbestos-related neoplasms were observed

in female rats or in groups exposed to short-range fibers. Similarly, an ingestion study of amosite asbestos in F344 rats using a design similar to that used in these studies failed to demonstrate a carcinogenic response (NTP, 1988b). In companion studies to this investigation, Syrian golden hamsters were exposed to either amosite asbestos or to short-range (fiber length) or intermediate-range chrysotile asbestos at a concentration of 1% in the diet for their natural lifespan (NTP, 1985b; NTP, 1988a). In both studies, no adverse effects were observed for body weight gain or survival, and no asbestos-related neoplasms were diagnosed.

Donham et al. (1980) reported equivocal results in F344 rats that were fed a diet containing 10% chrysotile for their lifetime. Although no significant ($P<0.05$) increase in the number of tumors in exposed animals was observed, the authors believed that there was a trend towards increased colon lesions in general, evidence of penetration of asbestos into the colonic mucosa, and possible cytotoxicity to colonic tissues; they also suggested a relationship to peritoneal mesothelioma. Another equivocal study was reported by Gibel et al. (1976) who described an increase in malignant tumors of the lung, kidney, liver, and reticuloendothelial system, but no increase in intestinal neoplasia, in Wistar rats fed asbestos filter material (20 mg per day) for 8-14 months. Cunningham et al. (1977) reported two studies (one 24-month and one 30-month) in male Wistar rats fed diets containing 1% chrysotile asbestos. These authors concluded that trace amounts of ingested asbestos can penetrate the walls of the gastrointestinal tract but that evidence of carcinogenicity was inconclusive. No evidence of carcinogenicity was found by Gross et al. (1974), who fed rats diets containing 5% chrysotile asbestos for 21 months.

An oral asbestos study in hamsters was reported by Smith et al. (1980). 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. No adverse effects on body weight or survival were observed in any of the groups. One peritoneal mesothelioma, one pulmonary carcinoma, and two early squamous carcinomas of the nonglandular stomach were found in hamsters exposed to amosite asbestos, but the incidence was not statistically significant ($P<0.05$). The authors concluded that the study was essentially negative. A subsequent study in rats using similar materials also failed to elicit a carcinogenic response (Hilding et al., 1981).

Except for the studies of Donham et al. (1980), Smith et al. (1980), and the NTP, the other studies were conducted with relatively small numbers of animals. Also, some were conducted for an insufficient period of time to adequately test the carcinogenic potential of ingested asbestos.

The experimental and tabulated data for the NTP Technical Report on crocidolite asbestos were examined for accuracy, consistency, completeness, and compliance with Good Laboratory Practice regulations. As summarized in Appendix I, the audit revealed no major problems with the conduct of the studies or with collection and documentation of the experimental data. No discrepancies were found that influenced the final interpretation of the results of these studies.

Under the conditions of these feed studies, crocidolite asbestos was not overtly toxic and did not cause a carcinogenic response when ingested at a concentration of 1% in the diet by male and female F344/N rats for their lifetime.

V. REFERENCES

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APPENDIX A

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

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS

	Untreated Control	1% Crocidolite Asbestos
ANIMALS INITIALLY IN STUDY	118	250
ANIMALS NECROPSIED	118	250
ANIMALS EXAMINED HISTOPATHOLOGICALLY	118	250
INTEGUMENTARY SYSTEM		
*Multiple organs	(118)	(250)
Fibrous histiocytoma, malignant	1 (1%)	
*Skin	(118)	(250)
Squamous cell papilloma	1 (1%)	6 (2%)
Squamous cell carcinoma	2 (2%)	3 (1%)
Basal cell tumor	1 (1%)	1 (0%)
Basal cell carcinoma	2 (2%)	10 (4%)
Trichoepithelioma		1 (0%)
Keratoacanthoma	4 (3%)	11 (4%)
Fibroma	1 (1%)	
Fibrosarcoma	2 (2%)	1 (0%)
Myxosarcoma	1 (1%)	
Neurofibroma		1 (0%)
Neurofibrosarcoma		3 (1%)
*Subcutaneous tissue	(118)	(250)
Keratoacanthoma		1 (0%)
Sarcoma, NOS	1 (1%)	
Sarcoma, NOS, invasive		1 (0%)
Fibroma	17 (14%)	‡27 (11%)
Fibrosarcoma	6 (5%)	6 (2%)
Lipoma	1 (1%)	3 (1%)
Osteosarcoma		2 (1%)
Neurofibroma	3 (3%)	8 (3%)
Neurofibrosarcoma		1 (0%)
RESPIRATORY SYSTEM		
#Trachea	(117)	(248)
C-cell carcinoma, invasive	1 (1%)	1 (0%)
#Lung	(117)	(250)
Neoplasm, NOS, metastatic		1 (0%)
Squamous cell carcinoma	1 (1%)	
Squamous cell carcinoma, metastatic	1 (1%)	2 (1%)
Alveolar/bronchiolar adenoma	1 (1%)	2 (1%)
Alveolar/bronchiolar carcinoma	2 (2%)	2 (1%)
C-cell carcinoma, metastatic	1 (1%)	1 (0%)
Pheochromocytoma, metastatic		5 (2%)
Liposarcoma, metastatic		3 (1%)
Mesothelioma, metastatic		2 (1%)
Osteosarcoma, metastatic		2 (1%)
HEMATOPOIETIC SYSTEM		
*Multiple organs	(118)	(250)
Malignant lymphoma, undifferentiated type		1 (0%)
Malignant lymphoma, histiocytic type	1 (1%)	3 (1%)
Monocytic leukemia	42 (36%)	110 (44%)
#Spleen	(117)	(250)
Pheochromocytoma, metastatic		1 (0%)
Fibrosarcoma		1 (0%)
Fibrosarcoma, metastatic		1 (0%)
Leukemia, mononuclear cell		1 (0%)
#Mandibular lymph node	(117)	(250)
Squamous cell carcinoma, metastatic	1 (1%)	1 (0%)
Sarcoma, NOS, invasive		1 (0%)

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
HEMATOPOIETIC SYSTEM (Continued)		
#Mediastinal lymph node	(117)	(250)
C-cell carcinoma, metastatic		1 (0%)
Pheochromocytoma, metastatic		1 (0%)
Rhabdomyosarcoma, metastatic		1 (0%)
Mesothelioma, metastatic	1 (1%)	
#Liver	(117)	(250)
Malignant lymphoma, histiocytic type		1 (0%)
Kupffer cell sarcoma		1 (0%)
Monocytic leukemia		3 (1%)
#Thymus	(88)	(182)
Papillary adenocarcinoma		1 (1%)
Granulocytic leukemia	1 (1%)	
CIRCULATORY SYSTEM		
*Multiple organs	(118)	(250)
Hemangiosarcoma, metastatic		1 (0%)
*Skin	(118)	(250)
Hemangiopericytoma, malignant		1 (0%)
*Subcutaneous tissue	(118)	(250)
Hemangiosarcoma		2 (1%)
#Bone marrow	(117)	(248)
Hemangiosarcoma	1 (1%)	
#Spleen	(117)	(250)
Hemangiosarcoma, metastatic		1 (0%)
*Vertebral column	(118)	(250)
Hemangiosarcoma		1 (0%)
#Lung	(117)	(250)
Hemangiosarcoma, metastatic	1 (1%)	1 (0%)
*Costal pleura	(118)	(250)
Hemangiosarcoma	1 (1%)	
#Heart	(117)	(250)
Hemangiosarcoma	1 (1%)	
#Myocardium	(117)	(250)
Alveolar/bronchiolar carcinoma, invasive		1 (0%)
Neurilemoma	1 (1%)	
*Mesentery	(118)	(250)
Hemangiosarcoma		1 (0%)
DIGESTIVE SYSTEM		
*Oral mucous membrane	(118)	(250)
Squamous cell carcinoma	4 (3%)	2 (1%)
*Tongue	(118)	(250)
Squamous cell papilloma		1 (0%)
#Salivary gland	(115)	(249)
Adenoma, NOS		1 (0%)
Sarcoma, NOS	1 (1%)	5 (2%)
#Liver	(117)	(250)
Neoplastic nodule	8 (7%)	16 (6%)
Hepatocellular carcinoma	4 (3%)	3 (1%)
Sarcoma, NOS	1 (1%)	
#Pancreas	(117)	(249)
Acinar cell adenoma	8 (7%)	15 (6%)
Acinar cell carcinoma		2 (1%)
*Pharynx	(118)	(250)
Squamous cell carcinoma		1 (0%)

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
DIGESTIVE SYSTEM (Continued)		
#Stomach	(116)	(249)
Carcinoma in-situ, NOS	1 (1%)	
Carcinoma, NOS		1 (0%)
Squamous cell papilloma		1 (0%)
Squamous cell carcinoma		1 (0%)
Basal cell carcinoma		1 (0%)
Fibrosarcoma		1 (0%)
Leiomyosarcoma		1 (0%)
#Duodenum	(117)	(249)
Fibrosarcoma	1 (1%)	1 (0%)
#Jejunum	(117)	(249)
Mucinous cystadenocarcinoma		1 (0%)
Fibrosarcoma	1 (1%)	
#Ileum	(117)	(249)
Adenocarcinoma, NOS	1 (1%)	
Leiomyosarcoma		1 (0%)
#Cecum	(117)	(249)
Adenomatous polyp, NOS	1 (1%)	
Lipoma		1 (0%)
#Ascending colon	(117)	(249)
Adenomatous polyp, NOS		1 (0%)
Leiomyosarcoma		1 (0%)
#Transverse colon	(117)	(249)
Carcinoma, NOS	1 (1%)	
#Descending colon	(117)	(249)
Adenomatous polyp, NOS		3 (1%)
URINARY SYSTEM		
#Kidney	(117)	(250)
Tubular cell adenoma		2 (1%)
Tubular cell adenocarcinoma		5 (2%)
Mixed tumor, malignant	1 (1%)	1 (0%)
#Urinary bladder	(116)	(250)
Transitional cell papilloma	2 (2%)	
ENDOCRINE SYSTEM		
#Pituitary	(117)	(245)
Carcinoma, NOS	3 (3%)	4 (2%)
Adenoma, NOS	15 (13%)	41 (17%)
#Adrenal	(117)	(250)
Cortical adenoma	2 (2%)	8 (3%)
Pheochromocytoma	29 (25%)	46 (18%)
Pheochromocytoma, malignant	2 (2%)	6 (2%)
#Adrenal medulla	(117)	(250)
Pheochromocytoma	4 (3%)	8 (3%)
Pheochromocytoma, malignant		2 (1%)
#Thyroid	(116)	(249)
Follicular cell adenoma	7 (6%)	15 (6%)
Follicular cell carcinoma	3 (3%)	22 (9%)
C-cell adenoma	13 (11%)	34 (14%)
C-cell carcinoma	19 (16%)	48 (19%)
#Pancreatic islets	(117)	(249)
Islet cell adenoma	2 (2%)	
Islet cell carcinoma	11 (9%)	11 (4%)

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
REPRODUCTIVE SYSTEM		
*Mammary gland	(118)	(250)
Adenoma, NOS		1 (0%)
Adenocarcinoma, NOS	1 (1%)	4 (2%)
Fibroadenoma	18 (15%)	18 (7%)
*Preputial gland	(118)	(250)
Squamous cell carcinoma	3 (3%)	16 (6%)
#Prostate	(116)	(250)
Carcinoma, NOS		1 (0%)
#Testis	(118)	(249)
Interstitial cell tumor	116 (98%)	237 (95%)
#Rete testis	(118)	(249)
Adenocarcinoma, NOS		1 (0%)
*Epididymis	(118)	(250)
Lipoma	1 (1%)	1 (0%)
Mesothelioma, NOS	1 (1%)	
NERVOUS SYSTEM		
#Cerebrum	(117)	(249)
Carcinoma, NOS, invasive	1 (1%)	1 (0%)
Granular cell tumor, NOS		1 (0%)
Astrocytoma		2 (1%)
#Cerebellum	(117)	(249)
Meningioma		1 (0%)
#Medulla oblongata	(117)	(249)
Meningioma, invasive		1 (0%)
*Cauda equina	(118)	(250)
Liposarcoma, invasive		1 (0%)
*Cranial nerve	(118)	(250)
Ganglioneuroma	1 (1%)	
SPECIAL SENSE ORGANS		
*Harderian gland	(118)	(250)
Squamous cell carcinoma, invasive		1 (0%)
Adenoma, NOS		1 (0%)
*Ear canal	(118)	(250)
Squamous cell carcinoma	1 (1%)	
*Zymbal gland	(118)	(250)
Squamous cell carcinoma	4 (3%)	5 (2%)
Keratoacanthoma	1 (1%)	1 (0%)
MUSCULOSKELETAL SYSTEM		
*Mandible	(118)	(250)
Squamous cell carcinoma, invasive		1 (0%)
Osteosarcoma	1 (1%)	
*Scapula	(118)	(250)
Osteosarcoma	1 (1%)	
*Rib	(118)	(250)
Osteosarcoma		1 (0%)
*Muscle of back	(118)	(250)
Rhabdomyosarcoma		1 (0%)
*Muscle of neck	(118)	(250)
C-cell carcinoma, invasive	2 (2%)	1 (0%)

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
BODY CAVITIES		
*Mediastinum	(118)	(250)
Alveolar/bronchiolar carcinoma, invasive		1 (0%)
*Abdominal cavity	(118)	(250)
Lipoma	1 (1%)	
Leiomyosarcoma, invasive		1 (0%)
*Peritoneum	(118)	(250)
Liposarcoma		1 (0%)
*Pleura	(118)	(250)
Mesothelioma, malignant	1 (1%)	
*Mesentery	(118)	(250)
Fibrosarcoma		1 (0%)
Mesothelioma, malignant		1 (0%)
*Tunica vaginalis	(118)	(250)
Mesothelioma, NOS	1 (1%)	1 (0%)
Mesothelioma, malignant	3 (3%)	4 (2%)
ALL OTHER SYSTEMS		
*Multiple organs	(118)	(250)
Squamous cell carcinoma, invasive	4 (3%)	2 (1%)
Squamous cell carcinoma, metastatic	1 (1%)	
Alveolar/bronchiolar carcinoma, invasive	1 (1%)	
C-cell carcinoma, metastatic		1 (0%)
Sarcoma, NOS, invasive		1 (0%)
Fibrosarcoma, invasive		1 (0%)
Liposarcoma, metastatic		1 (0%)
Mesothelioma, invasive	4 (3%)	5 (2%)
Osteosarcoma, invasive	1 (1%)	
Osteosarcoma, metastatic	1 (1%)	
ANIMAL DISPOSITION SUMMARY		
Animals initially in study	118	250
Natural death	15	32
Moribund sacrifice	92	186
Terminal sacrifice	11	29
Accidentally killed, nda		3
TUMOR SUMMARY		
Total animals with primary tumors**	118	248
Total primary tumors	395	831
Total animals with benign tumors	117	242
Total benign tumors	251	498
Total animals with malignant tumors	97	209
Total malignant tumors	134	315
Total animals with secondary tumors##	17	37
Total secondary tumors	21	48
Total animals with tumors-- uncertain benign or malignant	9	18
Total uncertain tumors	10	18

* Number of animals receiving complete necropsy examination; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
# Number of animals examined microscopically at this site
Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ
‡ Multiple occurrence of morphology; tissues are counted once only.

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS: UNTREATED CONTROL

ANIMAL NUMBER	51 12	51 15	53 37	49 96	47 70	51 18	43 37	53 39	50 04	47 72	49 99	43 38	44 41	46 68	48 83	53 35	48 85	51 11	51 16	54 41	47 74	51 19	45 50	43 36	49 95
WEEKS ON STUDY	06 00	07 01	07 74	07 76	07 78	07 78	08 83	08 84	08 86	08 89	08 89	09 00	09 00	09 92	09 95	09 95	09 98	09 98	09 98	09 98	09 99	10 00	10 01	10 03	10 04
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell tumor																									
Basal cell carcinoma																									
Keratoacanthoma																									
Fibroma																									
Fibrosarcoma																									
Myxosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																									
Fibroma									X								X								
Fibrosarcoma										X		X								X					
Lipoma																									
Neurofibroma																									X
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
C cell carcinoma, metastatic																									
Hemangiosarcoma, metastatic			X																						
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell carcinoma, invasive																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Mesothelioma, metastatic																									
Thymus	+	+	+	+	+	+	+	+	−	+	−	+	−	−	+	−	+	+	+	+	+	+	−	+	+
Granulocytic leukemia																		X							
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Neurilemoma																									
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 carcinoma																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma																									
Sarcoma, NOS																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Esophagus	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma in situ, NOS							X																		
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS						X																			
Fibrosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenomatous polyp, NOS																									
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Transitional cell papilloma																									

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

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

ANIMAL NUMBER	49 7	52 9	53 8	46 3	45 1	49 4	50 9	52 4	50 5	54 4	54 7	46 6	53 6	45 2	45 8	45 5	45 6	46 7	52 2	47 1	49 0	53 2	43 4	47 5	48 8
WEEKS ON STUDY	104	104	105	106	108	108	108	108	110	110	110	111	111	112	112	113	113	113	113	114	115	115	116	116	116
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma				X																					
Basal cell tumor																									
Basal cell carcinoma																									
Keratoacanthoma																						X			
Fibroma																									
Fibrosarcoma																									
Myxosarcoma																						X			
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																									
Fibroma																X						X			
Fibrosarcoma																									
Lipoma																									
Neurofibroma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																								X	
C-cell carcinoma, metastatic											X														
Hemangiosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell carcinoma, invasive																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Mesothelioma, metastatic																									
Thymus	−	+	+	−	−	+	−	−	+	+	+	+	−	−	−	+	+	+	+	+	+	+	+	−	−
Granulocytic leukemia																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Neurilemoma																									
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 carcinoma																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
Sarcoma, NOS																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma																									
Sarcoma, NOS											X														
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma in situ, NOS																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Fibrosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenomatous polyp, NOS																									
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Transitional cell papilloma																									

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

ANIMAL NUMBER	54 2	54 5	44 9	50 7	51 7	43 2	46 9	53 3	48 6	51 3	45 3	47 9	50 3	51 4	44 2	47 6	49 3	50 8	49 2	52 0	50 2	52 3	53 0	44 4	52 6
WEEKS ON STUDY	116	116	117	117	117	118	118	118	119	119	120	120	122	122	123	123	123	123	124	124	126	126	126	127	127
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma		X																							
Squamous cell carcinoma																									
Basal cell tumor																									
Basal cell carcinoma										X															
Keratoacanthoma								X		X															
Fibroma																									
Fibrosarcoma																					X				
Myxosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS			X																						
Fibroma		X													X		X		X			X			
Fibrosarcoma																									
Lipoma										X															
Neurofibroma																		X							
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Hemangiosarcoma, metastatic																									
Trachea	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C cell carcinoma, invasive												X													
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Spleen	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																							X		
Mesothelioma, metastatic																									
Thymus	+	−	−	−	−	+	+	+	+	−	+	+	+	−	+	+	−	+	+	−	−	+	+	+	+
Granulocytic leukemia																									
CIRCULATORY SYSTEM																									
Heart	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma														X											
Neurilemoma																									
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 carcinoma																							X		
Salivary gland	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																									
Liver	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule		X																				X			
Hepatocellular carcinoma																									
Sarcoma, NOS																									
Bile duct	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																					X	X			
Esophagus	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma in situ, NOS																									
Small intestine	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Fibrosarcoma																					X				
Large intestine	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenomatous polyp, NOS																									
URINARY SYSTEM																									
Kidney	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mixed tumor, malignant																									
Urinary bladder	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Transitional cell papilloma																									

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

ANIMAL NUMBER	440	525	528	531	433	510	447	448	454	465	481	506	534	540	445	457	484	500	548	435	521	477	482	543	546
WEEKS ON STUDY	128	128	128	128	129	129	130	130	130	130	130	130	130	130	131	131	132	132	132	133	133	133	134	135	137
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell tumor																						X			
Basal cell carcinoma						X																			
Keratoacanthoma																									
Fibroma																									X
Fibrosarcoma																		X							
Myxosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																									
Fibroma			X							X							X			X					
Fibrosarcoma									X															X	
Lipoma																									
Neurofibroma																					X				
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma							X																		
C-cell carcinoma, metastatic																									
Hemangiosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell carcinoma, invasive																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Mesothelioma, metastatic																									
Thymus	+	+	+	+	+	+	+	+	−	+	+	−	+	+	−	+	+	−	+	+	+	+	+	+	+
Granulocytic leukemia																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Neurilemoma																									
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 carcinoma				X	X																				
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule	X		X					X																	
Hepatocellular carcinoma			X														X						X		
Sarcoma, NOS																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma	X	X												X											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma in situ, NOS																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Fibrosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS							X																		
Adenomatous polyp, NOS							X																		
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mixed tumor, malignant													X												
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+
Transitional cell papilloma																X									

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

ANIMAL NUMBER	461	478	527	460	446	489	501	439	443	459	462	464	473	480	487	491	498	549	TOTAL TISSUES TUMORS
WEEKS ON STUDY	138	138	138	139	140	140	141	142	142	142	142	142	142	142	142	142	142	142	
INTEGUMENTARY SYSTEM																			
Skin	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	*118
Squamous cell papilloma																			1
Squamous cell carcinoma																	X		2
Basal cell tumor																			1
Basal cell carcinoma																			2
Keratoacanthoma			X																4
Fibroma																			1
Fibrosarcoma																			2
Myxosarcoma																			1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	*118
Sarcoma, NOS																			1
Fibroma	X						X	X			X								17
Fibrosarcoma																X			6
Lipoma																			1
Neurofibroma																			3
RESPIRATORY SYSTEM																			
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Squamous cell carcinoma									X										1
Squamous cell carcinoma, metastatic																	X		1
Alveolar/bronchiolar adenoma					X														1
Alveolar/bronchiolar carcinoma																			2
C-cell carcinoma, metastatic																			1
Hemangiosarcoma, metastatic																			1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
C cell carcinoma, invasive																			1
HEMATOPOIETIC SYSTEM																			
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Hemangiosarcoma	X																		1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Squamous cell carcinoma, metastatic																			1
Mesothelioma, metastatic												X							1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	88
Granulocytic leukemia																			1
CIRCULATORY SYSTEM																			
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Hemangiosarcoma																			1
Neurilemoma									X										1
DIGESTIVE SYSTEM																			
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Squamous cell carcinoma					X														4
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	115
Sarcoma, NOS																	X		1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Neoplastic nodule	X								X								X		8
Hepatocellular carcinoma		X																	4
Sarcoma, NOS																			1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Acinar cell adenoma	X						X				X								8
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	115
Stomach	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	116
Carcinoma in situ, NOS																			1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Adenocarcinoma, NOS																			1
Fibrosarcoma	X																		2
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Carcinoma, NOS																			1
Adenomatous polyp, NOS																			1
URINARY SYSTEM																			
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Mixed tumor, malignant																			1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	116
Transitional cell papilloma									X										2

* Animals necropsied

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

ANIMAL NUMBER	512	515	537	496	470	518	437	539	504	472	499	438	441	468	483	535	488	511	516	541	474	519	450	436	495
WEEKS ON STUDY	060	071	074	076	078	078	083	084	086	089	089	090	090	092	095	095	098	098	098	098	099	100	101	103	104
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																X									
Adenoma NOS											X				X										
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma													X												
Pheochromocytoma, malignant																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																						X			
C-cell adenoma						X														X					
C-cell carcinoma																		X							
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																		X							
Islet cell carcinoma															X										
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
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	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
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
Lipoma																									
Mesothelioma, NOS															X										
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
Ganglioneuroma	X																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																X									
SPECIAL SENSE ORGANS																									
Ear	+	N	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Zymbal 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
Squamous cell carcinoma																						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	N
Osteosarcoma																									
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
C-cell carcinoma, invasive																									
BODY CAVITIES																									
Pleura	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, malignant																									
Hemangiosarcoma			X																						
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																									
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, NOS															X										
Mesothelioma, malignant													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
Squamous cell carcinoma, invasive																									
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar carcinoma, invasive																									
Fibrous histiocytoma, malignant																									
Mesothelioma, invasive													X												
Osteosarcoma, invasive																									
Osteosarcoma, metastatic																									
Malignant lymphoma, histiocytic type																									
Monocytic leukemia		X		X							X			X					X				X	X	

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

ANIMAL NUMBER	49 7	52 9	53 8	46 3	45 1	49 4	50 9	52 4	50 5	54 4	54 7	46 6	53 6	45 2	45 8	45 5	45 6	46 7	52 2	47 1	49 0	53 2	43 4	47 5	48 8
WEEKS ON STUDY	104	104	105	106	108	108	108	108	110	110	110	111	111	112	112	113	113	113	113	114	115	115	116	116	116
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																							X		
Adenoma, NOS									X				X												
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																		X							
Pheochromocytoma					X			X			X	X		X	X		X					X		X	
Pheochromocytoma, malignant																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+
Follicular cell adenoma					X													X				X			
Follicular cell carcinoma																									
C-cell adenoma																	X								
C-cell carcinoma	X										X				X										
Parathyroid	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	–	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
Islet cell carcinoma	X					X						X													
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	N	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Fibroadenoma								X			X				X					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	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
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
Lipoma								X																	
Mesothelioma, NOS																									
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
Ganglioneuroma																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
SPECIAL SENSE ORGANS																									
Ear	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+
Squamous cell carcinoma																									
Zymbal 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
Squamous cell carcinoma																									
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																									
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
C-cell carcinoma, invasive											X														
BODY CAVITIES																									
Pleura	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, malignant																									
Hemangiosarcoma																									
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																									
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, NOS																									
Mesothelioma, malignant		X							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
Squamous cell carcinoma, invasive																									
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar carcinoma, invasive																								X	
Fibrous histiocytoma, malignant																									
Mesothelioma, invasive		X							X																
Osteosarcoma, invasive																									
Osteosarcoma, metastatic																									
Malignant lymphoma, histiocytic type																									
Monocytic leukemia			X				X			X				X		X		X	X	X					X

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

ANIMAL NUMBER	54201	54501	44901	50701	51701	43201	46901	53301	48601	51301	45301	47901	50301	51401	44201	47601	49301	50801	49201	52001	50201	52301	53001	44401	52601
WEEKS ON STUDY	11106	11106	11107	11107	11107	11108	11108	11108	11109	11109	12000	12000	12202	12202	12303	12303	12303	12303	12404	12404	12406	12406	12606	12707	12707
ENDOCRINE SYSTEM																									
Pituitary	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS														X											X
Adrenal	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma												X													
Pheochromocytoma							X			X			X			X			X	X			X		X
Pheochromocytoma, malignant																									
Thyroid	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma															X	X									
Follicular cell carcinoma																									
C-cell adenoma		X					X	X						X		X			X						
C cell carcinoma											X	X	X		X									X	X
Parathyroid	–	+	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+
Pancreatic islets	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
Islet cell carcinoma				X																					
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
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	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
Squamous cell carcinoma								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
Lipoma																									
Mesothelioma, NOS																									
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
Ganglioneuroma																									
Brain	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
SPECIAL SENSE ORGANS																									
Ear	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Zymbal 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
Squamous cell carcinoma								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	N
Osteosarcoma																									
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
C-cell carcinoma, invasive												X													
BODY CAVITIES																									
Pleura	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, malignant																									
Hemangiosarcoma																									
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									X																
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, NOS																									
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
Squamous cell carcinoma, invasive																							X		
Squamous cell carcinoma, metastatic								X																	
Alveolar/bronchiolar carcinoma, invasive																									
Fibrous histiocytoma, malignant																									
Mesothelioma, invasive																									
Osteosarcoma, invasive																									
Osteosarcoma, metastatic																									
Malignant lymphoma, histiocytic type						X																			
Monocytic leukemia	X	X			X						X		X		X	X	X					X			

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

ANIMAL NUMBER	44 0	52 5	52 8	53 1	43 3	51 0	44 7	44 8	45 4	46 5	48 1	50 6	53 4	54 0	44 5	45 7	48 4	50 0	54 8	43 5	52 1	47 7	48 2	54 3	54 6
WEEKS ON STUDY	12 8	12 8	12 8	12 8	12 9	12 9	13 0	13 0	13 0	13 0	13 0	13 0	13 0	13 0	13 1	13 1	13 2	13 2	13 2	13 3	13 3	13 4	13 4	13 5	13 7
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS														X	X										X
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma	X					X					X								X					X	
Pheochromocytoma, malignant					X																				
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma															X										
Follicular cell carcinoma																			X			X			
C-cell adenoma															X										
C cell carcinoma								X		X															
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma							X																		
Islet cell carcinoma	X						X				X				X										X
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS						X																			
Fibroadenoma		X									X	X	X		X			X		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	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
Squamous cell carcinoma										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
Lipoma																									
Mesothelioma, NOS																									
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
Ganglioneuroma																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
SPECIAL SENSE ORGANS																									
Ear	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																	X								
Zymbal 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
Squamous cell carcinoma								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	N
Osteosarcoma	X																					X			
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
C-cell carcinoma, invasive																									
BODY CAVITIES																									
Pleura	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, malignant																									
Hemangiosarcoma																									
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																									
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, NOS																									
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
Squamous cell carcinoma, invasive				X	X																				
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar carcinoma, invasive																									
Fibrous histiocytoma, malignant		X																							
Mesothelioma, invasive																									
Osteosarcoma, invasive																						X			
Osteosarcoma, metastatic	X																								
Malignant lymphoma, histiocytic type																									
Monocytic leukemia			X			X					X	X	X			X			X		X		X		X

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

ANIMAL NUMBER	46 1	47 8	52 7	46 0	44 6	48 9	50 1	43 9	44 3	45 9	46 2	46 4	47 3	48 0	48 7	49 1	49 8	54 9	TOTAL TISSUES TUMORS
WEEKS ON STUDY	13 8	13 8	13 8	13 9	14 0	14 0	14 1	14 2	14 2	14 2	14 2	14 2	14 2	14 2	14 2	14 2	14 2	14 2	
ENDOCRINE SYSTEM																			
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Carcinoma, NOS		X																	3
Adenoma, NOS							X		X			X		X		X	X		15
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Cortical adenoma																			2
Pheochromocytoma		X		X	X	X	X	X	X		X				X	X			33
Pheochromocytoma, malignant														X					2
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	116
Follicular cell adenoma	X																		7
Follicular cell carcinoma																			3
C-cell adenoma	X								X				X						13
C-cell carcinoma				X			X			X		X			X	X	X		19
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	111
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Islet cell adenoma																			2
Islet cell carcinoma				X															11
REPRODUCTIVE SYSTEM																			
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*118
Adenocarcinoma, NOS																			1
Fibroadenoma			X	X				X						X		X			18
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	118
Interstitial cell tumor	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	116
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	116
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Squamous cell carcinoma				X															3
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Lipoma																			1
Mesothelioma, NOS																			1
NERVOUS SYSTEM																			
Nerves	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Ganglioneuroma																			1
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Carcinoma, NOS, invasive																			1
SPECIAL SENSE ORGANS																			
Ear	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*118
Squamous cell carcinoma																			1
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Squamous cell carcinoma											X								4
Keratoacanthoma																			1
MUSCULOSKELETAL SYSTEM																			
Bone	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	*118
Osteosarcoma																			2
Muscle	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
C-cell carcinoma, invasive																			2
BODY CAVITIES																			
Pleura	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Mesothelioma, malignant												X							1
Hemangiosarcoma																			1
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Lipoma																			1
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*118
Mesothelioma, NOS																			1
Mesothelioma, malignant																			3
ALL OTHER SYSTEMS																			
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Squamous cell carcinoma, invasive					X														4
Squamous cell carcinoma, metastatic																			1
Alveolar/bronchiolar carcinoma, invas																			1
Fibrous histiocytoma, malignant																			1
Mesothelioma, invasive												X							4
Osteosarcoma, invasive																			1
Osteosarcoma, metastatic																			1
Malignant lymphoma, histiocytic type																			1
Monocytic leukemia	X		X	X				X	X				X				X		42

* Animals necropsied

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

ANIMAL NUMBER	869	692	746	686	737	831	818	678	715	876	802	887	866	778	709	575	669	702	822	683	680	877	706	895	720
WEEKS ON STUDY	017	042	061	073	081	082	083	085	085	086	088	088	090	091	093	094	095	095	095	096	098	098	100	100	101
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell tumor																									
Basal cell carcinoma																									
Trichoepithelioma																									
Keratoacanthoma																									
Fibrosarcoma																									
Hemangiopericytoma, malignant																									
Neurofibroma																									
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Sarcoma, NOS, invasive																									
Fibroma											X				X										
Fibrosarcoma																	X								
Lipoma																									
Hemangiosarcoma																			X	X					
Osteosarcoma						X																			
Neurofibroma																									
Neurofibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS, metastatic																									
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																				X					
C cell carcinoma, metastatic																									
Pheochromocytoma, metastatic					X																				
Liposarcoma, metastatic			X																						
Mesothelioma, metastatic																									
Hemangiosarcoma, metastatic		X																							
Osteosarcoma, metastatic				X		X																			
Trachea	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–
C-cell carcinoma, invasive																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma, metastatic																									
Fibrosarcoma																									
Fibrosarcoma, metastatic																									
Hemangiosarcoma, metastatic																				X					
Leukemia, mononuclear cell																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Sarcoma, NOS, invasive																									
Rhabdomyosarcoma, metastatic													X												
Thymus	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	–	–	–	+	+	+
Papillary adenocarcinoma																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, invasive																									
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																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Sarcoma, NOS												X													
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									X
Hepatocellular carcinoma																									
Malignant lymphoma, histiocytic type																									
Kupffer cell sarcoma																									
Monocytic leukemia																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Acinar cell carcinoma																									
Esophagus	–	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell carcinoma																									
Fibrosarcoma																									
Leiomyosarcoma																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma																									
Fibrosarcoma																									
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS																									
Lipoma																									
Leiomyosarcoma																									

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

ANIMAL NUMBER	7 3 0	7 5 9	7 8 1	8 3 4	8 8 8	6 7 2	6 7 9	6 9 9	7 2 5	7 2 9	7 7 1	7 8 0	8 7 4	7 0 0	7 7 9	7 9 9	7 5 1	9 0 2	9 1 6	7 4 7	8 2 7	8 5 1	8 6 1	9 1 1	8 0 9
WEEKS ON STUDY	1 0 2	1 0 2	1 0 2	1 0 2	1 0 2	1 0 3	1 0 3	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 5	1 0 5	1 0 5	1 0 6	1 0 6	1 0 6	1 0 7	1 0 8	1 0 8	1 0 8	1 0 8	1 0 9
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell tumor																									
Basal cell carcinoma																									
Trichoepithelioma																									
Keratoacanthoma																									
Fibrosarcoma																									
Hemangiopericytoma, malignant																									
Neurofibroma																						X			
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Sarcoma, NOS, invasive																									
Fibroma												X													
Fibrosarcoma				X												X									
Lipoma																									
Hemangiosarcoma																									
Osteosarcoma																									
Neurofibroma				X																					
Neurofibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS, metastatic																									
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																			X						
C cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic																									
Mesothelioma, metastatic																									
Hemangiosarcoma, metastatic																									
Osteosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C cell carcinoma, invasive																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma, metastatic																									
Fibrosarcoma																									
Fibrosarcoma, metastatic																									
Hemangiosarcoma, metastatic																									
Leukemia, mononuclear cell																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metasatatic																									
C cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Sarcoma, NOS, invasive																									
Rhabdomyosarcoma, metastatic																									
Thymus	+	+	–	+	+	+	–	-	+	–	+	+	–	–	+	+	–	–	+	–	+	+	+	+	+
Papillary adenocarcinoma																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, invasive																			X						
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																									X
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma NOS																									
Sarcoma, NOS								X																	
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma																									
Malignant lymphoma, histiocytic type																									
Kupffer cell sarcoma																									
Monocytic leukemia																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																					X				
Squamous cell carcinoma																									
Basal cell carcinoma																									
Fibrosarcoma	X																								
Leiomyosarcoma																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma																									
Fibrosarcoma																									
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS												X													
Lipoma																									
Leiomyosarcoma																									

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

ANIMAL NUMBER	8 3 3	6 9 3	6 9 4	7 1 1	7 1 3	7 3 5	7 4 3	7 6 3	7 7 5	8 8 2	7 5 2	7 7 7	7 9 2	8 1 9	8 7 3	8 7 8	6 9 0	7 3 9	7 9 7	8 4 7	8 5 3	7 1 8	8 5 8	6 9 5	7 0 5
WEEKS ON STUDY	1 0 9	1 1 0	1 1 0	1 1 0	1 1 0	1 1 0	1 1 0	1 1 0	1 1 0	1 1 0	1 1 1	1 1 1	1 1 1	1 1 1	1 1 1	1 1 1	1 1 2	1 1 2	1 1 2	1 1 2	1 1 2	1 1 3	1 1 3	1 1 4	1 1 4
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																							X		
Squamous cell carcinoma		X																							
Basal cell tumor																									
Basal cell carcinoma																					X				
Trichoepithelioma																									
Keratoacanthoma																									
Fibrosarcoma																									
Hemangiopericytoma, malignant																									
Neurofibroma																									
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Sarcoma, NOS, invasive																									
Fibroma																		@X							
Fibrosarcoma																									
Lipoma																									
Hemangiosarcoma																									
Osteosarcoma																									
Neurofibroma																									
Neurofibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS, metastatic																									
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic																									
Mesothelioma, metastatic																					X				
Hemangiosarcoma, metastatic																									
Osteosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C cell carcinoma, invasive																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma, metastatic																									
Fibrosarcoma																									
Fibrosarcoma, metastatic																									
Hemangiosarcoma, metastatic																									
Leukemia, mononuclear cell																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic		X																							
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Sarcoma, NOS, invasive																									
Rhabdomyosarcoma, metastatic																									
Thymus	+	+	–	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	–	+	+	+	–	–	+
Papillary adenocarcinoma																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, invasive																									
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																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Sarcoma, NOS																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma																									
Malignant lymphoma, histiocytic type																									
Kupffer cell sarcoma																									
Monocytic leukemia																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell carcinoma																									
Fibrosarcoma																									
Leiomyosarcoma								X																	
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma																									
Fibrosarcoma																									
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS																									
Lipoma																									
Leiomyosarcoma	X																								

@ Multiple occurrence of morphology

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

ANIMAL NUMBER	862	880	905	817	820	838	856	868	871	885	726	741	791	815	825	826	828	829	837	842	900	906	908	673	685
WEEKS ON STUDY	125	125	125	126	126	126	126	126	126	126	127	127	127	127	127	127	127	127	127	127	127	127	127	128	128
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell tumor																									
Basal cell carcinoma																				X					
Trichoepithelioma																									
Keratoacanthoma															X										
Fibrosarcoma																									
Hemangiopericytoma, malignant																									
Neurofibroma																									
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Sarcoma, NOS, invasive																									
Fibroma		X				X						X	X	X		X							X		
Fibrosarcoma																									
Lipoma																									
Hemangiosarcoma																									
Osteosarcoma						X																			
Neurofibroma															X										
Neurofibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS, metastatic																									
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic				X																					
Liposarcoma, metastatic																									
Mesothelioma, metastatic																									
Hemangiosarcoma, metastatic																									
Osteosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell carcinoma, invasive																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma, metastatic																									
Fibrosarcoma																									
Fibrosarcoma, metastatic																									
Hemangiosarcoma, metastatic																									
Leukemia, mononuclear cell																			X						
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Sarcoma, NOS, invasive																									
Rhabdomyosarcoma, metastatic																									
Thymus	+	–	+	+	+	+	+	–	–	+	+	–	+	+	+	–	+	–	+	+	–	–	–	–	–
Papillary adenocarcinoma							X																		
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, invasive																									
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																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS											X														
Sarcoma, NOS																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule					X				X							X	X								X
Hepatocellular carcinoma																									
Malignant lymphoma, histiocytic type																									
Kupffer cell sarcoma																									
Monocytic leukemia																			X						
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma								X	X	X															
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell carcinoma																									
Fibrosarcoma																									
Leiomyosarcoma																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+
Mucinous cystadenocarcinoma																									
Fibrosarcoma																									
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+
Adenomatous polyp, NOS																									
Lipoma																									
Leiomyosarcoma																									

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

ANIMAL NUMBER	75 53	76 61	76 62	80 03	67 64	74 49	75 50	76 65	80 00	67 70	70 01	72 27	73 11	75 55	79 95	87 22	88 66	89 99	67 11	72 22	78 89	71 16	85 57	91 13	72 23
WEEKS ON STUDY	12 28	12 28	12 28	12 28	12 29	12 29	12 29	12 29	12 29	13 30	13 30	13 30	13 30	13 30	13 30	13 30	13 30	13 30	13 31	13 31	13 31	13 32	13 32	13 32	13 33
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma												X													
Squamous cell carcinoma																									
Basal cell tumor																									
Basal cell carcinoma	X																								
Trichoepithelioma																									
Keratoacanthoma							X	X		X				X											
Fibrosarcoma																									X
Hemangiopericytoma, malignant																									
Neurofibroma																									
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Sarcoma, NOS, invasive																									
Fibroma			X		X							X	X				X				X		X		
Fibrosarcoma														X								X			
Lipoma						X	X																		
Hemangiosarcoma																									
Osteosarcoma																									
Neurofibroma										X															
Neurofibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS, metastatic				X																					
Squamous cell carcinoma, metastatic											X														
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic													X												
Mesothelioma, metastatic									X																
Hemangiosarcoma, metastatic																									
Osteosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell carcinoma, invasive																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma, metastatic																									
Fibrosarcoma																									
Fibrosarcoma, metastatic																									
Hemangiosarcoma, metastatic																									
Leukemia, mononuclear cell																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Sarcoma, NOS, invasive																									
Rhabdomyosarcoma, metastatic																									
Thymus	+	+	+	+	+	–	+	+	–	+	–	+	+	+	+	–	+	+	–	–	+	+	+	+	+
Papillary adenocarcinoma																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, invasive																									
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															X										
Squamous cell carcinoma																			X						
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Sarcoma, NOS																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule								X																	
Hepatocellular carcinoma																									
Malignant lymphoma, histiocytic type																									
Kupffer cell sarcoma																									
Monocytic leukemia								X																	
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma							X										X						X		
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell carcinoma																									
Fibrosarcoma																									
Leiomyosarcoma																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma																									
Fibrosarcoma																									
Leiomyosarcoma																	X								
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS																								X	
Lipoma																									
Leiomyosarcoma																									

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

ANIMAL NUMBER	7 7 3	8 1 6	8 2 4	8 8 9	8 9 4	7 7 2	7 7 4	8 0 6	7 6 4	7 8 8	6 6 8	6 7 7	7 3 3	8 5 0	7 5 8	7 6 0	7 9 4	8 6 3	8 6 4	8 6 5	8 9 3	7 1 2	8 2 3	8 3 5	8 4 4
WEEKS ON STUDY	1 1 4	1 1 4	1 1 4	1 1 4	1 1 4	1 1 6	1 1 6	1 1 6	1 1 7	1 1 7	1 1 8	1 1 8	1 1 8	1 1 8	1 1 9	1 1 9	1 1 9	1 1 9	1 1 9	1 1 9	1 1 9	1 2 0	1 2 0	1 2 0	1 2 0
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																	X								
Squamous cell carcinoma																									
Basal cell tumor																									
Basal cell carcinoma																	X								
Trichoepithelioma																									
Keratoacanthoma																									
Fibrosarcoma																									
Hemangiopericytoma, malignant										X															
Neurofibroma																									
Neurofibrosarcoma							X																		
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Sarcoma, NOS, invasive																									
Fibroma				X			X																		
Fibrosarcoma																									
Lipoma																									
Hemangiosarcoma																									
Osteosarcoma																									
Neurofibroma			X																						
Neurofibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS, metastatic																									
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic																									
Mesothelioma, metastatic																									
Hemangiosarcoma, metastatic																									
Osteosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C cell carcinoma, invasive																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma, metastatic																									
Fibrosarcoma																									
Fibrosarcoma, metastatic																									
Hemangiosarcoma, metastatic																									
Leukemia, mononuclear cell																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Sarcoma, NOS, invasive																									
Rhabdomyosarcoma, metastatic																									
Thymus	−	−	+	+	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	−	+	
Papillary adenocarcinoma																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, invasive																									
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																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Sarcoma, NOS		X																							
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule								X																	
Hepatocellular carcinoma																									
Malignant lymphoma, histiocytic type																									
Kupffer cell sarcoma																									
Monocytic leukemia														X											
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell carcinoma																									
Fibrosarcoma																									
Leiomyosarcoma																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma																									
Fibrosarcoma																									
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS							X																		
Lipoma																									
Leiomyosarcoma																									

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

ANIMAL NUMBER	9 1 7	7 6 8	7 8 2	7 8 7	8 9 1	8 9 2	7 3 8	8 3 2	9 0 9	6 8 9	6 9 7	6 9 8	7 1 9	8 1 0	8 4 8	6 8 2	7 2 4	7 8 3	7 8 4	7 9 6	8 6 0	9 0 3	7 1 4	7 3 4	7 7 6
WEEKS ON STUDY	1 2 0	1 2 1	1 2 1	1 2 1	1 2 1	1 2 1	1 2 2	1 2 2	1 2 2	1 2 3	1 2 3	1 2 3	1 2 3	1 2 3	1 2 3	1 2 4	1 2 4	1 2 4	1 2 4	1 2 4	1 2 4	1 2 4	1 2 5	1 2 5	1 2 5
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell tumor						X																			
Basal cell carcinoma																							X		
Trichoepithelioma															X										
Keratoacanthoma	X				X																				
Fibrosarcoma																									
Hemangiopericytoma, malignant																									
Neurofibroma																									
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Sarcoma, NOS, invasive											X														
Fibroma														X											
Fibrosarcoma						X																			
Lipoma																									
Hemangiosarcoma																									
Osteosarcoma																									
Neurofibroma							X										X								
Neurofibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS, metastatic																									
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar adenoma												X													
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic																									
Mesothelioma, metastatic																									
Hemangiosarcoma, metastatic																									
Osteosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell carcinoma, invasive																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma, metastatic																									
Fibrosarcoma				X																					
Fibrosarcoma, metastatic																									
Hemangiosarcoma, metastatic																									
Leukemia, mononuclear cell																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Sarcoma, NOS, invasive											X														
Rhabdomyosarcoma, metastatic																									
Thymus	+	–	–	+	+	–	–	–	+	+	–	+	+	+	+	–	–	–	+	–	+	–	–	+	+
Papillary adenocarcinoma																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, invasive																									
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						X																			
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Sarcoma, NOS											X														
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule												X										X		X	
Hepatocellular carcinoma													X									X			
Malignant lymphoma, histiocytic type																									
Kupffer cell sarcoma																									
Monocytic leukemia																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma			X																						
Acinar cell carcinoma																							X		
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell carcinoma																									
Fibrosarcoma																									
Leiomyosarcoma																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma		X																							
Fibrosarcoma																									
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS																									
Lipoma																				X					
Leiomyosarcoma																									

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

ANIMAL NUMBER	769	801	805	836	846	852	883	907	681	841	915	745	785	798	875	890	898	910	717	767	855	867	904	684	688
WEEKS ON STUDY	133	133	133	133	133	133	133	133	134	134	134	135	135	135	135	135	135	135	136	136	136	136	136	137	137
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma														X									X		
Squamous cell carcinoma			X			X																			
Basal cell tumor																									
Basal cell carcinoma														X	X										
Trichoepithelioma																									
Keratoacanthoma				X																X	X				
Fibrosarcoma																									
Hemangiopericytoma, malignant																									
Neurofibroma																									
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Sarcoma, NOS, invasive																									
Fibroma													X												
Fibrosarcoma																									
Lipoma																					X				
Hemangiosarcoma																									
Osteosarcoma																									
Neurofibroma																									
Neurofibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS, metastatic																									
Squamous cell carcinoma, metastatic						X																			
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic																									
Mesothelioma, metastatic																									
Hemangiosarcoma, metastatic																									
Osteosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell carcinoma, invasive																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma, metastatic										X															
Fibrosarcoma																									
Fibrosarcoma, metastatic																								X	
Hemangiosarcoma, metastatic																									
Leukemia, mononuclear cell																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Sarcoma, NOS, invasive																									
Rhabdomyosarcoma, metastatic																									
Thymus	+	−	+	+	+	+	+	−	+	+	+	+	−	+	+	+	+	+	+	+	−	+	+	+	+
Papillary adenocarcinoma																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, invasive																									
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																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Sarcoma, NOS																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule														X			X								
Hepatocellular carcinoma																									
Malignant lymphoma, histiocytic type																									
Kupffer cell sarcoma																									
Monocytic leukemia																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma								X						X											
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																			X						
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell carcinoma						X																			
Fibrosarcoma																									
Leiomyosarcoma																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma																									
Fibrosarcoma																								X	
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS																									
Lipoma																									
Leiomyosarcoma																									

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

ANIMAL NUMBER	748	756	821	843	704	710	849	896	813	740	790	804	814	870	879	901	912	887	766	845	881	875	876	891	996
WEEKS ON STUDY	137	137	137	137	138	138	138	138	139	140	140	140	140	140	140	140	140	141	141	141	141	142	142	142	142
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																					X				
Squamous cell carcinoma																									
Basal cell tumor																									
Basal cell carcinoma																									
Trichoepithelioma																									
Keratoacanthoma																									
Fibrosarcoma																									
Hemangiopericytoma, malignant																									
Neurofibroma																									
Neurofibrosarcoma								X																	
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Sarcoma, NOS, invasive																									
Fibroma	X																	X							
Fibrosarcoma																									
Lipoma																									
Hemangiosarcoma																									
Osteosarcoma																									
Neurofibroma			X																						
Neurofibrosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS, metastatic																									
Squamous cell carcinoma, metastatic																									
Alveolar/bronchiolar adenoma																		X							
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic		X																							
Liposarcoma, metastatic																		X							
Mesothelioma, metastatic																									
Hemangiosarcoma, metastatic																									
Osteosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell carcinoma, invasive																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma, metastatic																									
Fibrosarcoma																									
Fibrosarcoma, metastatic																									
Hemangiosarcoma, metastatic																									
Leukemia, mononuclear cell																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Sarcoma, NOS, invasive																									
Rhabdomyosarcoma, metastatic																									
Thymus	–	–	+	+	–	+	+	+	+	+	–	–	+	–	+	+	+	+	+	+	+	+	+	+	+
Papillary adenocarcinoma																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, invasive																									
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																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Sarcoma, NOS																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule								X																	
Hepatocellular carcinoma																									
Malignant lymphoma, histiocytic type													X												
Kupffer cell sarcoma				X																					
Monocytic leukemia																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma		X				X																			
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Basal cell carcinoma																									
Fibrosarcoma																									
Leiomyosarcoma																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma																									
Fibrosarcoma																									
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS																							X		
Lipoma																									
Leiomyosarcoma																									

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

ANIMAL NUMBER	703	707	708	721	728	732	736	742	744	754	770	786	793	807	808	811	812	830	839	840	854	859	884	897	914	TOTAL:
WEEKS ON STUDY	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*250
Squamous cell papilloma																										6
Squamous cell carcinoma																										3
Basal cell tumor																										1
Basal cell carcinoma											X		X				X									10
Trichoepithelioma																										1
Keratoacanthoma		X																								11
Fibrosarcoma																										1
Hemangiopericytoma, malignant																										1
Neurofibroma																										1
Neurofibrosarcoma																X										3
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*250
Keratoacanthoma															X											1
Sarcoma, NOS, invasive																										1
Fibroma	X												X											X		27
Fibrosarcoma																										6
Lipoma																										3
Hemangiosarcoma																										2
Osteosarcoma																										2
Neurofibroma			X																							8
Neurofibrosarcoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Neoplasm, NOS, metastatic																										1
Squamous cell carcinoma, metastatic																										2
Alveolar/bronchiolar adenoma																										2
Alveolar/bronchiolar carcinoma																										2
C cell carcinoma, metastatic																							X			1
Pheochromocytoma, metastatic	X		X																							5
Liposarcoma, metastatic																										3
Mesothelioma, metastatic																										2
Hemangiosarcoma, metastatic																										1
Osteosarcoma, metastatic																										2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	248
C-cell carcinoma, invasive															X											1
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	248
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Pheochromocytoma, metastatic																										1
Fibrosarcoma																										1
Fibrosarcoma, metastatic																										1
Hemangiosarcoma, metastatic																										1
Leukemia, mononuclear cell																										1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Squamous cell carcinoma, metastatic																										1
C-cell carcinoma, metastatic																							X			1
Pheochromocytoma, metastatic	X																									1
Sarcoma, NOS, invasive																										1
Rhabdomyosarcoma, metastatic																										1
Thymus	+	+	+	+	+	−	−	+	+	+	+	+	+	−	+	+	+	−	+	−	+	+	+	+	+	182
Papillary adenocarcinoma																										1
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Alveolar/bronchiolar carcinoma, invasiv																										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	*250
Squamous cell papilloma																										1
Squamous cell carcinoma																										3
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Adenoma, NOS																										1
Sarcoma, NOS			X																							5
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Neoplastic nodule		X													X											16
Hepatocellular carcinoma																		X								3
Malignant lymphoma, histiocytic type																										1
Kupffer cell sarcoma																										1
Monocytic leukemia																										3
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Acinar cell adenoma		X									X		X							X						15
Acinar cell carcinoma																								X		2
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	247
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Carcinoma, NOS																										1
Squamous cell papilloma																										1
Squamous cell carcinoma																							X			1
Basal cell carcinoma																										1
Fibrosarcoma																										1
Leiomyosarcoma																										1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Mucinous cystadenocarcinoma																										1
Fibrosarcoma																										1
Leiomyosarcoma																										1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Adenomatous polyp, NOS																										4
Lipoma																										1
Leiomyosarcoma																										1

* Animals necropsied

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

ANIMAL NUMBER	869	692	746	686	737	831	818	678	715	876	802	887	866	778	709	575	669	702	822	683	680	877	706	895	720
WEEKS ON STUDY	017	042	061	073	081	082	083	085	085	086	088	088	090	091	093	094	095	095	095	096	098	098	100	100	101
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																									
Tubular cell adenocarcinoma																									
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	−	−	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																X									
Adenoma, NOS																						X			
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma																									
Pheochromocytoma, malignant					X																				
Thyroid	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma											X							X							
Follicular cell carcinoma																									
C-cell adenoma											X			X				X			X				
C-cell carcinoma																	X						X		
Parathyroid	−	−	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−
Pancreatic islets	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS																									
Fibroadenoma																									
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Interstitial cell tumor					X	X		X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, 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
Squamous cell carcinoma										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
Lipoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Granular cell tumor, NOS																									
Astrocytoma																									
Meningioma																					X				
Meningioma, invasive																					X				
Spinal cord	N	+	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	+	N	N	N	N	N	N	N
Liposarcoma, invasive																									
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
Squamous cell carcinoma, invasive																							X		
Adenoma, NOS																							X		
Zymbal 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
Squamous cell carcinoma																							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	N
Squamous cell carcinoma, invasive																									
Hemangiosarcoma		X																							
Osteosarcoma				X																					
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
C-cell carcinoma, invasive																									
Rhabdomyosarcoma													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
Alveolar/bronchiolar carcinoma, invasive																									
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
Liposarcoma																									
Leiomyosarcoma, invasive																									
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
Fibrosarcoma																									
Mesothelioma, malignant																									
Hemangiosarcoma																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
Squamous cell carcinoma, invasive																									
C-cell carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Fibrosarcoma, invasive																									
Liposarcoma, metastatic																									
Mesothelioma, invasive																									
Hemangiosarcoma, metastatic																X									
Malignant lymphoma, undifferentiated type																									
Malignant lymphoma, histiocytic type																									
Monocytic leukemia							X	X	X															X	X

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

ANIMAL NUMBER	730	759	781	834	888	672	879	699	725	729	771	780	874	700	779	799	751	902	916	747	827	851	861	911	809
WEEKS ON STUDY	102	102	102	102	102	103	103	104	104	104	104	104	104	105	105	105	106	106	106	107	108	108	108	108	109
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																									
Tubular cell adenocarcinoma																									
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																				X					
Adenoma, NOS			X																						
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma							X									X				X					
Pheochromocytoma, malignant																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma														X											
Follicular cell carcinoma																									
C-cell adenoma							X					X													
C cell carcinoma			X									X													X
Parathyroid	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell carcinoma								X																	
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS																									
Fibroadenoma																		X							
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
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
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, 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
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
Lipoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Granular cell tumor, NOS																									
Astrocytoma																									
Meningioma																									
Meningioma, invasive																									
Spinal cord	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, invasive																									
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
Squamous cell carcinoma, invasive																									
Adenoma, NOS																									
Zymbal 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
Squamous cell carcinoma																									
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
Squamous cell carcinoma, invasive																									
Hemangiosarcoma																									
Osteosarcoma																									
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
C-cell carcinoma, invasive																									
Rhabdomyosarcoma																									
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
Alveolar/bronchiolar carcinoma, invasive																				X					
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
Liposarcoma																									
Leiomyosarcoma, invasive																									
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
Fibrosarcoma																									
Mesothelioma, malignant																									
Hemangiosarcoma																									
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
Squamous cell carcinoma, invasive																									
C-cell carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Fibrosarcoma, invasive																									
Liposarcoma, metastatic																									
Mesothelioma, invasive																									
Hemangiosarcoma, metastatic																									
Malignant lymphoma, undifferentiated type																									
Malignant lymphoma, histiocytic type																									
Monocytic leukemia		X			X	X			X		X			X	X	X	X	X	X				X	X	

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

ANIMAL NUMBER	8 3 3	6 9 3	6 9 4	7 1 1	7 1 3	7 3 5	7 4 3	7 6 3	7 7 5	8 8 2	7 5 2	7 7 7	7 9 2	8 1 9	8 7 3	8 7 8	8 9 0	7 3 9	7 9 7	8 4 7	8 5 3	7 1 8	8 5 8	6 9 5	7 0 5
WEEKS ON STUDY	1 0 9	1 1 0	1 1 0	1 1 0	1 1 0	1 1 0	1 1 0	1 1 0	1 1 0	1 1 0	1 1 1	1 1 1	1 1 1	1 1 1	1 1 1	1 1 1	1 1 2	1 1 2	1 1 2	1 1 2	1 1 2	1 1 3	1 1 3	1 1 4	1 1 4
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																									
Tubular cell adenocarcinoma																									
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS																									
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									X
Pheochromocytoma								X			X														
Pheochromocytoma, malignant																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma		X																							
Follicular cell carcinoma				X																					
C-cell adenoma	X	X						X							X			X		X	X				X
C-cell carcinoma														X											
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell carcinoma															X										
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS																									
Fibroadenoma												X													
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
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
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, 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
Squamous cell carcinoma					X													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
Lipoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Granular cell tumor, NOS																									
Astrocytoma																									
Meningioma																									
Meningioma, invasive																									
Spinal cord	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, invasive																									
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
Squamous cell carcinoma, invasive																									
Adenoma, NOS																									
Zymbal 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
Squamous cell carcinoma																									
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
Squamous cell carcinoma, invasive																									
Hemangiosarcoma																									
Osteosarcoma																									
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
C-cell carcinoma, invasive																									
Rhabdomyosarcoma																									
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
Alveolar/bronchiolar carcinoma, invasive																									
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
Liposarcoma																									
Leiomyosarcoma, invasive								X																	
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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
Fibrosarcoma																									
Mesothelioma, malignant																					X				
Hemangiosarcoma																									
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
Squamous cell carcinoma, invasive																									
C-cell carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Fibrosarcoma, invasive																									
Liposarcoma, metastatic																									
Mesothelioma, invasive																X					X				
Hemangiosarcoma, metastatic																									
Malignant lymphoma, undifferentiated type			X																						
Malignant lymphoma, histiocytic type																	X								
Monocytic leukemia		X	X	X	X	X	X	X	X	X	X		X		X					X		X	X		X

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

ANIMAL NUMBER	7737	8116	8244	8889	8994	7772	7744	8006	7664	7888	6668	6773	7383	8550	7558	7600	7994	8663	8664	8665	8993	7123	8223	8335	8444
WEEKS ON STUDY	114	114	114	114	114	116	116	116	117	117	118	118	118	118	119	119	119	119	119	119	119	120	120	120	120
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																									
Tubular cell adenocarcinoma																									
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																					X				
Adenoma, NOS	X			X	X				X			X	X												
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma								X		X						X			X						X
Pheochromocytoma, malignant																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma	X																X								
Follicular cell carcinoma				X										X	X										
C-cell adenoma							X																		
C-cell carcinoma				X		X						X						X							X
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS															X										
Fibroadenoma																									
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Preputial/chtoral 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
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
Lipoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																					X				
Granular cell tumor, NOS																									
Astrocytoma																									
Meningioma																									
Meningioma, invasive																									
Spinal cord	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, invasive																									
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
Squamous cell carcinoma, invasive																									
Adenoma, NOS																									
Zymbal 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
Squamous cell carcinoma																									
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
Squamous cell carcinoma, invasive																									
Hemangiosarcoma																									
Osteosarcoma																									
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
C-cell carcinoma, invasive																									
Rhabdomyosarcoma																									
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
Alveolar/bronchiolar carcinoma, invasive																									
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
Liposarcoma																									
Leiomyosarcoma, invasive																									
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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
Fibrosarcoma																									
Mesothelioma, malignant																									
Hemangiosarcoma																									
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
Squamous cell carcinoma, invasive																									
C-cell carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Fibrosarcoma, invasive																									
Liposarcoma, metastatic																									
Mesothelioma, invasive			X																						
Hemangiosarcoma, metastatic																									
Malignant lymphoma, undifferentiated type																									
Malignant lymphoma, histiocytic type																									
Monocytic leukemia		X				X		X			X		X					X	X			X	X	X	X

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

ANIMAL NUMBER	917	768	782	787	891	892	738	832	909	689	697	698	719	810	848	682	724	783	784	796	860	903	714	734	776
WEEKS ON STUDY	120	121	121	121	121	121	122	122	122	123	123	123	123	123	123	124	124	124	124	124	124	124	125	125	125
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																									
Tubular cell adenocarcinoma																									
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS				X																			X		
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma							X					X													
Pheochromocytoma		X	X	X	X								X	X				X				X		X	X
Pheochromocytoma, malignant																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma			X																						
Follicular cell carcinoma									X				X											X	
C-cell adenoma										X			X						X	X	X				
C-cell carcinoma								X			X														
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	N	+	+	N	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS																									
Fibroadenoma																	X								
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
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	
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, 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
Squamous cell carcinoma			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
Lipoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Granular cell tumor, NOS																									
Astrocytoma																									
Meningioma																									
Meningioma, invasive																									
Spinal cord	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, invasive																									
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
Squamous cell carcinoma, invasive																									
Adenoma, NOS																									
Zymbal 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
Squamous cell carcinoma								X									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
Squamous cell carcinoma, invasive																									
Hemangiosarcoma																									
Osteosarcoma																									
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
C-cell carcinoma, invasive																									
Rhabdomyosarcoma																									
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
Alveolar/bronchiolar carcinoma, invasive																									
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
Liposarcoma																									
Leiomyosarcoma, invasive																									
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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
Fibrosarcoma																									
Mesothelioma, malignant																									
Hemangiosarcoma																									
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
Squamous cell carcinoma, invasive						X																			
C-cell carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Fibrosarcoma, invasive																									
Liposarcoma, metastatic																									
Mesothelioma, invasive					X																				
Hemangiosarcoma, metastatic																									
Malignant lymphoma, undifferentiated type																									
Malignant lymphoma, histiocytic type																									
Monocytic leukemia	X				X					X		X		X	X	X			X			X		X	

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

ANIMAL NUMBER	86 2	88 0	90 5	81 7	82 0	83 8	85 6	86 8	87 1	88 5	72 6	74 1	79 1	81 5	82 5	82 6	82 8	82 9	83 7	84 2	90 0	90 6	90 8	67 3	68 5
WEEKS ON STUDY	125	125	125	126	126	126	126	126	126	126	127	127	127	127	127	127	127	127	127	127	127	127	127	128	128
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma											X														
Tubular cell adenocarcinoma																									
Mixed tumor, malignant																		X							
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS							X						X	X							X		X		
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma				X																					
Pheochromocytoma								X		X					X						X				
Pheochromocytoma, malignant				X																					
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma							X									X			X						
Follicular cell carcinoma		X							X								X					X			X
C-cell adenoma																	X		X						
C-cell carcinoma						X	X	X					X								X				X
Parathyroid	+	–	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell carcinoma																		X							
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS		X																							
Fibroadenoma			X										X												
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
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
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS													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
Squamous cell carcinoma								X		X	X											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
Lipoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Granular cell tumor, NOS																									
Astrocytoma		X																							
Meningioma																									
Meningioma, invasive																									
Spinal cord	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, invasive																									
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
Squamous cell carcinoma, invasive																									
Adenoma, NOS																									
Zymbal 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
Squamous cell carcinoma																									
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
Squamous cell carcinoma, invasive																									
Hemangiosarcoma																									
Osteosarcoma																									
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
C-cell carcinoma, invasive																									
Rhabdomyosarcoma																									
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
Alveolar/bronchiolar carcinoma, invasive																									
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
Liposarcoma																									
Leiomyosarcoma, invasive																									
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
Fibrosarcoma																									
Mesothelioma, malignant																									
Hemangiosarcoma																									
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
Squamous cell carcinoma, invasive																									
C-cell carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Fibrosarcoma, invasive																									
Liposarcoma, metastatic																									
Mesothelioma, invasive																									
Hemangiosarcoma, metastatic																									
Malignant lymphoma, undifferentiated type																									
Malignant lymphoma, histiocytic type																									
Monocytic leukemia			X		X				X	X	X	X					X							X	X

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

ANIMAL NUMBER	753	761	762	803	674	749	750	765	800	670	701	727	731	755	795	872	886	899	671	722	789	716	857	913	723
WEEKS ON STUDY	128	128	128	128	129	129	129	129	129	130	130	130	130	130	130	130	130	130	131	131	131	132	132	132	133
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																									
Tubular cell adenocarcinoma														X											
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																				X					
Adenoma, NOS			X	X	X		X							X	X							X			X
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma												X		X											
Pheochromocytoma		X			X								X		X							X			
Pheochromocytoma, malignant																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma														X											
Follicular cell carcinoma												X								X					
C-cell adenoma														X		X	X					X			
C-cell carcinoma							X	X		X		X									X				
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell carcinoma			X																				X		X
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS								X																	
Adenocarcinoma, NOS																									
Fibroadenoma																		X					X		
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, 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
Squamous cell carcinoma												X								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
Lipoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Granular cell tumor, NOS																									
Astrocytoma																	X								
Meningioma																									
Meningioma, invasive																									
Spinal cord	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, invasive																									
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
Squamous cell carcinoma, invasive																									
Adenoma, NOS																									
Zymbal 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
Squamous cell carcinoma											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
Squamous cell carcinoma, invasive																			X						
Hemangiosarcoma																									
Osteosarcoma																									
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
C-cell carcinoma, invasive																									
Rhabdomyosarcoma																									
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
Alveolar/bronchiolar carcinoma, invasive																									
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
Liposarcoma													X												
Leiomyosarcoma, invasive																									
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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
Fibrosarcoma																									
Mesothelioma, malignant																									
Hemangiosarcoma																									
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
Squamous cell carcinoma, invasive											X														
C-cell carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Fibrosarcoma, invasive																									
Liposarcoma, metastatic																									
Mesothelioma, invasive									X																
Hemangiosarcoma, metastatic																									
Malignant lymphoma, undifferentiated type																									
Malignant lymphoma, histiocytic type								X																	
Monocytic leukemia		X		X	X	X	X			X		X					X							X	X

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

ANIMAL NUMBER	769	801	805	836	846	852	883	907	681	841	915	745	785	798	875	890	898	910	717	767	855	867	904	684	688
WEEKS ON STUDY	133	133	133	133	133	133	133	133	134	134	134	135	135	135	135	135	135	135	136	136	136	136	136	137	137
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																									
Tubular cell adenocarcinoma																									
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS					X		X		X					X	X			X		X					
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma				X		X			X				X		X	X	X	X	X						X
Pheochromocytoma, malignant										X			X												
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma									X				X												
Follicular cell carcinoma																		X							
C-cell adenoma				X					X											X					X
C-cell carcinoma			X	X	X	X	X										X	X	X		X		X		
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS																									
Fibroadenoma											X				X		X				X	X			
Testis	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
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
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, 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
Squamous cell carcinoma														X						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
Lipoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Granular cell tumor, NOS																									
Astrocytoma																									
Meningioma																									
Meningioma, invasive																									
Spinal cord	N	N	+	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Liposarcoma, invasive			X																						
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
Squamous cell carcinoma, invasive																									
Adenoma, NOS																									
Zymbal 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
Squamous cell carcinoma																									
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
Squamous cell carcinoma, invasive																									
Hemangiosarcoma																									
Osteosarcoma																									
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
C-cell carcinoma, invasive																									
Rhabdomyosarcoma																									
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
Alveolar/bronchiolar carcinoma, invasive																									
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
Liposarcoma																									
Leiomyosarcoma, invasive																									
Tunica vaginalis	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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
Fibrosarcoma																									
Mesothelioma, malignant																									
Hemangiosarcoma																									
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
Squamous cell carcinoma, invasive																									
C-cell carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Fibrosarcoma, invasive																									
Liposarcoma, metastatic			X																						
Mesothelioma, invasive																									
Hemangiosarcoma, metastatic																									
Malignant lymphoma, undifferentiated type																									
Malignant lymphoma, histiocytic type																									
Monocytic leukemia		X	X	X		X		X			X			X		X	X				X			X	X

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

ANIMAL NUMBER	74 48	75 56	82 21	84 43	70 04	71 10	84 49	89 96	81 13	74 00	79 90	80 04	81 14	87 70	87 79	90 01	91 12	68 87	76 66	84 45	88 81	67 75	67 76	69 91	69 96
WEEKS ON STUDY	137	137	137	137	138	138	138	138	139	140	140	140	140	140	140	140	140	141	141	141	141	142	142	142	142
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																									X
Tubular cell adenocarcinoma																									X
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS				X		X			X			X					X		X						
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma									X																
Pheochromocytoma	X			X	X				X		X									X		X	X		X
Pheochromocytoma, malignant		X				X																			
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma									X								X								
Follicular cell carcinoma						X																			
C-cell adenoma													X										X		X
C-cell carcinoma									X				X	X						X				X	
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell carcinoma						X									X		X		X						
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS																			X						
Fibroadenoma									X										X				X		
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, 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
Squamous cell carcinoma												X						X					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
Lipoma								X																	
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Granular cell tumor, NOS																									
Astrocytoma																									
Meningioma																									
Meningioma, invasive																									
Spinal cord	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, invasive																									
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
Squamous cell carcinoma, invasive																									
Adenoma, NOS																									
Zymbal 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
Squamous cell carcinoma			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	N
Squamous cell carcinoma, invasive																									
Hemangiosarcoma																									
Osteosarcoma																									
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
C-cell carcinoma, invasive																									
Rhabdomyosarcoma																									
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
Alveolar/bronchiolar carcinoma, invasive																									
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
Liposarcoma																									
Leiomyosarcoma, invasive																									
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
Fibrosarcoma																					X				
Mesothelioma, malignant																									
Hemangiosarcoma																									
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
Squamous cell carcinoma, invasive																									
C-cell carcinoma, metastatic																									
Sarcoma, NOS, invasive																									
Fibrosarcoma, invasive																					X				
Liposarcoma, metastatic																									
Mesothelioma, invasive																									
Hemangiosarcoma, metastatic																									
Malignant lymphoma, undifferentiated type																									
Malignant lymphoma, histiocytic type																									
Monocytic leukemia				X		X	X	X	X		X							X	X	X		X	X	X	

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

ANIMAL NUMBER	70 03	70 07	70 08	72 21	72 28	73 32	73 36	74 42	74 44	75 54	77 70	78 86	79 93	80 07	80 08	81 11	81 12	83 30	83 39	84 40	85 54	85 59	88 84	89 97	91 14	TOTAL TISSUES TUMORS
WEEKS ON STUDY	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	142	
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Tubular cell adenoma																										2
Tubular cell adenocarcinoma				X			X															X				5
Mixed tumor, malignant																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
ENDOCRINE SYSTEM																										
Pituitary	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	245
Carcinoma, NOS														X												4
Adenoma, NOS				X					X				X											X		41
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Cortical adenoma										X																8
Pheochromocytoma			X				X						X		X	X							X		54
Pheochromocytoma, malignant	X		X																							8
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Follicular cell adenoma																										15
Follicular cell carcinoma		X						X	X					X						X				X		22
C-cell adenoma																					X					34
C-cell carcinoma								X	X	X		X		X		X						X	X		X	48
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	238
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Islet cell carcinoma							X																			11
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*250
Adenoma, NOS																										1
Adenocarcinoma, NOS																		X								4
Fibroadenoma																X	X			X						18
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Adenocarcinoma, NOS																				X						1
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	237
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Carcinoma, NOS																										1
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	*250
Squamous cell carcinoma																								X		16
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Carcinoma, NOS, invasive																										1
Granular cell tumor, NOS												X														1
Astrocytoma																										2
Meningioma																										1
Meningioma, invasive																										1
Spinal cord	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, invasive																										1
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*250
Squamous cell carcinoma, invasive																										1
Adenoma, NOS																										1
Zymbal 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
Squamous cell carcinoma																										5
Keratoacanthoma																										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
Squamous cell carcinoma, invasive																										1
Hemangiosarcoma																										1
Osteosarcoma																										1
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	*250
C-cell carcinoma, invasive															X											1
Rhabdomyosarcoma																										1
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	*250
Alveolar/bronchiolar carcinoma, invasive																										1
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
Liposarcoma																										1
Leiomyosarcoma, invasive																										1
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*250
Mesothelioma, NOS							X																			1
Mesothelioma, malignant																										4
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
Fibrosarcoma																										1
Mesothelioma, malignant																										1
Hemangiosarcoma																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*250
Squamous cell carcinoma, invasive																										2
C-cell carcinoma, metastatic															X											1
Sarcoma, NOS, invasive			X																							1
Fibrosarcoma, invasive																										1
Liposarcoma, metastatic																										1
Mesothelioma, invasive																										5
Hemangiosarcoma, metastatic																										1
Malig lymphoma, undifferentiated type																										1
Malignant lymphoma, histiocytic type																								X		3
Monocytic leukemia		X	X		X	X	X	X	X	X		X				X	X						X			110

*Animals necropsied

TABLE A3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS

	Control	1% Crocidolite Asbestos
Integumentary System: Fibroma		
Overall Rates (a)	18/118 (15%)	27/250 (11%)
Adjusted Rates (b)	48.8%	29.6%
Terminal Rates (c)	2/11 (18%)	3/29 (10%)
Week of First Observation	86	88
Life Table Test (d)		P=0.054N
Incidental Tumor Test (d)		P=0.103N
Fisher Exact Test (d)		P=0.148N
Integumentary System: Fibroma or Neurofibroma		
Overall Rates (a)	21/118 (18%)	36/250 (14%)
Adjusted Rates (b)	52.5%	36.9%
Terminal Rates (c)	2/11 (18%)	4/29 (14%)
Week of First Observation	86	88
Life Table Test (d)		P=0.093N
Incidental Tumor Test (d)		P=0.184N
Fisher Exact Test (d)		P=0.245N
Integumentary System: Fibroma or Fibrosarcoma		
Overall Rates (a)	26/118 (22%)	34/250 (14%)
Adjusted Rates (b)	61.5%	33.6%
Terminal Rates (c)	3/11 (27%)	3/29 (10%)
Week of First Observation	86	88
Life Table Test (d)		P=0.006N
Incidental Tumor Test (d)		P=0.016N
Fisher Exact Test (d)		P=0.032N
Integumentary System: Neurofibroma or Neurofibrosarcoma		
Overall Rates (a)	3/118 (3%)	13/250 (5%)
Adjusted Rates (b)	6.9%	16.2%
Terminal Rates (c)	0/11 (0%)	2/29 (7%)
Week of First Observation	104	102
Life Table Test (d)		P=0.287
Incidental Tumor Test (d)		P=0.210
Fisher Exact Test (d)		P=0.188
Integumentary System: Sarcoma, Fibrosarcoma, Neurofibrosarcoma, or Myxosarcoma		
Overall Rates (a)	10/118 (8%)	11/250 (4%)
Adjusted Rates (b)	25.2%	12.1%
Terminal Rates (c)	1/11 (9%)	1/29 (3%)
Week of First Observation	89	95
Life Table Test (d)		P=0.042N
Incidental Tumor Test (d)		P=0.075N
Fisher Exact Test (d)		P=0.094N
Integumentary System: Fibroma, Neurofibroma, Sarcoma, Fibrosarcoma, Neurofibrosarcoma, or Myxosarcoma		
Overall Rates (a)	30/118 (25%)	45/250 (18%)
Adjusted Rates (b)	64.8%	44.4%
Terminal Rates (c)	3/11 (27%)	5/29 (17%)
Week of First Observation	86	88
Life Table Test (d)		P=0.014N
Incidental Tumor Test (d)		P=0.037N
Fisher Exact Test (d)		P=0.068N
Hematopoietic System: Monocytic Leukemia		
Overall Rates (a)	42/118 (36%)	113/250 (45%)
Adjusted Rates (b)	73.5%	81.2%
Terminal Rates (c)	4/11 (36%)	15/29 (52%)
Week of First Observation	71	83
Life Table Test (d)		P=0.401
Incidental Tumor Test (d)		P=0.062
Fisher Exact Test (d)		P=0.051

TABLE A3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Control	1% Crocidolite Asbestos
Hematopoietic System: Leukemia		
Overall Rates (a)	43/118 (36%)	113/250 (45%)
Adjusted Rates (b)	73.7%	81.2%
Terminal Rates (c)	4/11 (36%)	15/29 (52%)
Week of First Observation	71	83
Life Table Test (d)		P=0.452
Incidental Tumor Test (d)		P=0.082
Fisher Exact Test (d)		P=0.070
Liver: Neoplastic Nodule		
Overall Rates (a)	8/117 (7%)	16/250 (6%)
Adjusted Rates (b)	30.8%	19.1%
Terminal Rates (c)	2/11 (18%)	2/29 (7%)
Week of First Observation	116	101
Life Table Test (d)		P=0.361N
Incidental Tumor Test (d)		P=0.449N
Fisher Exact Test (d)		P=0.518N
Liver: Neoplastic Nodule or Hepatocellular Carcinoma		
Overall Rates (a)	11/117 (9%)	18/250 (7%)
Adjusted Rates (b)	40.1%	22.7%
Terminal Rates (c)	2/11 (18%)	3/29 (10%)
Week of First Observation	116	101
Life Table Test (d)		P=0.152N
Incidental Tumor Test (d)		P=0.218N
Fisher Exact Test (d)		P=0.297N
Pancreas: Acinar Cell Adenoma		
Overall Rates (a)	8/117 (7%)	15/249 (6%)
Adjusted Rates (b)	30.0%	24.8%
Terminal Rates (c)	1/11 (9%)	4/29 (14%)
Week of First Observation	126	121
Life Table Test (d)		P=0.293N
Incidental Tumor Test (d)		P=0.365N
Fisher Exact Test (d)		P=0.464N
Pancreas: Acinar Cell Adenoma or Carcinoma		
Overall Rates (a)	8/117 (7%)	17/249 (7%)
Adjusted Rates (b)	30.0%	28.3%
Terminal Rates (c)	1/11 (9%)	5/29 (17%)
Week of First Observation	126	121
Life Table Test (d)		P=0.392N
Incidental Tumor Test (d)		P=0.481N
Fisher Exact Test (d)		P=0.578N
Pituitary Gland: Adenoma		
Overall Rates (a)	15/117 (13%)	41/245 (17%)
Adjusted Rates (b)	59.1%	45.4%
Terminal Rates (c)	5/11 (45%)	4/28 (14%)
Week of First Observation	89	98
Life Table Test (d)		P=0.499
Incidental Tumor Test (d)		P=0.337
Fisher Exact Test (d)		P=0.211
Pituitary Gland: Adenoma or Carcinoma		
Overall Rates (a)	18/117 (15%)	45/245 (18%)
Adjusted Rates (b)	62.3%	48.8%
Terminal Rates (c)	5/11 (45%)	5/28 (18%)
Week of First Observation	89	95
Life Table Test (d)		P=0.502N
Incidental Tumor Test (d)		P=0.439
Fisher Exact Test (d)		P=0.293

TABLE A3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Control	1% Crocidolite Asbestos
Adrenal Gland: Pheochromocytoma		
Overall Rates (a)	33/117 (28%)	54/250 (22%)
Adjusted Rates (b)	75.7%	58.9%
Terminal Rates (c)	5/11 (45%)	9/29 (31%)
Week of First Observation	90	103
Life Table Test (d)		P=0.017N
Incidental Tumor Test (d)		P=0.053N
Fisher Exact Test (d)		P=0.106N
Adrenal Gland: Pheochromocytoma or Malignant Pheochromocytoma		
Overall Rates (a)	35/117 (30%)	60/250 (24%)
Adjusted Rates (b)	80.3%	63.7%
Terminal Rates (c)	6/11 (55%)	10/29 (34%)
Week of First Observation	90	81
Life Table Test (d)		P=0.024N
Incidental Tumor Test (d)		P=0.076N
Fisher Exact Test (d)		P=0.142N
Thyroid Gland: Follicular Cell Adenoma		
Overall Rates (a)	7/116 (6%)	15/249 (6%)
Adjusted Rates (b)	15.5%	14.2%
Terminal Rates (c)	0/11 (0%)	0/29 (0%)
Week of First Observation	108	88
Life Table Test (d)		P=0.443N
Incidental Tumor Test (d)		P=0.562N
Fisher Exact Test (d)		P=0.582N
Thyroid Gland: Follicular Cell Carcinoma		
Overall Rates (a)	3/116 (3%)	22/249 (9%)
Adjusted Rates (b)	9.0%	31.7%
Terminal Rates (c)	0/11 (0%)	6/29 (21%)
Week of First Observation	100	110
Life Table Test (d)		P=0.061
Incidental Tumor Test (d)		P=0.034
Fisher Exact Test (d)		P=0.019
Thyroid Gland: Follicular Cell Adenoma or Carcinoma		
Overall Rates (a)	10/116 (9%)	37/249 (15%)
Adjusted Rates (b)	23.1%	41.5%
Terminal Rates (c)	0/11 (0%)	6/29 (21%)
Week of First Observation	100	88
Life Table Test (d)		P=0.196
Incidental Tumor Test (d)		P=0.095
Fisher Exact Test (d)		P=0.065
Thyroid Gland: C-Cell Adenoma		
Overall Rates (a)	13/116 (11%)	34/249 (14%)
Adjusted Rates (b)	34.8%	31.2%
Terminal Rates (c)	2/11 (18%)	3/29 (10%)
Week of First Observation	78	88
Life Table Test (d)		P=0.518
Incidental Tumor Test (d)		P=0.321
Fisher Exact Test (d)		P=0.319
Thyroid Gland: C-Cell Carcinoma		
Overall Rates (a)	19/116 (16%)	48/249 (19%)
Adjusted Rates (b)	62.5%	57.8%
Terminal Rates (c)	5/11 (45%)	10/29 (34%)
Week of First Observation	98	95
Life Table Test (d)		P=0.497N
Incidental Tumor Test (d)		P=0.436
Fisher Exact Test (d)		P=0.304

TABLE A3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Control	1% Crocidolite Asbestos
Thyroid Gland: C-Cell Adenoma or Carcinoma		
Overall Rates (a)	32/116 (28%)	79/249 (32%)
Adjusted Rates (b)	80.1%	71.6%
Terminal Rates (c)	7/11 (64%)	13/29 (45%)
Week of First Observation	78	88
Life Table Test (d)		P=0.458N
Incidental Tumor Test (d)		P=0.353
Fisher Exact Test (d)		P=0.250
Pancreatic Islets: Islet Cell Carcinoma		
Overall Rates (a)	11/117 (9%)	11/249 (4%)
Adjusted Rates (b)	25.7%	17.5%
Terminal Rates (c)	0/11 (0%)	1/29 (3%)
Week of First Observation	95	104
Life Table Test (d)		P=0.020N
Incidental Tumor Test (d)		P=0.028N
Fisher Exact Test (d)		P=0.055N
Pancreatic Islets: Islet Cell Adenoma or Carcinoma		
Overall Rates (a)	12/117 (10%)	11/249 (4%)
Adjusted Rates (b)	26.4%	17.5%
Terminal Rates (c)	0/11 (0%)	1/29 (3%)
Week of First Observation	95	104
Life Table Test (d)		P=0.010N
Incidental Tumor Test (d)		P=0.015N
Fisher Exact Test (d)		P=0.031N
Mammary Gland: Fibroadenoma		
Overall Rates (a)	18/118 (15%)	18/250 (7%)
Adjusted Rates (b)	52.4%	29.1%
Terminal Rates (c)	3/11 (27%)	4/29 (14%)
Week of First Observation	78	106
Life Table Test (d)		P=0.002N
Incidental Tumor Test (d)		P=0.005N
Fisher Exact Test (d)		P=0.015N
Mammary Gland: Adenoma or Fibroadenoma		
Overall Rates (a)	18/118 (15%)	19/250 (8%)
Adjusted Rates (b)	52.4%	29.8%
Terminal Rates (c)	3/11 (27%)	4/29 (14%)
Week of First Observation	78	106
Life Table Test (d)		P=0.003N
Incidental Tumor Test (d)		P=0.007N
Fisher Exact Test (d)		P=0.021N
Mammary Gland: Adenoma, Fibroadenoma, or Adenocarcinoma		
Overall Rates (a)	19/118 (16%)	22/250 (9%)
Adjusted Rates (b)	53.6%	33.6%
Terminal Rates (c)	3/11 (27%)	5/29 (17%)
Week of First Observation	78	106
Life Table Test (d)		P=0.005N
Incidental Tumor Test (d)		P=0.012N
Fisher Exact Test (d)		P=0.031N
Preputial Gland: Squamous Cell Carcinoma		
Overall Rates (a)	3/118 (3%)	16/250 (6%)
Adjusted Rates (b)	10.6%	21.3%
Terminal Rates (c)	0/11 (0%)	2/29 (7%)
Week of First Observation	118	86
Life Table Test (d)		P=0.183
Incidental Tumor Test (d)		P=0.109
Fisher Exact Test (d)		P=0.091

TABLE A3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Control	1% Crocidolite Asbestos
Testis: Interstitial Cell Tumor		
Overall Rates (a)	116/118 (98%)	237/249 (95%)
Adjusted Rates (b)	100.0%	100.0%
Terminal Rates (c)	11/11 (100%)	29/29 (100%)
Week of First Observation	60	81
Life Table Test (d)		P=0.023N
Incidental Tumor Test (d)		P=0.047N
Fisher Exact Test (d)		P=0.119N
All Sites: Benign Tumors		
Overall Rates (a)	117/118 (99%)	242/250 (97%)
Adjusted Rates (b)	100.0%	100.0%
Terminal Rates (c)	11/11 (100%)	29/29 (100%)
Week of First Observation	60	81
Life Table Test (d)		P=0.029N
Incidental Tumor Test (d)		P=0.050N
Fisher Exact Test (d)		P=0.159N
All Sites: Malignant Tumors		
Overall Rates (a)	97/118 (82%)	209/250 (84%)
Adjusted Rates (b)	98.8%	98.3%
Terminal Rates (c)	10/11 (91%)	26/29 (90%)
Week of First Observation	71	42
Life Table Test (d)		P=0.089N
Incidental Tumor Test (d)		P=0.498
Fisher Exact Test (d)		P=0.422
All Sites: All Tumors		
Overall Rates (a)	118/118 (100%)	248/250 (99%)
Adjusted Rates (b)	100.0%	100.0%
Terminal Rates (c)	11/11 (100%)	29/29 (100%)
Week of First Observation	60	42
Life Table Test (d)		P=0.042N
Incidental Tumor Test (d)		P=0.314N
Fisher Exact Test (d)		P=0.461N

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

TABLE A4a. HISTORICAL INCIDENCE OF LEUKEMIA IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES (a)

Asbestos Studies	Incidence in Controls
Chrysotile (short range)	37/88
Chrysotile (intermediate range)	31/88
Tremolite	43/118
Crocidolite	43/118
Amosite	38/117
TOTAL	192/529 (36.3%)
SD (b)	3.48%
Range	
High	37/88 (42.0%)
Low	38/117 (32.5%)

(a) All studies conducted by Hazleton Laboratories; age at start of terminal kill, 138-146 weeks.
(b) Standard deviation

TABLE A4b. HISTORICAL INCIDENCE OF THYROID GLAND FOLLICULAR CELL TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES (a)

Asbestos Studies	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Chrysotile (short range)	4/86	2/86	6/86
Chrysotile (intermediate range)	1/84	5/84	6/84
Tremolite	5/117	6/117	11/117
Crocidolite	7/116	3/116	10/116
Amosite	4/117	7/117	11/117
TOTAL	21/520 (4.0%)	23/520 (4.4%)	44/520 (8.5%)
SD (b)	1.79%	1.81%	1.19%
Range			
High	7/116 (6.0%)	7/117 (6.0%)	11/117 (9.4%)
Low	1/84 (1.2%)	2/86 (2.3%)	6/86 (7.0%)

(a) All studies conducted by Hazleton Laboratories; age at start of terminal kill, 138-146 weeks.
(b) Standard deviation

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS

	Untreated Control	1% Crocidolite Asbestos
ANIMALS INITIALLY IN STUDY	118	250
ANIMALS NECROPSIED	118	250
ANIMALS EXAMINED HISTOPATHOLOGICALLY	118	250
INTEGUMENTARY SYSTEM		
*Skin	(118)	(250)
Epidermal inclusion cyst	2 (2%)	3 (1%)
Edema, NOS		1 (0%)
Hemorrhage		1 (0%)
Inflammation, acute		1 (0%)
Inflammation, acute focal		1 (0%)
Abscess, NOS		2 (1%)
Inflammation, acute/chronic	1 (1%)	
Necrosis, focal		2 (1%)
Hyperplasia, focal		1 (0%)
Hyperkeratosis	1 (1%)	2 (1%)
Acanthosis	1 (1%)	2 (1%)
Metaplasia, osseous	1 (1%)	
*Subcutaneous tissue	(118)	(250)
Abscess, NOS		2 (1%)
Inflammation, chronic		1 (0%)
Fibrosis		1 (0%)
RESPIRATORY SYSTEM		
*Nasal cavity	(118)	(250)
Hyperkeratosis		1 (0%)
Metaplasia, squamous		1 (0%)
*Nasal turbinate	(118)	(250)
Inflammation, chronic		1 (0%)
#Trachea	(117)	(248)
Inflammation, chronic		1 (0%)
#Lung	(117)	(250)
Bronchiectasis		1 (0%)
Congestion, NOS	7 (6%)	8 (3%)
Hemorrhage	5 (4%)	14 (6%)
Inflammation, interstitial	2 (2%)	1 (0%)
Pneumonia, aspiration		1 (0%)
Inflammation, acute		1 (0%)
Inflammation, acute focal		1 (0%)
Inflammation, acute diffuse	1 (1%)	
Pneumonia, chronic murine		1 (0%)
Inflammation, chronic	98 (84%)	214 (86%)
Granuloma, NOS	1 (1%)	5 (2%)
Necrosis, focal		1 (0%)
Pigmentation, NOS	2 (2%)	7 (3%)
Hyperplasia, alveolar epithelium	3 (3%)	10 (4%)
Metaplasia, squamous		1 (0%)
#Lung/alveoli	(117)	(250)
Histiocytosis	4 (3%)	4 (2%)
HEMATOPOIETIC SYSTEM		
*Mediastinum	(118)	(250)
Hematopoiesis		1 (0%)
#Bone marrow	(117)	(248)
Congestion, NOS	1 (1%)	
Hemorrhage	1 (1%)	
Necrosis, focal		1 (0%)
Hypoplasia, NOS	3 (3%)	8 (3%)
Hyperplasia, NOS	3 (3%)	7 (3%)

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE *LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)*

	Untreated Control	1% Crocidolite Asbestos
HEMATOPOIETIC SYSTEM (Continued)		
#Spleen	(117)	(250)
Hemorrhage		6 (2%)
Fibrosis		1 (0%)
Fibrosis, focal	3 (3%)	21 (8%)
Fibrosis, multifocal		6 (2%)
Fibrosis, diffuse	2 (2%)	2 (1%)
Necrosis, NOS		1 (0%)
Necrosis, focal	1 (1%)	13 (5%)
Amyloidosis	1 (1%)	
Pigmentation, NOS		2 (1%)
Hemosiderosis	14 (12%)	48 (19%)
Hyperplasia, reticulum cell		1 (0%)
Hyperplasia, lymphoid	1 (1%)	
Hematopoiesis	21 (18%)	49 (20%)
#Splenic capsule	(117)	(250)
Fibrosis, multifocal		1 (0%)
#Splenic follicles	(117)	(250)
Atrophy, NOS	1 (1%)	6 (2%)
#Submandibular lymph node	(117)	(250)
Hyperplasia, lymphoid		1 (0%)
#Mandibular lymph node	(117)	(250)
Hemorrhage	1 (1%)	1 (0%)
Inflammation, acute diffuse		1 (0%)
Inflammation, chronic diffuse		1 (0%)
Fibrosis, focal	1 (1%)	
Hyperplasia, lymphoid	14 (12%)	37 (15%)
#Cervical lymph node	(117)	(250)
Pigmentation, NOS		1 (0%)
Erythrophagocytosis		1 (0%)
#Mediastinal lymph node	(117)	(250)
Congestion, NOS		1 (0%)
Hemorrhage	5 (4%)	16 (6%)
Pigmentation, NOS	12 (10%)	36 (14%)
Atrophy, NOS		1 (0%)
Erythrophagocytosis	4 (3%)	16 (6%)
Hyperplasia, reticulum cell	1 (1%)	
Hyperplasia, lymphoid	1 (1%)	7 (3%)
#Pancreatic lymph node	(117)	(250)
Hemorrhage		3 (1%)
Pigmentation, NOS	1 (1%)	15 (6%)
Atrophy, NOS		1 (0%)
Hyperplasia, reticulum cell	2 (2%)	6 (2%)
#Mesenteric lymph node	(117)	(250)
Congestion, NOS	1 (1%)	
Hemorrhage	1 (1%)	2 (1%)
Pigmentation, NOS	1 (1%)	3 (1%)
Atrophy, NOS	1 (1%)	1 (0%)
Erythrophagocytosis	1 (1%)	6 (2%)
Hyperplasia, reticulum cell	37 (32%)	58 (23%)
Hyperplasia, lymphoid	3 (3%)	9 (4%)
Mastocytosis	1 (1%)	
#Ileocolic lymph node	(117)	(250)
Edema, NOS	1 (1%)	
Inflammation, acute diffuse	1 (1%)	
Inflammation, chronic diffuse		1 (0%)
Necrosis, NOS	1 (1%)	
Pigmentation, NOS		2 (1%)
#Renal lymph node	(117)	(250)
Pigmentation, NOS	1 (1%)	2 (1%)
Hyperplasia, reticulum cell		1 (0%)

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE *LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS* (Continued)

	Untreated Control	1% Crocidolite Asbestos
HEMATOPOIETIC SYSTEM (Continued)		
#Iliac lymph node	(117)	(250)
Hemorrhage		1 (0%)
Hyperplasia, lymphoid		1 (0%)
#Lung	(117)	(250)
Leukocytosis, NOS	1 (1%)	
#Liver	(117)	(250)
Leukocytosis, NOS	5 (4%)	7 (3%)
Hematopoiesis	1 (1%)	2 (1%)
#Hepatic sinusoid	(117)	(250)
Leukocytosis, NOS		1 (0%)
#Kidney	(117)	(250)
Hematopoiesis		1 (0%)
#Adrenal	(117)	(250)
Hematopoiesis		1 (0%)
#Thymus	(88)	(182)
Cyst, NOS		1 (1%)
Congestion, NOS		1 (1%)
Hemorrhage		1 (1%)
Hyperplasia, epithelial		1 (1%)
CIRCULATORY SYSTEM		
*Eye	(118)	(250)
Thrombosis, NOS		1 (0%)
Embolus, septic		1 (0%)
#Spleen	(117)	(250)
Thrombosis, NOS		1 (0%)
#Mandibular lymph node	(117)	(250)
Lymphangiectasis	2 (2%)	5 (2%)
#Mediastinal lymph node	(117)	(250)
Lymphangiectasis	2 (2%)	
Thrombosis, NOS		1 (0%)
#Pancreatic lymph node	(117)	(250)
Lymphangiectasis		2 (1%)
#Mesenteric lymph node	(117)	(250)
Lymphangiectasis	12 (10%)	21 (8%)
#Ileocolic lymph node	(117)	(250)
Lymphangiectasis	3 (3%)	3 (1%)
#Iliac lymph node	(117)	(250)
Lymphangiectasis		2 (1%)
#Lung	(117)	(250)
Thrombosis, NOS		1 (0%)
#Heart	(117)	(250)
Embolus, septic		2 (1%)
#Heart/atrium	(117)	(250)
Thrombosis, NOS		5 (2%)
#Myocardium	(117)	(250)
Mineralization	1 (1%)	
Thrombosis, NOS		1 (0%)
Inflammation, acute focal		1 (0%)
Inflammation, chronic focal	40 (34%)	96 (38%)
Inflammation, chronic diffuse	33 (28%)	78 (31%)
Fibrosis, focal	3 (3%)	2 (1%)
Fibrosis, multifocal	1 (1%)	
Degeneration, NOS		2 (1%)
Necrosis, focal		1 (0%)
#Endocardium	(117)	(250)
Fibrosis		1 (0%)
#Cardiac valve	(117)	(250)
Inflammation, acute focal		1 (0%)
Inflammation, chronic		1 (0%)

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control		1% Crocidolite Asbestos	
CIRCULATORY SYSTEM (Continued)				
*Aorta	(118)		(250)	
Mineralization	1	(1%)	2	(1%)
Atherosclerosis			1	(0%)
*Coronary artery	(118)		(250)	
Mineralization			1	(0%)
*Pulmonary artery	(118)		(250)	
Inflammation, chronic	1	(1%)		
*Mesenteric artery	(118)		(250)	
Inflammation, chronic	1	(1%)		
*Vena cava	(118)		(250)	
Mineralization			1	(0%)
#Liver	(117)		(250)	
Thrombosis, NOS	3	(3%)	1	(0%)
#Pancreas	(117)		(249)	
Periarteritis	1	(1%)	6	(2%)
#Stomach	(116)		(249)	
Periarteritis			1	(0%)
*Mesentery	(118)		(250)	
Periarteritis			3	(1%)
#Kidney	(117)		(250)	
Thrombosis, NOS			1	(0%)
Embolism, NOS			1	(0%)
Embolus, septic			1	(0%)
#Testis	(118)		(249)	
Periarteritis	2	(2%)	4	(2%)
#Adrenal	(117)		(250)	
Thrombosis, NOS	2	(2%)		
#Adrenal cortex	(117)		(250)	
Thrombosis, NOS			1	(0%)
DIGESTIVE SYSTEM				
*Tongue	(118)		(250)	
Epidermal inclusion cyst			1	(0%)
Edema, NOS			1	(0%)
Inflammation, acute diffuse			1	(0%)
Inflammation, chronic focal			1	(0%)
Hyperkeratosis			2	(1%)
Acanthosis			1	(0%)
#Salivary gland	(115)		(249)	
Inflammation, acute focal	1	(1%)		
Inflammation, chronic focal	1	(1%)	1	(0%)
Inflammation, chronic diffuse	1	(1%)	5	(2%)
Degeneration, NOS			2	(1%)
Atrophy, diffuse			7	(3%)
#Submaxillary gland	(115)		(249)	
Inflammation, chronic	1	(1%)		
Atrophy, NOS	1	(1%)		
#Liver	(117)		(250)	
Congestion, NOS			2	(1%)
Hemorrhage	2	(2%)	5	(2%)
Inflammation, fibrinous			1	(0%)
Granuloma, NOS	9	(8%)	17	(7%)
Hepatitis, toxic	8	(7%)	37	(15%)
Degeneration, NOS	11	(9%)	30	(12%)
Necrosis, NOS	1	(1%)	1	(0%)
Necrosis, focal	18	(15%)	29	(12%)
Metamorphosis, fatty	28	(24%)	56	(22%)
Pigmentation, NOS	18	(15%)	50	(20%)
Hemosiderosis			1	(0%)
Focal cellular change	44	(38%)	89	(36%)
Angiectasis	1	(1%)	7	(3%)

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
DIGESTIVE SYSTEM (Continued)		
#Liver/hepatocytes	(117)	(250)
Cytomegaly		1 (0%)
Hepatocytomegaly		1 (0%)
#Bile duct	(117)	(250)
Calculus, unknown gross or micro		1 (0%)
Dilatation, NOS		1 (0%)
Cyst, NOS	1 (1%)	1 (0%)
Multilocular cyst		1 (0%)
Inflammation, chronic	15 (13%)	18 (7%)
Fibrosis	10 (9%)	9 (4%)
Hyperplasia, NOS	45 (38%)	79 (32%)
Hyperplasia, focal		2 (1%)
#Pancreas	(117)	(249)
Ectopia	4 (3%)	20 (8%)
Inflammation, acute diffuse	1 (1%)	
Inflammation, chronic focal	1 (1%)	2 (1%)
Inflammation, chronic diffuse	2 (2%)	
Atrophy, NOS		1 (0%)
Atrophy, focal	14 (12%)	50 (20%)
Atrophy, diffuse	3 (3%)	10 (4%)
Hyperplasia, focal		2 (1%)
#Pancreatic acinus	(117)	(249)
Hyperplasia, focal	4 (3%)	16 (6%)
#Esophagus	(115)	(247)
Hyperkeratosis	8 (7%)	17 (7%)
Acanthosis	1 (1%)	
#Stomach	(116)	(249)
Mineralization	4 (3%)	3 (1%)
Cyst, NOS		2 (1%)
Edema, NOS		2 (1%)
Hemorrhage		2 (1%)
Ulcer, NOS		1 (0%)
Inflammation, acute focal	2 (2%)	5 (2%)
Inflammation, acute diffuse		1 (0%)
Inflammation, chronic	5 (4%)	3 (1%)
Inflammation, chronic focal	7 (6%)	7 (3%)
Inflammation, chronic diffuse	13 (11%)	28 (11%)
Ulcer, perforated	10 (9%)	21 (8%)
Fibrosis, diffuse	2 (2%)	
Adhesion, NOS		1 (0%)
Necrosis, focal	19 (16%)	47 (19%)
Hyperplasia, epithelial	4 (3%)	1 (0%)
Hyperplasia, focal		1 (0%)
Hyperkeratosis	17 (15%)	47 (19%)
Acanthosis	28 (24%)	60 (24%)
#Gastric submucosa	(116)	(249)
Edema, NOS		1 (0%)
#Gastric muscularis	(116)	(249)
Degeneration, NOS		3 (1%)
#Small intestine	(117)	(249)
Inflammation, acute focal	1 (1%)	
Necrosis, focal	1 (1%)	
#Duodenum	(117)	(249)
Inflammation, acute focal		1 (0%)
Necrosis, focal	1 (1%)	1 (0%)
#Jejunum	(117)	(249)
Diverticulum	1 (1%)	
Ulcer, perforated		1 (0%)
#Large intestine	(117)	(249)
Parasitism		3 (1%)

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
DIGESTIVE SYSTEM (Continued)		
#Colon	(117)	(249)
Inflammation, chronic focal		2 (1%)
Inflammation, chronic diffuse	1 (1%)	
Fibrosis, focal	1 (1%)	
Parasitism	5 (4%)	9 (4%)
Necrosis, focal	2 (2%)	2 (1%)
Hyperplasia, focal		1 (0%)
#Colonic muscularis propria	(117)	(249)
Degeneration, NOS		1 (0%)
#Cecum	(117)	(249)
Hemorrhage	2 (2%)	
Inflammation, acute diffuse		1 (0%)
Inflammation, chronic diffuse	1 (1%)	1 (0%)
Parasitism		1 (0%)
Necrosis, focal	1 (1%)	2 (1%)
Necrosis, diffuse		1 (0%)
#Transverse colon	(117)	(249)
Inflammation, chronic focal		1 (0%)
Necrosis, focal		1 (0%)
URINARY SYSTEM		
#Kidney	(117)	(250)
Mineralization	12 (10%)	6 (2%)
Hydronephrosis		1 (0%)
Congestion, NOS		1 (0%)
Inflammation, acute focal	1 (1%)	
Abscess, NOS		1 (0%)
Inflammation, acute/chronic		1 (0%)
Inflammation, chronic	105 (90%)	220 (88%)
Inflammation, chronic diffuse		2 (1%)
Fibrosis, diffuse	1 (1%)	
Necrosis, focal		1 (0%)
Calcification, NOS		1 (0%)
Pigmentation, NOS	1 (1%)	1 (0%)
Hyperplasia, tubular cell	1 (1%)	1 (0%)
#Kidney/cortex	(117)	(250)
Cyst, NOS	5 (4%)	12 (5%)
Multiple cysts	1 (1%)	1 (0%)
#Renal papilla	(117)	(250)
Necrosis, NOS		1 (0%)
#Kidney/tubule	(117)	(250)
Pigmentation, NOS	43 (37%)	85 (34%)
Hyperplasia, focal		2 (1%)
*Ureter	(118)	(250)
Dilatation, NOS	1 (1%)	
Inflammation, chronic		1 (0%)
Hyperplasia, epithelial		1 (0%)
#Urinary bladder	(116)	(250)
Hemorrhage		5 (2%)
Inflammation, hemorrhagic	2 (2%)	1 (0%)
Inflammation, acute		1 (0%)
Inflammation, acute diffuse		1 (0%)
Inflammation, chronic		1 (0%)
Inflammation, chronic focal		2 (1%)
Inflammation, chronic diffuse	1 (1%)	3 (1%)
Granuloma, NOS		1 (0%)
Necrosis, NOS		1 (0%)
Necrosis, focal		1 (0%)
Pigmentation, NOS		1 (0%)

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE *LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS* (Continued)

	Untreated Control	1% Crocidolite Asbestos
URINARY SYSTEM		
#Urinary bladder (Continued)		
Hyperplasia, epithelial	2 (2%)	7 (3%)
Hyperplasia, diffuse		1 (0%)
Hyperplasia, papillary		3 (1%)
Polyp, inflammatory		2 (1%)
Metaplasia, squamous		1 (0%)
ENDOCRINE SYSTEM		
#Pituitary	(117)	(245)
Cyst, NOS		3 (1%)
Hemorrhage		1 (0%)
Abscess, NOS		1 (0%)
Necrosis, NOS		1 (0%)
Necrosis, focal		1 (0%)
Pigmentation, NOS		2 (1%)
Hyperplasia, focal	7 (6%)	12 (5%)
Angiectasis	7 (6%)	6 (2%)
#Adrenal	(117)	(250)
Congestion, NOS		1 (0%)
Hemorrhage		1 (0%)
Necrosis, NOS	1 (1%)	
Necrosis, focal	1 (1%)	1 (0%)
Metamorphosis, fatty		2 (1%)
Hyperplasia, focal	1 (1%)	
Angiectasis		5 (2%)
#Adrenal cortex	(117)	(250)
Congestion, NOS	2 (2%)	1 (0%)
Degeneration, NOS	1 (1%)	2 (1%)
Necrosis, focal		2 (1%)
Metamorphosis, fatty	31 (26%)	55 (22%)
Hyperplasia, focal	8 (7%)	19 (8%)
Angiectasis	4 (3%)	1 (0%)
#Adrenal medulla	(117)	(250)
Hyperplasia, NOS		1 (0%)
Hyperplasia, focal	30 (26%)	68 (27%)
Hyperplasia, diffuse		1 (0%)
#Thyroid	(116)	(249)
Follicular cyst, NOS	6 (5%)	22 (9%)
Hemorrhage		1 (0%)
Inflammation, chronic		1 (0%)
Pigmentation, NOS		1 (0%)
Hyperplasia, C-cell	13 (11%)	48 (19%)
Hyperplasia, follicular cell	1 (1%)	
#Parathyroid	(111)	(238)
Hyperplasia, NOS	16 (14%)	28 (12%)
#Pancreatic islets	(117)	(249)
Hyperplasia, focal	3 (3%)	7 (3%)
REPRODUCTIVE SYSTEM		
*Mammary gland	(118)	(250)
Galactocele	1 (1%)	2 (1%)
Cystic ducts	6 (5%)	7 (3%)
Fibrosis, focal	1 (1%)	
Pigmentation, NOS		1 (0%)
Hyperplasia, NOS	11 (9%)	11 (4%)
Hyperplasia, focal		2 (1%)
Hyperplasia, diffuse	1 (1%)	

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
REPRODUCTIVE SYSTEM (Continued)		
*Preputial gland	(118)	(250)
Cystic ducts	5 (4%)	11 (4%)
Abscess, NOS	2 (2%)	3 (1%)
Inflammation, chronic		1 (0%)
Inflammation, chronic diffuse		1 (0%)
Hyperplasia, NOS	1 (1%)	
Hyperplasia, diffuse	1 (1%)	2 (1%)
Hyperkeratosis	1 (1%)	2 (1%)
#Prostate	(116)	(250)
Cyst, NOS		3 (1%)
Cystic ducts		1 (0%)
Hemorrhage	1 (1%)	3 (1%)
Inflammation, acute	1 (1%)	
Inflammation, acute focal	2 (2%)	1 (0%)
Inflammation, acute diffuse	1 (1%)	3 (1%)
Abscess, NOS	8 (7%)	12 (5%)
Inflammation active chronic		1 (0%)
Inflammation, acute/chronic	1 (1%)	4 (2%)
Inflammation, chronic		1 (0%)
Inflammation, chronic focal	25 (22%)	71 (28%)
Inflammation, chronic diffuse	7 (6%)	23 (9%)
Hyperplasia, NOS		1 (0%)
Hyperplasia, epithelial	3 (3%)	9 (4%)
Hyperplasia, focal	4 (3%)	7 (3%)
Hyperplasia, diffuse		2 (1%)
Angiectasis		1 (0%)
*Seminal vesicle	(118)	(250)
Cyst, NOS		9 (4%)
Cystic ducts	2 (2%)	2 (1%)
Hemorrhage		1 (0%)
Inflammation, acute focal		2 (1%)
Abscess, NOS		1 (0%)
Inflammation, chronic	1 (1%)	
Inflammation, chronic diffuse	1 (1%)	1 (0%)
Hyperplasia, focal		1 (0%)
Hyperplasia, diffuse	1 (1%)	5 (2%)
Hyperplasia, papillary		1 (0%)
#Testis	(118)	(249)
Granuloma, spermatic		1 (0%)
Degeneration, NOS	12 (10%)	17 (7%)
Infarct, NOS		2 (1%)
Hyperplasia, interstitial cell	51 (43%)	98 (39%)
*Epididymis	(118)	(250)
Inflammation, chronic focal		1 (0%)
Necrosis, fat	1 (1%)	8 (3%)
*Scrotum	(118)	(250)
Hemorrhage		1 (0%)
NERVOUS SYSTEM		
#Brain/meninges	(117)	(249)
Abscess, NOS		1 (0%)
#Cerebrum	(117)	(249)
Hemorrhage	1 (1%)	
Gliosis		1 (0%)
Necrosis, focal		2 (1%)
Malacia	1 (1%)	
#Brain	(117)	(249)
Hydrocephalus, NOS		1 (0%)
Hemorrhage	3 (3%)	1 (0%)
Necrosis, focal	1 (1%)	

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
NERVOUS SYSTEM (Continued)		
*Spinal cord	(118)	(250)
Degeneration, NOS		1 (0%)
*Optic nerve	(118)	(250)
Necrosis, NOS		1 (0%)
SPECIAL SENSE ORGANS		
*Eye	(118)	(250)
Hemorrhage	5 (4%)	6 (2%)
Empyema	2 (2%)	3 (1%)
Synechia, anterior		1 (0%)
Synechia, posterior	2 (2%)	2 (1%)
Cataract	18 (15%)	24 (10%)
Phthisis bulbi	2 (2%)	4 (2%)
*Vitreous body	(118)	(250)
Inflammation, chronic		1 (0%)
Vascularization	1 (1%)	1 (0%)
*Eye/cornea	(118)	(250)
Inflammation, acute		1 (0%)
Inflammation, acute diffuse	1 (1%)	1 (0%)
Inflammation, chronic focal	2 (2%)	3 (1%)
Inflammation, chronic diffuse	7 (6%)	7 (3%)
Acanthosis		1 (0%)
*Eye/retina	(118)	(250)
Degeneration, NOS	41 (35%)	58 (23%)
*Eye/crystalline lens	(118)	(250)
Rupture		4 (2%)
*Eyelid	(118)	(250)
Hemorrhage		1 (0%)
Inflammation, acute		1 (0%)
Necrosis, NOS		1 (0%)
*Harderian gland	(118)	(250)
Inflammation, acute diffuse		1 (0%)
Inflammation, chronic diffuse	1 (1%)	1 (0%)
Atrophy, NOS		1 (0%)
*Ear canal	(118)	(250)
Necrosis, NOS	1 (1%)	
*Zymbal gland	(118)	(250)
Cystic ducts	17 (14%)	51 (20%)
Abscess, NOS	1 (1%)	2 (1%)
Inflammation, chronic	1 (1%)	
Inflammation, chronic focal		1 (0%)
Hyperkeratosis	1 (1%)	5 (2%)
Acanthosis		1 (0%)
MUSCULOSKELETAL SYSTEM		
*Skull	(118)	(250)
Osteopetrosis	1 (1%)	2 (1%)
*Mandible	(118)	(250)
Fibrous osteodystrophy		1 (0%)
*Sternum	(118)	(250)
Osteopetrosis		1 (0%)
Fibrous osteodystrophy	1 (1%)	
Hypoplasia, NOS		1 (0%)
*Rib	(118)	(250)
Degeneration, NOS		5 (2%)

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
BODY CAVITIES		
*Abdominal cavity	(118)	(250)
Steatitis	1 (1%)	2 (1%)
Necrosis, fat	5 (4%)	12 (5%)
*Pleura	(118)	(250)
Hemorrhage	1 (1%)	
Inflammation, chronic diffuse	1 (1%)	
*Mesentery	(118)	(250)
Hemorrhage	1 (1%)	
Inflammation, acute diffuse	1 (1%)	
Inflammation, chronic focal	3 (3%)	1 (0%)
Granuloma, NOS	2 (2%)	
Necrosis, fat		1 (0%)
Pigmentation, NOS	1 (1%)	
ALL OTHER SYSTEMS		
*Multiple organs	(118)	(250)
Mineralization	4 (3%)	2 (1%)
Cyst, NOS	1 (1%)	
Inflammation, acute		1 (0%)
Inflammation, chronic	8 (7%)	21 (8%)
Inflammation, chronic diffuse		2 (1%)
Degeneration, NOS		1 (0%)
Necrosis, focal		2 (1%)
Pigmentation, NOS	1 (1%)	2 (1%)
Hyperplasia, NOS	3 (3%)	3 (1%)
Diaphragm		
Hernia, NOS	2	1
SPECIAL MORPHOLOGY SUMMARY		
None		

* 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 CROCIDOLITE ASBESTOS

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS

	Untreated Control	1% Crocidolite Asbestos
ANIMALS INITIALLY IN STUDY	118	250
ANIMALS NECROPSIED	118	250
ANIMALS EXAMINED HISTOPATHOLOGICALLY	118	250
INTEGUMENTARY SYSTEM		
*Skin	(118)	(250)
Squamous cell papilloma		1 (0%)
Squamous cell carcinoma	1 (1%)	1 (0%)
Squamous cell carcinoma, invasive		1 (0%)
Basal cell tumor		1 (0%)
Basal cell carcinoma	1 (1%)	
Trichoepithelioma	1 (1%)	
Keratoacanthoma		1 (0%)
Fibroma	1 (1%)	
Fibrosarcoma	2 (2%)	2 (1%)
Neurofibrosarcoma		1 (0%)
*Subcutanaous tissue	(118)	(250)
Squamous cell papilloma		1 (0%)
Squamous cell carcinoma, invasive	1 (1%)	1 (0%)
Follicular cell carcinoma, invasive		1 (0%)
Sarcoma, NOS	1 (1%)	1 (0%)
Fibroma	5 (4%)	9 (4%)
Fibrosarcoma	1 (1%)	3 (1%)
Lipoma	2 (2%)	
Neurofibroma		1 (0%)
RESPIRATORY SYSTEM		
*Nasal turbinate	(118)	(250)
Squamous cell carcinoma		1 (0%)
Adenocarcinoma, NOS		1 (0%)
#Trachea	(117)	(250)
Follicular cell carcinoma, invasive		1 (0%)
#Lung	(118)	(250)
Squamous cell carcinoma, metastatic		1 (0%)
Adenocarcinoma, NOS, metastatic	1 (1%)	2 (1%)
Alveolar/bronchiolar adenoma		1 (0%)
Alveolar/bronchiolar carcinoma	1 (1%)	2 (1%)
Cortical carcinoma, metastatic	1 (1%)	
C-cell carcinoma, metastatic		1 (0%)
Granulosa cell carcinoma, metastatic	1 (1%)	
Pheochromocytoma, metastatic		1 (0%)
Liposarcoma, metastatic		1 (0%)
HEMATOPOIETIC SYSTEM		
*Multiple organs	(118)	(250)
Malignant lymphoma, lymphocytic type		1 (0%)
Myelomonocytic leukemia		4 (2%)
Monocytic leukemia	41 (35%)	118 (47%)
Leukemia, mononuclear cell	1 (1%)	
#Spleen	(118)	(250)
Fibrosarcoma	1 (1%)	
#Mandibular lymph node	(118)	(250)
Squamous cell carcinoma, metastatic		2 (1%)
#Axillary lymph node	(118)	(250)
Sarcoma, NOS, metastatic	1 (1%)	
#Liver	(118)	(250)
Monocytic leukemia	2 (2%)	
#Thymus	(91)	(187)
Thymoma		1 (1%)

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
CIRCULATORY SYSTEM		
#Heart	(117)	(250)
Alveolar/bronchiolar carcinoma, metastatic		1 (0%)
#Myocardium	(117)	(250)
Neurilemoma	1 (1%)	
DIGESTIVE SYSTEM		
*Oral mucous membrane	(118)	(250)
Squamous cell papilloma	1 (1%)	
Squamous cell carcinoma		3 (1%)
*Tongue	(118)	(250)
Squamous cell carcinoma	1 (1%)	
*Tooth	(118)	(250)
Squamous cell carcinoma, invasive		1 (0%)
#Salivary gland	(117)	(248)
Fibrosarcoma		1 (0%)
#Liver	(118)	(250)
Neoplastic nodule	3 (3%)	6 (2%)
Hepatocellular carcinoma		1 (0%)
#Pancreas	(118)	(249)
Acinar cell adenoma	2 (2%)	5 (2%)
Acinar cell carcinoma		1 (0%)
*Pharynx	(118)	(250)
Squamous cell carcinoma		1 (0%)
#Stomach	(118)	(250)
Carcinoma, NOS		1 (0%)
Squamous cell papilloma		1 (0%)
Squamous cell carcinoma		1 (0%)
Adenomatous polyp, NOS		1 (0%)
#Duodenum	(118)	(250)
Leiomyoma	1 (1%)	
#Jejunum	(118)	(250)
Carcinoid tumor, malignant		1 (0%)
Mucinous cystadenocarcinoma	1 (1%)	
Leiomyosarcoma	1 (1%)	
URINARY SYSTEM		
#Kidney	(117)	(250)
Tubular cell adenoma	2 (2%)	
Tubular cell adenocarcinoma	1 (1%)	
Lipoma	1 (1%)	
Mixed tumor, malignant	1 (1%)	
ENDOCRINE SYSTEM		
#Pituitary	(116)	(247)
Carcinoma, NOS	9 (8%)	8 (3%)
Adenoma, NOS	42 (36%)	101 (41%)
#Adrenal	(118)	(250)
Cortical adenoma	4 (3%)	18 (7%)
Cortical carcinoma	2 (2%)	1 (0%)
Pheochromocytoma	14 (12%)	36 (14%)
Pheochromocytoma, malignant		3 (1%)
Ganglioneuroma		2 (1%)
#Adrenal medulla	(118)	(250)
Pheochromocytoma	3 (3%)	3 (1%)
Pheochromocytoma, malignant	2 (2%)	

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
ENDOCRINE SYSTEM (Continued)		
#Thyroid	(117)	(250)
Follicular cell adenoma	8 (7%)	8 (3%)
Follicular cell carcinoma	3 (3%)	2 (1%)
C-cell adenoma	4 (3%)	23 (9%)
C-cell carcinoma	12 (10%)	46 (18%)
#Parathyroid	(108)	(224)
Adenoma, NOS	1 (1%)	1 (0%)
#Pancreatic islets	(118)	(249)
Islet cell adenoma	2 (2%)	5 (2%)
Islet cell carcinoma	3 (3%)	6 (2%)
REPRODUCTIVE SYSTEM		
*Mammary gland	(118)	(250)
Adenoma, NOS	2 (2%)	1 (0%)
Adenocarcinoma, NOS	16 (14%)	23 (9%)
Fibroadenoma	48 (41%)	112 (45%)
*Preputial gland	(118)	(250)
Carcinoma, NOS		1 (0%)
Squamous cell carcinoma	4 (3%)	22 (9%)
Basal cell carcinoma	1 (1%)	
Adenoma, NOS	1 (1%)	2 (1%)
Keratoacanthoma		1 (0%)
#Uterus	(116)	(248)
Adenocarcinoma, NOS	1 (1%)	2 (1%)
Papillary adenoma	1 (1%)	1 (0%)
Leiomyoma		1 (0%)
Leiomyosarcoma	1 (1%)	
Endometrial stromal polyp	19 (16%)	38 (15%)
Endometrial stromal sarcoma	1 (1%)	3 (1%)
#Cervix uteri	(116)	(248)
Squamous cell carcinoma		1 (0%)
Sarcoma, NOS		1 (0%)
Endometrial stromal sarcoma, invasive		1 (0%)
#Uterus/endometrium	(116)	(248)
Papillary adenoma		1 (0%)
#Fallopian tube	(116)	(248)
Granulosa cell carcinoma, invasive	1 (1%)	
#Ovary	(116)	(248)
Granulosa cell tumor	1 (1%)	4 (2%)
Granulosa cell carcinoma	1 (1%)	1 (0%)
NERVOUS SYSTEM		
#Brain/meninges	(118)	(248)
Meningioma	1 (1%)	
#Cerebrum	(118)	(248)
Carcinoma, NOS, invasive	4 (3%)	5 (2%)
Glioma, invasive	1 (1%)	
Astrocytoma		1 (0%)
Meningioma	1 (1%)	
#Brain	(118)	(248)
Carcinosarcoma, metastatic	1 (1%)	
#Cerebellum	(118)	(248)
Carcinoma, NOS, invasive	3 (3%)	3 (1%)
Granular cell tumor, NOS	1 (1%)	
Glioma, NOS	1 (1%)	
Astrocytoma	1 (1%)	

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
NERVOUS SYSTEM (Continued)		
#Medulla oblongata	(118)	(248)
Astrocytoma, invasive		1 (0%)
*Spinal cord	(118)	(250)
Astrocytoma	1 (1%)	
SPECIAL SENSE ORGANS		
*Eyelid	(118)	(250)
Squamous cell carcinoma		1 (0%)
*Eye/conjunctiva	(118)	(250)
Squamous cell carcinoma, invasive	1 (1%)	
*Harderian gland	(118)	(250)
Squamous cell carcinoma	1 (1%)	
Squamous cell carcinoma, metastatic	1 (1%)	
*Zymbal gland	(118)	(250)
Carcinoma in-situ, NOS		1 (0%)
Squamous cell papilloma		1 (0%)
Squamous cell carcinoma		4 (2%)
Carcinosarcoma	1 (1%)	
MUSCULOSKELETAL SYSTEM		
*Skull	(118)	(250)
Squamous cell carcinoma, invasive	1 (1%)	
*Maxilla	(118)	(250)
Squamous cell carcinoma, invasive		1 (0%)
*Mandible	(118)	(250)
Squamous cell carcinoma, invasive		3 (1%)
BODY CAVITIES		
*Mediastinum	(118)	(250)
Mesothelioma, malignant		1 (0%)
ALL OTHER SYSTEMS		
*Multiple organs	(118)	(250)
Squamous cell carcinoma, invasive		2 (1%)
Squamous cell carcinoma, metastatic		1 (0%)
Adenocarcinoma, NOS, invasive	1 (1%)	
Alveolar/bronchiolar carcinoma, metastatic	1 (1%)	
C-cell carcinoma, metastatic	1 (1%)	1 (0%)
Endometrial stromal sarcoma, invasive	1 (1%)	2 (1%)
Carcinosarcoma, invasive	1 (1%)	
Mesothelioma, invasive		1 (0%)
Orbital region		
Squamous cell carcinoma, metastatic	1	
Adipose tissue		
Cortical carcinoma, invasive		1

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
ANIMAL DISPOSITION SUMMARY		
Animals initially in study	118	250
Natural death	21	30
Moribund sacrifice	85	195
Terminal sacrifice	12	25
TUMOR SUMMARY		
Total animals with primary tumors**	115	242
Total primary tumors	291	661
Total animals with benign tumors	91	190
Total benign tumors	166	378
Total animals with malignant tumors	80	187
Total malignant tumors	120	273
Total animals with secondary tumors##	17	28
Total secondary tumors	24	36
Total animals with tumors-- uncertain benign or malignant	5	10
Total uncertain tumors	5	10

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

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS: UNTREATED CONTROL

ANIMAL NUMBER	57	59	64	60	57	58	62	61	56	59	63	55	56	64	55	56	56	63	56	61	63	65	62	65	65
	78	44	00	04	79	82	23	66	88	98	77	88	11	66	11	00	22	07	67	88	32	52	22	88	55
WEEKS ON STUDY	06	07	07	07	08	08	08	08	08	08	08	09	09	09	09	09	09	09	09	09	09	09	09	09	09
	00	00	00	79	33	33	44	55	66	77	87	11	11	11	22	22	33	44	55	55	55	52	66	66	77
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																								X	
Basal cell carcinoma																									
Trichoepithelioma																									
Fibroma																									
Fibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, invasive																									
Sarcoma, NOS																									
Fibroma																									
Fibrosarcoma																									
Lipoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic																									
Alveolar/bronchiolar carcinoma																									
Cortical carcinoma, metastatic																									
Granulosa cell carcinoma, metastatic																							X		
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS, metastatic																									
Thymus	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neurilemoma																									
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										X															
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Monocytic leukemia	X																								
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Esophagus	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma																									
Leiomyoma																									
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																									
Tubular cell adenocarcinoma																									
Lipoma																									
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

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

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

ANIMAL NUMBER	66 60	66 64	65 44	65 59	61 12	56 65	57 72	60 01	61 11	64 43	61 33	62 44	65 51	63 11	63 34	65 56	66 11	57 73	58 81	62 26	66 67	55 54	56 99	57 66	61 10
WEEKS ON STUDY	09 98	09 98	10 00	10 02	10 03	10 04	10 04	10 04	10 04	10 04	10 05	10 06	10 08	11 10	11 10	11 10	11 10	11 11	11 14	11 14	11 14	11 15	11 15	11 17	11 17
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Basal cell carcinoma																									
Trichoepithelioma																									
Fibroma																									
Fibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, invasive																									
Sarcoma, NOS																									
Fibroma	X	X																					X		
Fibrosarcoma																									
Lipoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic																									
Alveolar/bronchiolar carcinoma																									
Cortical carcinoma, metastatic																									
Granulosa cell carcinoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS, metastatic																									
Thymus	+	+	+	–	+	–	+	+	–	+	–	+	+	+	+	–	–	+	+	–	+	+	–	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neurilemoma																									
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																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule															X										
Monocytic leukemia																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma																									
Leiomyoma																									
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																									
Tubular cell adenocarcinoma																									
Lipoma																						X			
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+

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

ANIMAL NUMBER	63 6	55 9	56 4	57 4	58 3	58 9	55 7	58 4	60 8	59 2	60 6	55 0	60 2	61 4	60 3	64 1	66 3	64 5	55 6	58 5	58 7	59 5	61 5	62 5	66 2
WEEKS ON STUDY	117	118	118	118	118	118	121	121	122	123	124	125	125	125	126	126	126	127	128	128	128	128	128	128	129
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Basal cell carcinoma																									
Trichoepithelioma																									
Fibroma																									
Fibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, invasive						X																			
Sarcoma, NOS																									
Fibroma																									
Fibrosarcoma																									
Lipoma											X					X									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic																									
Alveolar/bronchiolar carcinoma																									
Cortical carcinoma, metastatic																									
Granulosa cell carcinoma, metastatic																									
Trachea	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS, metastatic																									
Thymus	–	+	–	–	+	+	+	+	+	–	–	–	+	–	+	–	+	+	–	–	+	–	+	+	–
CIRCULATORY SYSTEM																									
Heart	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neurilemoma																									
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																									
Salivary gland	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule		X																							
Monocytic leukemia																							X		
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma																	X								
Leiomyoma																									
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																									
Tubular cell adenocarcinoma																									
Lipoma																									
Mixed tumor, malignant																				X					
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

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

ANIMAL NUMBER	55 55	56 63	60 09	57 55	61 99	63 33	55 52	58 88	59 97	60 05	66 65	57 77	60 07	62 67	64 88	59 99	64 49	65 57	57 00	59 00	55 53	58 86	63 35	58 80	59 96
WEEKS ON STUDY	130	130	130	131	131	131	134	134	134	134	134	135	136	136	136	137	137	137	138	138	140	141	141	143	143
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Basal cell carcinoma																						X			
Trichoepithelioma																X									
Fibroma																	X								
Fibrosarcoma																						X			
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, invasive																									
Sarcoma, NOS																				X					
Fibroma														X									X		
Fibrosarcoma													X												
Lipoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic														X											
Alveolar/bronchiolar carcinoma						X																			
Cortical carcinoma, metastatic																									
Granulosa cell carcinoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS, metastatic																				X					
Thymus	+	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neurilemoma				X																					
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																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule													X												
Monocytic leukemia																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mucinous cystadenocarcinoma																									
Leiomyoma																									
Leiomyosarcoma					X																				
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																									
Tubular cell adenocarcinoma																							X		
Lipoma																									
Mixed tumor, malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

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

ANIMAL NUMBER	62 0	66 6	65 3	56 6	57 1	59 1	59 3	60 0	61 7	62 1	62 8	62 9	63 8	63 9	64 2	64 4	64 7	65 0	TOTAL TISSUES TUMORS
WEEKS ON STUDY	14 3	14 3	14 4	14 5	14 5	14 5	14 5	14 5	14 5	14 5	14 5	14 5	14 5	14 5	14 5	14 5	14 5	14 5	
INTEGUMENTARY SYSTEM																			
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*118
Squamous cell carcinoma																			1
Basal cell carcinoma																			1
Trichoepithelioma																			1
Fibroma																			1
Fibrosarcoma																X			2
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*118
Squamous cell carcinoma, invasive																			1
Sarcoma, NOS																			1
Fibroma																			5
Fibrosarcoma																			1
Lipoma																			2
RESPIRATORY SYSTEM																			
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	118
Adenocarcinoma, NOS, metastatic																			1
Alveolar/bronchiolar carcinoma																			1
Cortical carcinoma, metastatic																	X		1
Granulosa cell carcinoma, metastatic																			1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
HEMATOPOIETIC SYSTEM																			
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	116
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	118
Fibrosarcoma						X													1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	118
Sarcoma, NOS, metastatic																			1
Thymus	−	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	91
CIRCULATORY SYSTEM																			
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Neurilemoma																			1
DIGESTIVE SYSTEM																			
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Squamous cell papilloma	X																		1
Squamous cell carcinoma																			1
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	118
Neoplastic nodule																			3
Monocytic leukemia																			2
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	118
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	118
Acinar cell adenoma						X		X											2
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	116
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	118
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	118
Mucinous cystadenocarcinoma																			1
Leiomyoma																X			1
Leiomyosarcoma																			1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	118
URINARY SYSTEM																			
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Tubular cell adenoma							X						X						2
Tubular cell adenocarcinoma																			1
Lipoma																			1
Mixed tumor, malignant																			1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	116

* Animals necropsied

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

ANIMAL NUMBER	578	594	640	604	579	582	623	616	568	598	637	558	561	646	551	560	562	630	567	618	632	652	622	658	655
WEEKS ON STUDY	060	070	070	079	083	083	084	085	086	087	087	091	091	091	092	092	093	094	095	095	095	095	096	096	097
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS														X											
Adenoma, NOS		X		X	X	X	X				X	X										X			
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Cortical carcinoma																									
Pheochromocytoma							X																		
Pheochromocytoma, malignant																					X				
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																X		X							
Follicular cell carcinoma																									
C cell adenoma																									
C-cell carcinoma																									
Parathyroid	+	+	+	+	+	+	+	+	–	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS			X																						
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
Squamous cell carcinoma																									
Basal cell carcinoma																									
Adenoma, NOS																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Papillary adenoma																									
Granulosa cell carcinoma, invasive																							X		
Leiomyosarcoma																									
Endometrial stromal polyp													X												
Endometrial stromal sarcoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor																									
Granulosa cell carcinoma																							X		
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Carcinosarcoma, metastatic																									
Granular cell tumor, NOS																									
Glioma, NOS																									
Glioma, invasive																									
Astrocytoma																									
Meningioma																									
Spinal cord	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
Astrocytoma																									
SPECIAL SENSE ORGANS																									
Eye appendages	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																									
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
Squamous cell carcinoma																									
Squamous cell carcinoma, metastatic																								X	
Zymbal 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
Carcinosarcoma																									
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
Squamous cell carcinoma, invasive																								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
Adenocarcinoma, NOS, invasive																									
Alveolar/bronchiolar carcinoma, metastatic																									
C-cell carcinoma, metastatic																									
Endometrial stromal sarcoma, invasive																									
Carcinosarcoma, invasive																									
Monocytic leukemia					X		X					X		X	X				X						
Leukemia, mononuclear cell	X																								
Orbital region																									
Squamous cell carcinoma, metastatic																								X	

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

ANIMAL NUMBER	66 60	66 64	65 54	65 59	61 12	56 65	57 72	60 01	61 11	64 43	61 13	62 24	65 51	63 31	63 34	65 56	66 61	57 73	58 81	62 26	66 67	55 54	56 89	57 76	61 10
WEEKS ON STUDY	09 8	09 8	10 0	10 2	10 3	10 4	10 4	10 4	10 4	10 4	10 5	10 6	10 8	11 0	11 0	11 0	11 0	11 1	11 4	11 4	11 4	11 5	11 5	11 7	11 7
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS		X	X			X		X		X		X	X	X										X	
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Cortical carcinoma												X													
Pheochromocytoma									X	X													X		
Pheochromocytoma, malignant																			X						
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																									
C-cell adenoma																									
C-cell carcinoma																					X				
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	−	+	+	−
Adenoma, NOS																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																								X	
Adenocarcinoma, NOS																									X
Fibroadenoma	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
Squamous cell carcinoma																									
Basal cell carcinoma																									
Adenoma, NOS																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+
Adenocarcinoma, NOS																									
Papillary adenoma																									
Granulosa cell carcinoma, invasive																									
Leiomyosarcoma																									
Endometrial stromal polyp			X	X		X							X				X		X					X	
Endometrial stromal sarcoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+
Granulosa cell tumor																									
Granulosa cell carcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Carcinosarcoma, metastatic																									
Granular cell tumor, NOS																									
Glioma, NOS																									
Glioma, invasive																									
Astrocytoma											X														
Meningioma																									
Spinal cord	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
Astrocytoma																									
SPECIAL SENSE ORGANS																									
Eye appendages	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																									
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
Squamous cell carcinoma																									
Squamous cell carcinoma, metastatic																									
Zymbal 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
Carcinosarcoma																									
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
Squamous cell carcinoma, 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, invasive																									
Alveolar/bronchiolar carcinoma, metastatic																									
C-cell carcinoma, metastatic																									
Endometrial stromal sarcoma, invasive																									
Carcinosarcoma, invasive																									
Monocytic leukemia			X		X							X			X	X		X	X	X	X	X			X
Leukemia, mononuclear cell																									
Orbital region																									
Squamous cell carcinoma, metastatic																									

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

ANIMAL NUMBER	63 36	55 59	56 64	57 74	58 83	58 89	55 57	58 84	60 08	59 92	60 06	55 50	60 02	61 14	60 03	64 41	66 63	64 45	55 56	58 85	58 87	59 95	61 15	62 25	66 62
WEEKS ON STUDY	117	118	118	118	118	118	121	121	122	123	124	125	125	125	126	126	126	127	128	128	128	128	128	128	129
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS				X			X					X						X							
Adenoma, NOS	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																		
C-cell adenoma									X																
C-cell carcinoma													X									X			X
Parathyroid	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	–	+
Adenoma, NOS																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma											X						X								
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS							X																		
Adenocarcinoma, NOS								X				X	X		X										
Fibroadenoma				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
Squamous cell carcinoma																									
Basal cell carcinoma																									
Adenoma, NOS																		X							
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Papillary adenoma																									
Granulosa cell carcinoma, invasive																									
Leiomyosarcoma																									
Endometrial stromal polyp				X							X		X											X	
Endometrial stromal sarcoma										X															
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor																									
Granulosa cell carcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive				@X			X											X							
Carcinosarcoma, metastatic																X									
Granular cell tumor, NOS																									
Glioma, NOS																									
Glioma, invasive																									
Astrocytoma																									
Meningioma																									
Spinal cord	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Astrocytoma		X																							
SPECIAL SENSE ORGANS																									
Eye appendages	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						X																			
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
Squamous cell carcinoma						X																			
Squamous cell carcinoma, metastatic																									
Zymbal 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
Carcinosarcoma																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
Squamous cell carcinoma, 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, invasive																									
Alveolar/bronchiolar carcinoma, metastatic																									
C-cell carcinoma, metastatic													X												
Endometrial stromal sarcoma, invasive										X															
Carcinosarcoma, invasive																X									
Monocytic leukemia			X						X						X						X	X		X	
Leukemia, mononuclear cell																									
Orbital region																									
Squamous cell carcinoma, metastatic																									

@ Multiple occurrence of morphology

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

ANIMAL NUMBER	555	563	609	575	619	633	552	588	597	605	665	577	607	627	648	599	649	657	570	590	553	586	635	580	596
WEEKS ON STUDY	130	130	130	131	131	131	134	134	134	134	134	135	136	136	136	137	137	137	138	138	140	141	141	143	143
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS															X										X
Adenoma, NOS	X	X		X	X		X		X				X				X	X							
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Cortical carcinoma																									
Pheochromocytoma			X	X	X		X	X																	
Pheochromocytoma, malignant																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma			X						X						X										
Follicular cell carcinoma											X														
C-cell adenoma									X																
C-cell carcinoma							X							X				X						X	
Parathyroid	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																			X						
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
Islet cell carcinoma																							X		X
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS						X											X	X	X					X	
Fibroadenoma	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
Squamous cell carcinoma																		X							
Basal cell carcinoma																									
Adenoma, NOS																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS														X											
Papillary adenoma																									
Granulosa cell carcinoma, invasive																									
Leiomyosarcoma				X																					
Endometrial stromal polyp					X						X					X			X						
Endometrial stromal sarcoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor											X														
Granulosa cell carcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive															X										X
Carcinosarcoma, metastatic																									
Granular cell tumor, NOS																						X			
Glioma, NOS																									
Glioma, invasive																									
Astrocytoma																									
Meningioma																									
Spinal cord	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
Astrocytoma																									
SPECIAL SENSE ORGANS																									
Eye appendages	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																									
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
Squamous cell carcinoma																									
Squamous cell carcinoma, metastatic																									
Zymbal 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
Carcinosarcoma																									
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
Squamous cell carcinoma, 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, invasive														X											
Alveolar/bronchiolar carcinoma, metastatic						X																			
C cell carcinoma, metastatic																									
Endometrial stromal sarcoma, invasive																									
Carcinosarcoma, invasive																									
Monocytic leukemia	X	X	X				X	X	X	X		X				X	X			X		X	X	X	
Leukemia, mononuclear cell																									
Orbital region																									
Squamous cell carcinoma, metastatic																									

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

ANIMAL NUMBER	62 20	66 66	65 53	56 56	57 71	59 91	59 93	60 00	61 17	62 21	62 28	62 29	63 38	63 39	64 42	64 44	64 47	65 50	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	14 43	14 43	14 44	14 45	14 45	14 45	14 45	14 45	14 45	14 45	14 45	14 45	14 45	14 45	14 45	14 45	14 45	14 45	
ENDOCRINE SYSTEM																			
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	116
Carcinoma, NOS			X			X													9
Adenoma, NOS				X	X		X		X	X	X				X			X	42
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	118
Cortical adenoma							X					X	X						4
Cortical carcinoma																	X		2
Pheochromocytoma	X	X			X	X				X	X		X	X					17
Pheochromocytoma, malignant																			2
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	117
Follicular cell adenoma												X							8
Follicular cell carcinoma					X														3
C-cell adenoma											X						X		4
C-cell carcinoma			X										X		X	X			12
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	108
Adenoma, NOS																			1
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	118
Islet cell adenoma																			2
Islet cell carcinoma		X																	3
REPRODUCTIVE SYSTEM																			
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*118
Adenoma, NOS																			2
Adenocarcinoma, NOS		X	X				X									X		X	16
Fibroadenoma	X	X		X			X	X	X			X	X	X	X	X			48
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Squamous cell carcinoma	X								X		X								4
Basal cell carcinoma						X													1
Adenoma, NOS																			1
Uterus	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	116
Adenocarcinoma, NOS																			1
Papillary adenoma																X			1
Granulosa cell carcinoma, invasive																			1
Leiomyosarcoma																			1
Endometrial stromal polyp				X											X		X		19
Endometrial stromal sarcoma																			1
Ovary	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	116
Granulosa cell tumor																			1
Granulosa cell carcinoma																			1
NERVOUS SYSTEM																			
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	118
Carcinoma, NOS, invasive			X																6
Carcinosarcoma, metastatic																			1
Granular cell tumor, NOS																			1
Glioma, NOS		X																	1
Glioma, invasive		X																	1
Astrocytoma																			1
Meningioma																	@X		1
Spinal cord	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Astrocytoma																			1
SPECIAL SENSE ORGANS																			
Eye appendages	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Squamous cell carcinoma, invasive																			1
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Squamous cell carcinoma																			1
Squamous cell carcinoma, metastatic																			1
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Carcinosarcoma																			1
MUSCULOSKELETAL SYSTEM																			
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Squamous cell carcinoma, invasive																			1
ALL OTHER SYSTEMS																			
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*118
Adenocarcinoma, NOS, invasive																			1
Alveolar/bronchiolar carcinoma, meta																			1
C-cell carcinoma, metastatic																			1
Endometrial stromal sarcoma, invasive																			1
Carcinosarcoma, invasive																			1
Monocytic leukemia		X					X		X						X				41
Leukemia, mononuclear cell																			1
Orbital region																			
Squamous cell carcinoma, metastatic																			1

* Animals necropsied
@ Multiple occurrence of morphology

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS: 1% CROCIDOLITE ASBESTOS

ANIMAL NUMBER	0001	0023	1008	0889	1288	1558	0009	0091	0997	1331	9889	0110	9992	9770	9443	9551	0551	0337	0220	0766	1449	0229	1009	0116	0990
WEEKS ON STUDY	0455	0553	0557	0680	0660	0663	0771	0774	0776	0776	0776	0778	0778	0881	0882	0882	0883	0886	0887	0887	0887	0892	0997	0998	0998
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																									
Basal cell tumor																									
Keratoacanthoma																									
Fibrosarcoma																									
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma, invasive																									
Follicular cell carcinoma, invasive																									
Sarcoma, NOS																									
Fibroma																									
Fibrosarcoma																									
Neurofibroma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Adenocarcinoma, NOS, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma, invasive																									
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
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	–	+	–	–	+	+	–	–	+	+	+	+	+
Thymoma, benign																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, 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	N
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+
Acinar cell adenoma																									
Acinar cell carcinoma																									
Esophagus	–	–	–	–	–	–	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma							X																		
Squamous cell carcinoma																		X							
Adenomatous polyp, NOS																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoid tumor, malignant		X																							
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

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

ANIMAL NUMBER	9 9 8	9 4 0	9 4 8	0 6 0	9 2 9	9 3 5	0 0 8	1 1 3	1 4 1	9 7 8	9 4 7	9 5 3	9 6 3	1 1 9	1 2 2	0 0 4	0 4 8	0 5 0	0 6 9	0 8 0	1 6 1	9 7 5	9 3 9	0 5 8	1 2 7
WEEKS ON STUDY	0 9 8	0 9 9	0 9 9	1 0 0	1 0 0	1 0 0	1 0 1	1 0 1	1 0 1	1 0 1	1 0 2	1 0 2	1 0 2	1 0 3	1 0 3	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 6	1 0 7	1 0 7
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																									
Basal cell tumor																									
Keratoacanthoma																									
Fibrosarcoma																									
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma, invasive																									
Follicular cell carcinoma, invasive																									
Sarcoma, NOS																									
Fibroma											X														
Fibrosarcoma																									
Neurofibroma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Adenocarcinoma, NOS, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma, invasive																									
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
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Thymus	−	+	−	+	+	+	+	−	+	−	−	+	+	−	+	−	−	+	−	+	+	+	−	−	−
Thymoma, benign																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, 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	N
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																									
Salivary gland	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma														X											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Adenomatous polyp, NOS																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoid tumor, malignant																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

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

ANIMAL NUMBER	97 9	13 8	15 6	91 8	01 3	07 7	15 5	93 1	93 2	02 5	04 3	07 4	12 4	99 0	99 5	08 8	12 0	16 7	92 1	92 3	92 6	04 4	06 7	11 4	15 9
WEEKS ON STUDY	10 7	10 8	10 8	10 8	10 9	10 9	10 9	10 9	10 9	11 0	11 0	11 0	11 0	11 0	11 0	11 1	11 1	11 1	11 1	11 1	11 1	11 2	11 2	11 2	11 2
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																									
Basal cell tumor																									
Keratoacanthoma																									
Fibrosarcoma																									
Neurofibrosarcoma																			X						
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma, invasive																									
Follicular cell carcinoma, invasive																									
Sarcoma, NOS																									
Fibroma																									
Fibrosarcoma					X																				
Neurofibroma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic					X																				
Adenocarcinoma, NOS, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma, invasive																									
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
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Thymus	+	+	+	+	–	–	+	+	+	+	–	–	–	–	+	–	+	–	+	–	+	+	–	+	–
Thymoma, benign																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, 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	N
Squamous cell carcinoma								X																	
Squamous cell carcinoma, invasive																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Adenomatous polyp, NOS																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoid tumor, malignant																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+

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

ANIMAL NUMBER	92 20	92 28	93 30	14 48	09 92	10 00	16 60	03 35	05 54	15 52	94 49	96 60	05 53	13 37	13 39	99 96	06 64	16 63	02 27	03 31	14 47	93 38	95 58	98 83	00 07
WEEKS ON STUDY	112	112	112	113	114	114	114	115	115	115	115	115	116	116	116	116	117	117	118	118	118	118	118	118	119
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																									
Basal cell tumor																									
Keratoacanthoma																									
Fibrosarcoma																									
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma, invasive																									
Follicular cell carcinoma, invasive																									
Sarcoma, NOS																									
Fibroma																									
Fibrosarcoma																									
Neurofibroma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Adenocarcinoma, NOS, metastatic						X																			
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																				X					
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma, invasive																									
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
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Thymus	–	+	+	–	+	+	+	+	+	–	+	+	+	–	+	+	+	+	–	–	–	+	+	+	–
Thymoma, benign																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, 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	N
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																	X								
Hepatocellular carcinoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Adenomatous polyp, NOS																				X					
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoid tumor, malignant																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

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

ANIMAL NUMBER	011	106	111	126	154	980	997	066	071	078	162	985	006	057	105	165	924	994	017	079	093	993	033	034	101
WEEKS ON STUDY	119	119	119	119	119	119	120	121	121	121	121	121	122	122	122	122	122	122	123	123	123	123	124	124	124
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																			X						
Basal cell tumor																									
Keratoacanthoma																									
Fibrosarcoma																									
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma, invasive																									
Follicular cell carcinoma, invasive																									
Sarcoma, NOS									X																
Fibroma																								X	
Fibrosarcoma																									
Neurofibroma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Adenocarcinoma, NOS, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma, invasive																									
Nasal cavity	+	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																			X						
Adenocarcinoma, NOS																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Thymus	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymoma, benign																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, 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	N
Squamous cell carcinoma	X														X										
Squamous cell carcinoma, invasive																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma	X																								
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Adenomatous polyp, NOS																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoid tumor, malignant																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

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

ANIMAL NUMBER	1 0 4	9 1 9	0 3 8	0 4 7	0 6 1	1 6 4	9 5 2	9 7 2	0 2 6	0 5 9	0 7 2	9 7 6	9 7 7	9 8 7	0 3 0	1 0 7	1 5 0	0 4 0	0 5 6	1 0 3	1 4 3	9 3 7	9 6 4	0 0 5	0 1 2
WEEKS ON STUDY	1 2 4	1 2 4	1 2 5	1 2 5	1 2 5	1 2 5	1 2 5	1 2 5	1 2 6	1 2 6	1 2 6	1 2 6	1 2 6	1 2 6	1 2 7	1 2 7	1 2 7	1 2 8	1 2 8	1 2 8	1 2 8	1 2 8	1 2 8	1 2 9	1 2 9
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma						X																			
Squamous cell carcinoma, invasive																									
Basal cell tumor																									
Keratoacanthoma																									
Fibrosarcoma																									
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																			X						
Squamous cell carcinoma, invasive																									
Follicular cell carcinoma, invasive																									
Sarcoma, NOS																									
Fibroma																									
Fibrosarcoma									X																
Neurofibroma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Adenocarcinoma, NOS, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																X									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma, invasive																									
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
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic													X												
Thymus	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+
Thymoma, benign																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic																X									
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 carcinoma																									
Squamous cell carcinoma, invasive																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule														X	X							X			
Hepatocellular carcinoma															X										
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma								X																	
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Adenomatous polyp, NOS																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoid tumor, malignant																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

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

ANIMAL NUMBER	0212	0715	1233	1134	1336	1442	9442	9986	0118	0886	0073	0096	9554	9666	0882	0099	1117	1551	1557	0445	0449	0665	0995	1221	9611
WEEKS ON STUDY	129	129	129	129	129	129	129	129	130	130	131	131	131	131	132	132	132	132	132	133	134	134	134	134	134
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																									
Basal cell tumor																					X				
Keratoacanthoma																									
Fibrosarcoma															X										
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma, invasive																									
Follicular cell carcinoma, invasive																									
Sarcoma, NOS																									
Fibroma																					X				
Fibrosarcoma																		X							
Neurofibroma																		X							
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Adenocarcinoma, NOS, metastatic																									
Alveolar/bronchiolar adenoma			X																						
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic													X												
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma, invasive																									
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
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Thymus	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	−	−	+
Thymoma, benign													X												
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, 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	N
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																				X					
Hepatocellular carcinoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Adenomatous polyp, NOS																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoid tumor, malignant																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−

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

ANIMAL NUMBER	1 2 9	9 7 4	0 3 6	0 9 4	1 1 8	9 4 6	9 5 6	9 6 8	0 5 5	1 1 6	1 4 6	9 5 9	0 1 5	0 7 0	0 9 8	1 4 4	1 1 2	1 3 3	9 9 1	0 6 8	1 0 2	1 6 6	9 2 2	9 4 5	0 4 2
WEEKS ON STUDY	1 3 5	1 3 5	1 3 6	1 3 6	1 3 6	1 3 6	1 3 6	1 3 6	1 3 7	1 3 7	1 3 7	1 3 7	1 3 8	1 3 8	1 3 8	1 3 8	1 3 9	1 3 9	1 3 9	1 4 0	1 4 0	1 4 0	1 4 0	1 4 0	1 4 1
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																									
Basal cell tumor																									
Keratoacanthoma																									
Fibrosarcoma														X											
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Squamous cell carcinoma, invasive																									
Follicular cell carcinoma, invasive	X																								
Sarcoma, NOS																									
Fibroma						X																X			
Fibrosarcoma																									
Neurofibroma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Adenocarcinoma, NOS, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																									
Liposarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma, invasive	X																								
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
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Thymus	+	–	+	+	+	+	+	–	+	+	–	+	–	+	+	–	+	+	+	+	+	–	–	+	+
Thymoma, benign																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, 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	N
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma		X															X								
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
Adenomatous polyp, NOS																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoid tumor, malignant																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

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

ANIMAL NUMBER	13 2	00 0	08 5	94 1	95 7	96 5	96 7	00 2	05 2	06 2	11 0	12 5	14 5	92 7	94 4	98 1	04 1	08 1	08 4	93 4	99 9	00 3	01 4	01 9	02 2
WEEKS ON STUDY	141	142	142	142	142	142	142	143	143	143	143	143	143	143	143	143	144	144	144	144	144	145	145	145	145
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma													X												
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																									
Basal cell tumor																									
Keratoacanthoma											X														
Fibrosarcoma																									
Neurofibrosarcoma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma			X																						
Squamous cell carcinoma, invasive																									
Follicular cell carcinoma, invasive																									
Sarcoma, NOS																									
Fibroma	X							X																	
Fibrosarcoma																									
Neurofibroma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Adenocarcinoma, NOS, metastatic																									
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma										X															
C-cell carcinoma, metastatic																									
Pheochromocytoma, metastatic																				X					
Liposarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma, invasive																									
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
Squamous cell carcinoma																									
Adenocarcinoma, NOS																	X								
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic																									
Thymus	−	+	+	+	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	−	−	+	+
Thymoma, benign																									
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, 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	N
Squamous cell carcinoma																									
Squamous cell carcinoma, invasive																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Hepatocellular carcinoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell adenoma																									
Acinar cell carcinoma																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS										X															
Squamous cell papilloma																									
Squamous cell carcinoma																									
Adenomatous polyp, NOS																									
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoid tumor, malignant																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

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

ANIMAL NUMBER	0 2 4	0 2 8	0 3 2	0 3 9	0 4 6	0 6 3	0 8 3	0 8 7	1 1 5	1 3 0	1 3 5	1 4 0	1 5 3	9 2 5	9 3 3	9 3 6	9 5 0	9 5 5	9 6 2	9 6 9	9 7 1	9 7 3	9 8 2	9 8 4	9 8 8	TOTAL TISSUES TUMORS
WEEKS ON STUDY	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	
INTEGUMENTARY SYSTEM																										
Skin	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*250
Squamous cell papilloma																										1
Squamous cell carcinoma																										1
Squamous cell carcinoma, invasive																										1
Basal cell tumor																										1
Keratoacanthoma																										1
Fibrosarcoma																										2
Neurofibrosarcoma																										1
Subcutaneous tissue	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*250
Squamous cell papilloma																										1
Squamous cell carcinoma, invasive																										1
Follicular cell carcinoma, invasive																										1
Sarcoma, NOS																										1
Fibroma							X																X			9
Fibrosarcoma																										3
Neurofibroma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Squamous cell carcinoma, metastatic																										1
Adenocarcinoma, NOS, metastatic																									X	2
Alveolar/bronchiolar adenoma																										1
Alveolar/bronchiolar carcinoma																										2
C-cell carcinoma, metastatic																										1
Pheochromocytoma, metastatic																										1
Liposarcoma, metastatic																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Follicular cell carcinoma, invasive																										1
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	*250
Squamous cell carcinoma																										1
Adenocarcinoma, NOS																										1
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Squamous cell carcinoma, metastatic			X																							2
Thymus	+	+	+	+	+	−	+	+	+	+	−	−	−	+	+	+	−	+	+	+	+	+	−	+	+	187
Thymoma, benign																										1
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Alveolar/bronchiolar carcinoma, metast																										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	*250
Squamous cell carcinoma																	X									4
Squamous cell carcinoma, invasive																	X									1
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	248
Fibrosarcoma																										1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Neoplastic nodule																				X						6
Hepatocellular carcinoma																										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Acinar cell adenoma	X																									5
Acinar cell carcinoma				X																						1
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	239
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Carcinoma, NOS																										1
Squamous cell papilloma																										1
Squamous cell carcinoma																										1
Adenomatous polyp, NOS																										1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Carcinoid tumor, malignant																										1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	248

* Animals necropsied

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

ANIMAL NUMBER	0001	0023	1008	0889	1288	1558	0091	0091	0097	1331	9889	0110	9992	9970	9443	9951	0551	0337	0220	0766	1449	0229	1096	0116	0990
WEEKS ON STUDY	0455	0553	0557	0600	0600	0633	0711	0744	0766	0766	0766	0778	0778	0781	0822	0822	0833	0866	0877	0877	0877	0992	0997	0998	0998
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS						X		X						X					X				X		
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Cortical carcinoma																									
Pheochromocytoma																						X			
Pheochromocytoma, malignant				X																					
Ganglioneuroma	X			X																					
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS																					X				
Fibroadenoma									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																									
Squamous cell carcinoma																									
Adenoma, NOS																									
Keratoacanthoma																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
Papillary adenoma																									
Sarcoma, NOS																									
Leiomyoma																									
Endometrial stromal polyp					X																		X		
Endometrial stromal sarcoma							X																		
Endometrial stromal sarcoma, invasive																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor																									
Granulosa cell carcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Astrocytoma																									
Astrocytoma, invasive																									
SPECIAL SENSE ORGANS																									
Eye appendages	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																									
Zymbal 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 in situ, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma															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
Squamous cell carcinoma, 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
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
Squamous cell carcinoma, invasive																									
Squamous cell carcinoma, metastatic																									
C cell carcinoma, metastatic																									
Endometrial stromal sarcoma, invasive							X																		
Mesothelioma, invasive																									
Malignant lymphoma, lymphocytic type																									
Myelomonocytic leukemia																									
Monocytic leukemia										X	X	X		X		X	X			X			X		X
Adipose tissue																									
Cortical carcinoma, invasive																									

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

ANIMAL NUMBER	99 98	94 40	94 48	06 60	92 29	93 35	00 08	11 13	14 41	97 78	94 47	95 53	96 63	11 19	12 22	00 04	04 48	05 50	06 69	08 80	16 61	97 75	93 39	05 58	12 27
WEEKS ON STUDY	09 98	09 99	09 99	10 00	10 00	10 00	10 01	10 11	10 11	10 11	10 02	10 02	10 02	10 03	10 03	10 04	10 04	10 04	10 04	10 04	10 04	10 04	10 04	10 08	10 07	10 07
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS						X																			
Adenoma, NOS																	X							X	X
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																X									
Cortical carcinoma																									
Pheochromocytoma																									
Pheochromocytoma, malignant																									
Ganglioneuroma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																									
C cell adenoma																									X
C cell carcinoma		X												X											
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	−	+	+	−	−	+	−	−	−
Adenoma, NOS																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS																									
Fibroadenoma				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																									
Squamous cell carcinoma																									
Adenoma, NOS																									
Keratoacanthoma																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
Papillary adenoma																									
Sarcoma, NOS																									
Leiomyoma																									
Endometrial stromal polyp					X			X		X										X			X		
Endometrial stromal sarcoma																									
Endometrial stromal sarcoma, invasive																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor																									
Granulosa cell carcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive						X																			
Astrocytoma																									
Astrocytoma, invasive																									
SPECIAL SENSE ORGANS																									
Eye appendages	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																									
Zymbal 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 in situ, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma	X																			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
Squamous cell carcinoma, 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
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
Squamous cell carcinoma, invasive	X																								
Squamous cell carcinoma, metastatic																									
C cell carcinoma, metastatic																									
Endometrial stromal sarcoma, invasive																									
Mesothelioma, invasive																									
Malignant lymphoma, lymphocytic type																									
Myelomonocytic leukemia																									
Monocytic leukemia		X	X				X	X		X		X	X		X	X			X		X	X	X		
Adipose tissue																									
Cortical carcinoma, invasive																									

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

ANIMAL NUMBER	97 79	13 38	15 56	91 88	01 33	07 77	15 55	93 31	93 32	02 25	04 43	07 74	12 44	99 90	99 95	08 88	12 20	16 67	92 21	92 23	92 26	04 44	06 67	11 14	15 59
WEEKS ON STUDY	107	108	108	108	109	109	109	109	109	110	110	110	110	110	110	111	111	111	111	111	111	112	112	112	112
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS		X				X	X					X		X	X		X					X			X
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma										X													X		
Cortical carcinoma																									
Pheochromocytoma																									
Pheochromocytoma, malignant																									
Ganglioneuroma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																									
C-cell adenoma						X									X								X		
C-cell carcinoma																X	X								
Parathyroid	+	–	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	–	+	+	+	–	+
Adenoma, NOS																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
Islet cell carcinoma						X																			
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS																									
Fibroadenoma		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																									
Squamous cell carcinoma					X																X		X		
Adenoma, NOS																									
Keratoacanthoma																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
Papillary adenoma																									
Sarcoma, NOS																									
Leiomyoma																									
Endometrial stromal polyp											X	X				X									
Endometrial stromal sarcoma																									
Endometrial stromal sarcoma, invasive																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor																									
Granulosa cell carcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Astrocytoma																									
Astrocytoma, invasive																									
SPECIAL SENSE ORGANS																									
Eye appendages	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																									
Zymbal 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 in situ, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma		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
Squamous cell carcinoma, invasive								@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
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
Squamous cell carcinoma, invasive																									
Squamous cell carcinoma, metastatic																									
C cell carcinoma, metastatic																									
Endometrial stromal sarcoma, invasive																									
Mesothelioma, invasive																									
Malignant lymphoma, lymphocytic type																									
Myelomonocytic leukemia																									
Monocytic leukemia	X		X				X		X	X	X	X	X	X		X						X		X	X
Adipose tissue																									
Cortical carcinoma, invasive																									

@ Multiple occurrence of morphology

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

ANIMAL NUMBER	920	928	930	148	092	100	160	035	054	152	949	960	053	137	139	996	064	163	027	031	147	938	958	983	007
WEEKS ON STUDY	112	112	112	113	114	114	114	115	115	115	115	115	116	116	116	116	117	117	118	118	118	118	118	118	119
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																							X		
Adenoma, NOS	X		X							X	X	X									X			X	
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma															X										
Cortical carcinoma																									
Pheochromocytoma														X						X		X	X	X	
Pheochromocytoma, malignant																					X				
Ganglioneuroma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																			X						
Follicular cell carcinoma																					X				
C-cell adenoma							X																		
C-cell carcinoma		X								X					X					X				X	
Parathyroid	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS						X																			
Fibroadenoma				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																									
Squamous cell carcinoma				X					X																
Adenoma, NOS																								X	
Keratoacanthoma																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
Papillary adenoma							X																		
Sarcoma, NOS																									
Leiomyoma																									
Endometrial stromal polyp	X							X			X						X				X				
Endometrial stromal sarcoma																									
Endometrial stromal sarcoma, invasive																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor																									
Granulosa cell carcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																							@X		
Astrocytoma																						X			
Astrocytoma, invasive																						X			
SPECIAL SENSE ORGANS																									
Eye appendages	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																									
Zymbal 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 in situ, NOS																									
Squamous cell papilloma																				X					
Squamous cell carcinoma																									
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
Squamous cell carcinoma, 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
Mesothelioma, malignant																							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
Squamous cell carcinoma, invasive																									
Squamous cell carcinoma, metastatic																									
C cell carcinoma, metastatic																									
Endometrial stromal sarcoma, invasive																									
Mesothelioma, invasive																							X		
Malignant lymphoma, lymphocytic type																									
Myelomonocytic leukemia																			X						
Monocytic leukemia		X	X	X	X		X	X	X		X		X	X	X	X	X				X	X			X
Adipose tissue																									
Cortical carcinoma, invasive																									

@ Multiple occurrence of morphology

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

ANIMAL NUMBER	011	106	111	126	154	980	997	066	071	078	162	985	006	057	105	165	224	994	017	079	093	993	033	034	101
WEEKS ON STUDY	119	119	119	119	119	119	120	121	121	121	121	121	122	122	122	122	122	122	123	123	123	123	124	124	124
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS							X											X							
Adenoma, NOS		X	X						X	X	X	X	X			X	X			X		X	X		
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma														X						X					X
Cortical carcinoma																									
Pheochromocytoma					X																				
Pheochromocytoma, malignant																									
Ganglioneuroma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma													X												
Follicular cell carcinoma																									
C cell adenoma																				X					
C cell carcinoma		X			X												X					X			
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	–
Adenoma, NOS																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma														X											
Islet cell carcinoma					X																				
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS														X									X	X	
Fibroadenoma	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	
Squamous cell carcinoma														X											X
Adenoma, NOS																									
Keratoacanthoma																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
Papillary adenoma																									
Sarcoma, NOS																		X							
Leiomyoma																									
Endometrial stromal polyp												X													
Endometrial stromal sarcoma														X											
Endometrial stromal sarcoma, invasive														X											
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor																									
Granulosa cell carcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive							X											X							
Astrocytoma																									
Astrocytoma, invasive																									
SPECIAL SENSE ORGANS																									
Eye appendages	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																									
Zymbal 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 in situ, NOS																			X						
Squamous cell papilloma																									
Squamous cell carcinoma																									
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
Squamous cell carcinoma, invasive	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
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
Squamous cell carcinoma, invasive														X											
Squamous cell carcinoma, metastatic																			X						
C cell carcinoma, metastatic																									
Endometrial stromal sarcoma, invasive																									
Mesothelioma, invasive																									
Malignant lymphoma, lymphocytic type																									
Myelomonocytic leukemia	X					X							X												
Monocytic leukemia		X		X	X		X		X		X			X							X	X			X
Adipose tissue																									
Cortical carcinoma, invasive																									

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

ANIMAL NUMBER	1 0 4	9 1 9	0 3 8	0 4 7	0 6 1	1 6 4	9 5 2	9 7 2	0 2 6	0 5 9	0 7 2	9 7 6	9 7 7	9 8 7	0 3 0	1 0 7	1 5 0	0 4 0	0 5 6	1 0 3	1 4 3	9 3 7	9 6 4	0 0 5	0 1 2
WEEKS ON STUDY	1 2 4	1 2 4	1 2 5	1 2 5	1 2 5	1 2 5	1 2 5	1 2 5	1 2 6	1 2 6	1 2 6	1 2 6	1 2 6	1 2 6	1 2 7	1 2 7	1 2 7	1 2 8	1 2 8	1 2 8	1 2 8	1 2 8	1 2 8	1 2 9	1 2 9
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS								X					X												
Adenoma, NOS		X	X		X	X				X	X	X		X				X				X	X		
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma					X																				
Cortical carcinoma																									
Pheochromocytoma					X																			X	
Pheochromocytoma, malignant																									
Ganglioneuroma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																									
C cell adenoma																							X		
C-cell carcinoma		X							X			X									X	X	X		
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	–	+	+	+	+
Adenoma, NOS																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																								X	
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS											X														
Adenocarcinoma, NOS																		X				X			
Fibroadenoma		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																									
Squamous cell carcinoma													X					X			X				
Adenoma, NOS		X																							
Keratoacanthoma																						X			
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																			X						
Adenocarcinoma, NOS																									
Papillary adenoma																					X				
Sarcoma, NOS																									
Leiomyoma														X											
Endometrial stromal polyp								X	X	X								X							
Endometrial stromal sarcoma																									
Endometrial stromal sarcoma, invasive																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor																									
Granulosa cell carcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive													X												
Astrocytoma																									
Astrocytoma, invasive																									
SPECIAL SENSE ORGANS																									
Eye appendages	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													X												
Zymbal 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 in situ, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
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
Squamous cell carcinoma, 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
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
Squamous cell carcinoma, invasive																									
Squamous cell carcinoma, metastatic																									
C cell carcinoma, metastatic																									
Endometrial stromal sarcoma, invasive																									
Mesothelioma, invasive																									
Malignant lymphoma, lymphocytic type																									
Myelomonocytic leukemia																									
Monocytic leukemia	X			X		X		X		X				X	X	X	X		X	X		X	X	X	X
Adipose tissue																									
Cortical carcinoma, invasive																									

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

ANIMAL NUMBER	0211	0755	1233	1334	1336	1442	9442	9886	0118	0886	0773	0996	9554	9666	0882	0999	1117	1551	1557	0445	0449	0665	0995	1221	9611
WEEKS ON STUDY	1299	1299	1299	1299	1299	1299	1299	1299	1300	1300	1311	1311	1311	1311	1322	1322	1322	1322	1322	1323	1334	1334	1334	1334	1334
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		X	X	X							X
Pheochromocytoma, malignant																									
Ganglioneuroma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma													X							X		X			
Follicular cell carcinoma																									
C cell adenoma			X	X				X		X		X													
C-cell carcinoma	X				X												X	X	X				X		
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma	X																						X		
Islet cell carcinoma					X																				
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS							X				X														
Fibroadenoma	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																									
Squamous cell carcinoma			X																						
Adenoma, NOS																									
Keratoacanthoma																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
Papillary adenoma																									
Sarcoma, NOS																									
Leiomyoma																									
Endometrial stromal polyp		X		X										X						X					
Endometrial stromal sarcoma																X									
Endometrial stromal sarcoma, invasive																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–
Granulosa cell tumor				X																					
Granulosa cell carcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Astrocytoma																									
Astrocytoma, invasive																									
SPECIAL SENSE ORGANS																									
Eye appendages	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																									
Zymbal 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 in situ, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
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
Squamous cell carcinoma, 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
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
Squamous cell carcinoma, invasive																									
Squamous cell carcinoma, metastatic																									
C cell carcinoma, metastatic																			X						
Endometrial stromal sarcoma, invasive																X									
Mesothelioma, invasive																									
Malignant lymphoma, lymphocytic type																									
Myelomonocytic leukemia																									
Monocytic leukemia	X		X	X	X		X	X	X	X	X	X						X	X	X					X
Adipose tissue																									
Cortical carcinoma, invasive																									

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

ANIMAL NUMBER	1 2 9	9 7 4	0 3 6	0 9 4	1 1 8	9 4 6	9 5 6	9 6 8	0 5 5	1 1 6	1 4 6	9 5 9	0 1 5	0 7 0	0 9 8	1 4 4	1 1 2	1 3 3	9 9 1	0 6 8	1 0 2	1 6 6	9 2 2	9 4 5	0 4 2
WEEKS ON STUDY	1 3 5	1 3 5	1 3 6	1 3 6	1 3 6	1 3 6	1 3 6	1 3 6	1 3 7	1 3 7	1 3 7	1 3 7	1 3 8	1 3 8	1 3 8	1 3 8	1 3 9	1 3 9	1 3 9	1 4 0	1 4 0	1 4 0	1 4 0	1 4 0	1 4 1
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS	X	X		X			X				X		X	X	X		X	X		X	X				
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma									X			X	X		X	X									
Cortical carcinoma																									
Pheochromocytoma				X		X	X		X	X		X						X							
Pheochromocytoma, malignant																									
Ganglioneuroma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma	X																								
C-cell adenoma													X		X										
C-cell carcinoma						X	X	X								X		X							
Parathyroid	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
Islet cell carcinoma						X																			
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS							X								X			X							
Fibroadenoma	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																									
Squamous cell carcinoma								X	X			X	X												
Adenoma, NOS																									
Keratoacanthoma																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Adenocarcinoma, NOS																									
Papillary adenoma																									
Sarcoma, NOS																									
Leiomyoma																									
Endometrial stromal polyp	X	X				X									X	X									
Endometrial stromal sarcoma																									
Endometrial stromal sarcoma, invasive																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor											X														
Granulosa cell carcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
Astrocytoma																									
Astrocytoma, invasive																									
SPECIAL SENSE ORGANS																									
Eye appendages	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																									
Zymbal 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 in situ, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
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
Squamous cell carcinoma, 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
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
Squamous cell carcinoma, invasive																									
Squamous cell carcinoma, metastatic																									
C-cell carcinoma, metastatic																									
Endometrial stromal sarcoma, invasive																									
Mesothelioma, invasive																									
Malignant lymphoma, lymphocytic type																									
Myelomonocytic leukemia																									
Monocytic leukemia	X				X							X			X	X		X					X	X	
Adipose tissue																									
Cortical carcinoma, invasive																									

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

ANIMAL NUMBER	132	000	085	941	957	965	967	002	052	062	110	125	145	927	944	981	041	081	084	934	999	003	014	019	022
WEEKS ON STUDY	141	142	142	142	142	142	142	143	143	143	143	143	143	143	143	143	144	144	144	144	144	145	145	145	145
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS															X										
Adenoma, NOS	X	X	X	X	X			X		X		X	X			X	X	X	X				X		X
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Cortical carcinoma																		X							
Pheochromocytoma		X			X				X	X		X				X								X	X
Pheochromocytoma, malignant																				X					
Ganghoneuroma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma															X										
Follicular cell carcinoma																									
C cell adenoma								X					X			X					X				X
C cell carcinoma			X			X				X	X	X		X	X		X	X	X						
Parathyroid	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+
Adenoma, NOS																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma					X																				
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adenocarcinoma, NOS								X	X			X							X						
Fibroadenoma	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																									
Squamous cell carcinoma					X																X		X		
Adenoma, NOS																									
Keratoacanthoma																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Adenocarcinoma, NOS																X	X								
Papillary adenoma																									
Sarcoma, NOS																									
Leiomyoma																									
Endometrial stromal polyp								X		X			X	X								X			X
Endometrial stromal sarcoma																									
Endometrial stromal sarcoma, invasive																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor					X				X																
Granulosa cell carcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive															X										
Astrocytoma																									
Astrocytoma, invasive																									
SPECIAL SENSE ORGANS																									
Eye appendages	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																									
Zymbal 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 in situ, NOS																									
Squamous cell papilloma																									
Squamous cell carcinoma																									
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
Squamous cell carcinoma, 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
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
Squamous cell carcinoma, invasive																									
Squamous cell carcinoma, metastatic																									
C cell carcinoma, metastatic																									
Endometrial stromal sarcoma, invasive																									
Mesothelioma, invasive																									
Malignant lymphoma, lymphocytic type																									
Myelomonocytic leukemia																									
Monocytic leukemia		X	X		X			X	X	X	X			X	X		X		X		X			X	X
Adipose tissue																									
Cortical carcinoma, invasive																		X							

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

ANIMAL NUMBER	0 2 4	0 2 8	0 3 2	0 3 9	0 4 6	0 6 3	0 8 3	0 8 7	1 1 5	1 3 0	1 3 5	1 4 0	1 5 3	9 2 5	9 3 3	9 3 6	9 5 0	9 5 5	9 6 2	9 6 9	9 7 1	9 7 3	9 8 2	9 8 4	9 8 8	TOTAL. TISSUES TUMORS
WEEKS ON STUDY	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	1 4 5	
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	247
Carcinoma, NOS																	X									8
Adenoma, NOS		X		X	X		X		X	X	X	X	X					X	X		X		X		X	101
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Cortical adenoma		X		X																X					X	18
Cortical carcinoma																										1
Pheochromocytoma	X					X		X		X		X		X									X	X		39
Pheochromocytoma, malignant																										3
Ganglioneuroma																										2
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250
Follicular cell adenoma		X											X													8
Follicular cell carcinoma																										2
C-cell adenoma	X							X															X	X		23
C cell carcinoma		X	X							X		X				X			X							46
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	224
Adenoma, NOS							X																			1
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249
Islet cell adenoma																										5
Islet cell carcinoma																					X				X	6
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*250
Adenoma, NOS																										1
Adenocarcinoma, NOS						X					X				X				X	X		X			X	23
Fibroadenoma	X	X			X	X	X	X				X	X		X			X		X	X	X	X			112
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	*250
Carcinoma, NOS																										1
Squamous cell carcinoma												X	X	X							X					22
Adenoma, NOS																										2
Keratoacanthoma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	248
Squamous cell carcinoma																										1
Adenocarcinoma, NOS																										2
Papillary adenoma																										2
Sarcoma, NOS																										1
Leiomyoma																										1
Endometrial stromal polyp					X								X												X	38
Endometrial stromal sarcoma																										3
Endometrial stromal sarcoma, invasive																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	248
Granulosa cell tumor																										4
Granulosa cell carcinoma									X																	1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	248
Carcinoma, NOS, invasive																	X									7
Astrocytoma																										1
Astrocytoma, invasive																										1
SPECIAL SENSE ORGANS																										
Eye appendages	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																										1
Zymbal 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 in situ, NOS																										1
Squamous cell papilloma																										1
Squamous cell carcinoma																										4
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
Squamous cell carcinoma, invasive																	X									3
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	*250
Mesothelioma, malignant																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*250
Squamous cell carcinoma, invasive																										2
Squamous cell carcinoma, metastatic																										1
C cell carcinoma, metastatic																										1
Endometrial stromal sarcoma, invasive																										2
Mesothelioma, invasive																										1
Malignant lymphoma, lymphocytic type																	X									1
Myelomonocytic leukemia																										4
Monocytic leukemia															X	X		X			X	X		X		118
Adipose tissue																										
Cortical carcinoma, invasive																										1

* Animals necropsied

TABLE B3. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS

	Control	1% Crocidolite Asbestos
Integumentary System: Fibroma		
Overall Rates (a)	6/118 (5%)	9/250 (4%)
Adjusted Rates (b)	14.5%	15.8%
Terminal Rates (c)	0/15 (0%)	2/29 (7%)
Week of First Observation	98	102
Life Table Test (d)		P=0.307N
Incidental Tumor Test (d)		P=0.345N
Fisher Exact Test (d)		P=0.339N
Integumentary System: Fibroma or Neurofibroma		
Overall Rates (a)	6/118 (5%)	10/250 (4%)
Adjusted Rates (b)	14.5%	16.8%
Terminal Rates (c)	0/15 (0%)	2/29 (7%)
Week of First Observation	98	102
Life Table Test (d)		P=0.373N
Incidental Tumor Test (d)		P=0.416N
Fisher Exact Test (d)		P=0.409N
Integumentary System: Fibroma or Fibrosarcoma		
Overall Rates (a)	9/118 (8%)	14/250 (6%)
Adjusted Rates (b)	26.3%	20.1%
Terminal Rates (c)	1/15 (7%)	2/29 (7%)
Week of First Observation	98	102
Life Table Test (d)		P=0.252N
Incidental Tumor Test (d)		P=0.293N
Fisher Exact Test (d)		P=0.297N
Integumentary System: Fibroma, Neurofibroma, Sarcoma, Fibrosarcoma, or Neurofibrosarcoma		
Overall Rates (a)	10/118 (8%)	16/250 (6%)
Adjusted Rates (b)	29.3%	21.1%
Terminal Rates (c)	1/15 (7%)	2/29 (7%)
Week of First Observation	98	102
Life Table Test (d)		P=0.248N
Incidental Tumor Test (d)		P=0.298N
Fisher Exact Test (d)		P=0.301N
Hematopoietic System: Monocytic Leukemia		
Overall Rates (a)	43/118 (36%)	118/250 (47%)
Adjusted Rates (b)	66.7%	74.9%
Terminal Rates (c)	3/15 (20%)	8/29 (28%)
Week of First Observation	60	76
Life Table Test (d)		P=0.152
Incidental Tumor Test (d)		P=0.032
Fisher Exact Test (d)		P=0.033
Hematopoietic System: Myelomonocytic Leukemia		
Overall Rates (a)	0/118 (0%)	4/250 (2%)
Adjusted Rates (b)	0.0%	2.7%
Terminal Rates (c)	0/15 (0%)	0/29 (0%)
Week of First Observation		118
Life Table Test (d)		P=0.227
Incidental Tumor Test (d)		P=0.238
Fisher Exact Test (d)		P=0.211
Hematopoietic System: All Leukemia		
Overall Rates (a)	43/118 (36%)	122/250 (49%)
Adjusted Rates (b)	66.7%	75.6%
Terminal Rates (c)	3/15 (20%)	8/29 (28%)
Week of First Observation	60	76
Life Table Test (d)		P=0.111
Incidental Tumor Test (d)		P=0.018
Fisher Exact Test (d)		P=0.017

TABLE B3. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Control	1% Crocidolite Asbestos
Pituitary Gland: Adenoma		
Overall Rates (a)	42/116 (36%)	101/247 (41%)
Adjusted Rates (b)	76.0%	82.9%
Terminal Rates (c)	8/14 (57%)	16/29 (55%)
Week of First Observation	70	63
Life Table Test (d)		P=0.383
Incidental Tumor Test (d)		P=0.239
Fisher Exact Test (d)		P=0.231
Pituitary Gland: Carcinoma		
Overall Rates (a)	9/116 (8%)	8/247 (3%)
Adjusted Rates (b)	26.1%	9.6%
Terminal Rates (c)	1/14 (7%)	1/29 (3%)
Week of First Observation	91	100
Life Table Test (d)		P=0.045N
Incidental Tumor Test (d)		P=0.034N
Fisher Exact Test (d)		P=0.055N
Pituitary Gland: Adenoma or Carcinoma		
Overall Rates (a)	51/116 (44%)	109/247 (44%)
Adjusted Rates (b)	84.1%	85.3%
Terminal Rates (c)	9/14 (64%)	17/29 (59%)
Week of First Observation	70	63
Life Table Test (d)		P=0.415N
Incidental Tumor Test (d)		P=0.517N
Fisher Exact Test (d)		P=0.534
Adrenal Gland: Cortical Adenoma		
Overall Rates (a)	4/118 (3%)	18/250 (7%)
Adjusted Rates (b)	21.6%	25.3%
Terminal Rates (c)	3/15 (20%)	4/29 (14%)
Week of First Observation	128	104
Life Table Test (d)		P=0.131
Incidental Tumor Test (d)		P=0.126
Fisher Exact Test (d)		P=0.111
Adrenal Gland: Cortical Adenoma or Carcinoma		
Overall Rates (a)	6/118 (5%)	19/250 (8%)
Adjusted Rates (b)	29.0%	27.5%
Terminal Rates (c)	4/15 (27%)	4/29 (14%)
Week of First Observation	106	104
Life Table Test (d)		P=0.278
Incidental Tumor Test (d)		P=0.266
Fisher Exact Test (d)		P=0.255
Adrenal Gland: Pheochromocytoma		
Overall Rates (a)	17/118 (14%)	39/250 (16%)
Adjusted Rates (b)	54.7%	55.4%
Terminal Rates (c)	6/15 (40%)	10/29 (34%)
Week of First Observation	84	92
Life Table Test (d)		P=0.484
Incidental Tumor Test (d)		P=0.490
Fisher Exact Test (d)		P=0.448
Adrenal Gland: Pheochromocytoma or Malignant Pheochromocytoma		
Overall Rates (a)	19/118 (16%)	42/250 (17%)
Adjusted Rates (b)	55.8%	57.2%
Terminal Rates (c)	6/15 (40%)	10/29 (34%)
Week of First Observation	84	60
Life Table Test (d)		P=0.537
Incidental Tumor Test (d)		P=0.561N
Fisher Exact Test (d)		P=0.497

TABLE B3. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Control	1% Crocidolite Asbestos
Thyroid Gland: Follicular Cell Adenoma		
Overall Rates (a)	8/117 (7%)	8/250 (3%)
Adjusted Rates (b)	18.8%	13.5%
Terminal Rates (c)	1/15 (7%)	2/29 (7%)
Week of First Observation	92	118
Life Table Test (d)		P=0.092N
Incidental Tumor Test (d)		P=0.084N
Fisher Exact Test (d)		P=0.097N
Thyroid Gland: Follicular Cell Adenoma or Carcinoma		
Overall Rates (a)	11/117 (9%)	10/250 (4%)
Adjusted Rates (b)	28.2%	15.2%
Terminal Rates (c)	2/15 (13%)	2/29 (7%)
Week of First Observation	92	118
Life Table Test (d)		P=0.032N
Incidental Tumor Test (d)		P=0.025N
Fisher Exact Test (d)		P=0.037N
Thyroid Gland: C-Cell Adenoma		
Overall Rates (a)	4/117 (3%)	23/250 (9%)
Adjusted Rates (b)	17.1%	34.3%
Terminal Rates (c)	2/15 (13%)	5/29 (17%)
Week of First Observation	122	107
Life Table Test (d)		P=0.046
Incidental Tumor Test (d)		P=0.038
Fisher Exact Test (d)		P=0.034
Thyroid Gland: C-Cell Carcinoma		
Overall Rates (a)	12/117 (10%)	46/250 (18%)
Adjusted Rates (b)	39 9%	53.4%
Terminal Rates (c)	3/15 (20%)	6/29 (21%)
Week of First Observation	114	99
Life Table Test (d)		P=0.054
Incidental Tumor Test (d)		P=0.041
Fisher Exact Test (d)		P=0.030
Thyroid Gland: C-Cell Adenoma or Carcinoma		
Overall Rates (a)	16/117 (14%)	68/250 (27%)
Adjusted Rates (b)	52 2%	71 2%
Terminal Rates (c)	5/15 (33%)	11/29 (38%)
Week of First Observation	114	99
Life Table Test (d)		P=0.008
Incidental Tumor Test (d)		P=0 003
Fisher Exact Test (d)		P=0.002
Mammary Gland: Fibroadenoma		
Overall Rates (a)	48/118 (41%)	112/250 (45%)
Adjusted Rates (b)	85 7%	85 7%
Terminal Rates (c)	9/15 (60%)	17/29 (59%)
Week of First Observation	83	76
Life Table Test (d)		P=0 417
Incidental Tumor Test (d)		P=0 322
Fisher Exact Test (d)		P=0 264
Mammary Gland: Adenoma or Fibroadenoma		
Overall Rates (a)	49/118 (42%)	112/250 (45%)
Adjusted Rates (b)	86 0%	85.7%
Terminal Rates (c)	9/15 (60%)	17/29 (59%)
Week of First Observation	83	76
Life Table Test (d)		P=0.467
Incidental Tumor Test (d)		P=0.385
Fisher Exact Test (d)		P=0 316

TABLE B3. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Control	1% Crocidolite Asbestos
Mammary Gland: Adenocarcinoma		
Overall Rates (a)	16/118 (14%)	23/250 (9%)
Adjusted Rates (b)	46.6%	39.2%
Terminal Rates (c)	3/15 (20%)	7/29 (24%)
Week of First Observation	70	87
Life Table Test (d)		P=0 131N
Incidental Tumor Test (d)		P=0.102N
Fisher Exact Test (d)		P=0 140N
Mammary Gland: Adenoma or Adenocarcinoma		
Overall Rates (a)	18/118 (15%)	24/250 (10%)
Adjusted Rates (b)	48.2%	39 8%
Terminal Rates (c)	3/15 (20%)	7/29 (24%)
Week of First Observation	70	87
Life Table Test (d)		P=0 074N
Incidental Tumor Test (d)		P=0.049N
Fisher Exact Test (d)		P=0 081N
Mammary Gland: Adenoma, Fibroadenoma, or Adenocarcinoma		
Overall Rates (a)	58/118 (49%)	125/250 (50%)
Adjusted Rates (b)	90.5%	90.6%
Terminal Rates (c)	10/15 (67%)	20/29 (69%)
Week of First Observation	70	76
Life Table Test (d)		P=0 459N
Incidental Tumor Test (d)		P=0.508N
Fisher Exact Test (d)		P=0 484
Preputial (Clitoral) Gland Squamous Cell Carcinoma		
Overall Rates (a)	4/118 (3%)	22/250 (9%)
Adjusted Rates (b)	20.6%	31.6%
Terminal Rates (c)	2/15 (13%)	5/29 (17%)
Week of First Observation	137	109
Life Table Test (d)		P=0.058
Incidental Tumor Test (d)		P=0 053
Fisher Exact Test (d)		P=0 042
Preputial (Clitoral) Gland Carcinoma or Squamous Cell Carcinoma		
Overall Rates (a)	4/118 (3%)	23/250 (9%)
Adjusted Rates (b)	20.6%	32 2%
Terminal Rates (c)	2/15 (13%)	5/29 (17%)
Week of First Observation	137	109
Life Table Test (d)		P=0 047
Incidental Tumor Test (d)		P=0 043
Fisher Exact Test (d)		P=0 032
Preputial (Clitoral) Gland Adenoma, Carcinoma, or Squamous Cell Carcinoma		
Overall Rates (a)	5/118 (4%)	25/250 (10%)
Adjusted Rates (b)	22 2%	33 1%
Terminal Rates (c)	2/15 (13%)	5/29 (17%)
Week of First Observation	127	109
Life Table Test (d)		P=0 060
Incidental Tumor Test (d)		P=0 056
Fisher Exact Test (d)		P=0.041
Uterus: Endometrial Stromal Polyp		
Overall Rates (a)	19/116 (16%)	38/248 (15%)
Adjusted Rates (b)	41 8%	40.7%
Terminal Rates (c)	3/14 (21%)	5/29 (17%)
Week of First Observation	91	60
Life Table Test (d)		P=0 375N
Incidental Tumor Test (d)		P=0 440N
Fisher Exact Test (d)		P=0.454N

TABLE B3. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Control	1% Crocidolite Asbestos
All Sites: Benign Tumors		
Overall Rates (a)	91/118 (77%)	190/250 (76%)
Adjusted Rates (b)	100.0%	98.2%
Terminal Rates (c)	15/15 (100%)	26/29 (90%)
Week of First Observation	70	45
Life Table Test (d)		P=0.312N
Incidental Tumor Test (d)		P=0.377N
Fisher Exact Test (d)		P=0.462N
All Sites: Malignant Tumors		
Overall Rates (a)	80/118 (68%)	187/250 (75%)
Adjusted Rates (b)	93.4%	95.8%
Terminal Rates (c)	10/15 (67%)	23/29 (79%)
Week of First Observation	60	53
Life Table Test (d)		P=0.389
Incidental Tumor Test (d)		P=0.128
Fisher Exact Test (d)		P=0.101
All Sites: All Tumors		
Overall Rates (a)	115/118 (97%)	242/250 (97%)
Adjusted Rates (b)	100.0%	100.0%
Terminal Rates (c)	15/15 (100%)	29/29 (100%)
Week of First Observation	60	45
Life Table Test (d)		P=0.297N
Incidental Tumor Test (d)		P=0.513N
Fisher Exact Test (d)		P=0.509N

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

TABLE B4a. HISTORICAL INCIDENCE OF LEUKEMIA IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME FEED STUDIES (a)

Asbestos Studies	Incidence in Controls
Chrysotile (short range)	28/88
Chrysotile (intermediate range)	34/88
Tremolite	56/118
Crocidolite	43/118
Amosite	40/117
TOTAL	201/529 (38.0%)
SD (b)	6.01%
Range	
High	56/118 (47.5%)
Low	28/88 (31.8%)

(a) All studies conducted by Hazleton Laboratories; age at start of terminal kill, 138-146 weeks.
(b) Standard deviation

TABLE B4b. HISTORICAL INCIDENCE OF THYROID GLAND FOLLICULAR CELL TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME FEED STUDIES (a)

Asbestos Studies	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Chrysotile (short range)	1/87	4/87	5/87
Chrysotile (intermediate range)	6/87	1/87	7/87
Tremolite	3/118	5/118	7/118
Crocidolite	8/117	3/117	11/117
Amosite	2/116	7/116	9/116
TOTAL	20/525 (3.8%)	20/525 (3.8%)	39/525 (7.4%)
SD (b)	2.82%	1.89%	1.54%
Range			
High	6/87 (6.9%)	7/116 (6.0%)	11/117 (9.4%)
Low	1/87 (1.1%)	1/87 (1.1%)	5/87 (5.7%)

(a) All studies conducted by Hazleton Laboratories; age at start of terminal kill, 138-146 weeks.
(b) Standard deviation

TABLE B4c. HISTORICAL INCIDENCE OF THYROID GLAND C-CELL TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME FEED STUDIES (a)

Asbestos Studies	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Chrysotile (short range)	11/87	7/87	17/87
Chrysotile (intermediate range)	11/87	11/87	21/87
Tremolite	7/118	18/118	25/118
Crocidolite	4/117	12/117	16/117
Amosite	14/116	10/116	24/116
TOTAL	47/525 (9.0%)	58/525 (11.0%)	103/525 (19.6%)
SD (b)	4.36%	2.99%	3.84%
Range			
High	1/87 (12.6%)	18/116 (15.5%)	21/87 (24.1%)
Low	4/117 (3.4%)	7/87 (8.0%)	16/117 (13.7%)

(a) All studies conducted by Hazleton Laboratories; age at start of terminal kill, 138-146 weeks.
(b) Standard deviation

TABLE B4d. HISTORICAL INCIDENCE OF CLITORAL GLAND TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME FEED STUDIES (a)

Asbestos Studies	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Chrysotile (short range)	1/88	2/88	3/88
Chrysotile (intermediate range)	0/88	1/88	1/88
Tremolite	0/118	6/118	6/118
Crocidolite	1/118	4/118	5/118
Amosite	0/117	6/117	6/117
TOTAL	2/529 (0.2%)	19/529 (3.6%)	21/529 (4.0%)
SD (b)	0.55%	1.75%	1.65%
Range			
High	0/118 (0%)	6/117 (5.1%)	6/117 (5.1%)
Low	1/88 (1.1%)	1/88 (1.1%)	1/88 (1.1%)

(a) All studies conducted by Hazleton Laboratories; age at start of terminal kill, 138-146 weeks.
(b) Standard deviation

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS

	Untreated Control	1% Crocidolite Asbestos
ANIMALS INITIALLY IN STUDY	118	250
ANIMALS NECROPSIED	118	250
ANIMALS EXAMINED HISTOPATHOLOGICALLY	118	250
INTEGUMENTARY SYSTEM		
*Skin	(118)	(250)
Abscess, NOS		2 (1%)
Fibrosis, focal		1 (0%)
Hyperplasia, NOS	‡1 (1%)	
Hyperkeratosis	1 (1%)	1 (0%)
Acanthosis	1 (1%)	2 (1%)
*Subcutaneous tissue	(118)	(250)
Inflammation, pyogranulomatous		1 (0%)
RESPIRATORY SYSTEM		
*Nasal cavity	(118)	(250)
Congestion, NOS	1 (1%)	
*Nasal turbinate	(118)	(250)
Abscess, NOS		1 (0%)
Inflammation, chronic		1 (0%)
#Trachea	(117)	(250)
Abscess, NOS	1 (1%)	
#Lung	(118)	(250)
Mineralization		1 (0%)
Atelectasis		1 (0%)
Congestion, NOS	2 (2%)	2 (1%)
Hemorrhage	4 (3%)	9 (4%)
Inflammation, interstitial	2 (2%)	6 (2%)
Inflammation, acute diffuse		1 (0%)
Inflammation, chronic	96 (81%)	218 (87%)
Granuloma, NOS	2 (2%)	3 (1%)
Necrosis, focal		1 (0%)
Pigmentation, NOS	5 (4%)	3 (1%)
Hyperplasia, alveolar epithelium	3 (3%)	5 (2%)
#Lung/alveoli	(118)	(250)
Histiocytosis	6 (5%)	11 (4%)
HEMATOPOIETIC SYSTEM		
#Bone marrow	(116)	(249)
Osteopetrosis		2 (1%)
Hypoplasia, NOS	5 (4%)	7 (3%)
Histiocytosis	1 (1%)	
#Spleen	(118)	(250)
Hemorrhage	1 (1%)	6 (2%)
Hemorrhagic cyst	1 (1%)	
Inflammation, fibrinous		2 (1%)
Inflammation, chronic diffuse		1 (0%)
Granuloma, NOS		1 (0%)
Fibrosis, focal		4 (2%)
Fibrosis, multifocal	1 (1%)	2 (1%)
Fibrosis, diffuse		8 (3%)
Necrosis, NOS		2 (1%)
Necrosis, focal		6 (2%)
Infarct, NOS		1 (0%)
Metamorphosis, fatty		1 (0%)
Pigmentation, NOS		1 (0%)
Hemosiderosis	29 (25%)	46 (18%)
Metaplasia, osseous		1 (0%)
Hyperplasia, reticulum cell	1 (1%)	
Hyperplasia, lymphoid	3 (3%)	1 (0%)
Hematopoiesis	22 (19%)	61 (24%)

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control		1% Crocidolite Asbestos	
HEMATOPOIETIC SYSTEM (Continued)				
#Splenic follicles	(118)		(250)	
Atrophy, NOS	2	(2%)	3	(1%)
#Mandibular lymph node	(118)		(250)	
Congestion, NOS			1	(0%)
Edema, NOS			1	(0%)
Hemorrhage	1	(1%)		
Pigmentation, NOS			1	(0%)
Atrophy, NOS			1	(0%)
Hyperplasia, reticulum cell			1	(0%)
Hyperplasia, lymphoid	21	(18%)	28	(11%)
#Cervical lymph node	(118)		(250)	
Pigmentation, NOS			1	(0%)
Erythrophagocytosis			3	(1%)
#Mediastinal lymph node	(118)		(250)	
Congestion, NOS	2	(2%)	1	(0%)
Hemorrhage	5	(4%)	6	(2%)
Pigmentation, NOS	18	(15%)	32	(13%)
Erythrophagocytosis	6	(5%)	9	(4%)
Hyperplasia, reticulum cell	1	(1%)	1	(0%)
Hyperplasia, lymphoid	4	(3%)	4	(2%)
#Pancreatic lymph node	(118)		(250)	
Hemorrhage			1	(0%)
Pigmentation, NOS	2	(2%)	4	(2%)
Erythrophagocytosis			1	(0%)
Hyperplasia, reticulum cell	3	(3%)	8	(3%)
Hyperplasia, lymphoid			2	(1%)
Hematopoiesis			1	(0%)
#Mesenteric lymph node	(118)		(250)	
Hemorrhage	3	(3%)	2	(1%)
Pigmentation, NOS	3	(3%)	7	(3%)
Atrophy, NOS			2	(1%)
Erythrophagocytosis	4	(3%)	11	(4%)
Hyperplasia, reticulum cell	44	(37%)	68	(27%)
Hyperplasia, lymphoid	6	(5%)	10	(4%)
#Ileocolic lymph node	(118)		(250)	
Hemorrhage	1	(1%)		
Hyperplasia, lymphoid	2	(2%)	1	(0%)
#Renal lymph node	(118)		(250)	
Hemorrhage			1	(0%)
Pigmentation, NOS			2	(1%)
Atrophy, NOS	2	(2%)		
Erythrophagocytosis	2	(2%)	4	(2%)
Hyperplasia, reticulum cell	1	(1%)	2	(1%)
Hyperplasia, lymphoid	1	(1%)	1	(0%)
#Iliac lymph node	(118)		(250)	
Inflammation, acute diffuse			1	(0%)
Hyperplasia, lymphoid			1	(0%)
*Sternum	(118)		(250)	
Myelofibrosis			1	(0%)
#Liver	(118)		(250)	
Leukocytosis, NOS	5	(4%)	7	(3%)
Hematopoiesis	1	(1%)	2	(1%)
#Adrenal	(118)		(250)	
Hematopoiesis	1	(1%)	1	(0%)
#Thymus	(91)		(187)	
Multilocular cyst			1	(1%)
Hemorrhage	1	(1%)		

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
CIRCULATORY SYSTEM		
#Spleen	(118)	(250)
Thrombosis, NOS		4 (2%)
#Mesenteric lymph node	(118)	(250)
Lymphangiectasis	2 (2%)	3 (1%)
#Ileocolic lymph node	(118)	(250)
Lymphangiectasis	2 (2%)	1 (0%)
#Renal lymph node	(118)	(250)
Lymphangiectasis	1 (1%)	
#Iliac lymph node	(118)	(250)
Lymphangiectasis		1 (0%)
#Heart	(117)	(250)
Inflammation, chronic focal		1 (0%)
Inflammation, chronic diffuse		1 (0%)
#Heart/atrium	(117)	(250)
Thrombosis, NOS	1 (1%)	3 (1%)
#Myocardium	(117)	(250)
Inflammation, chronic		1 (0%)
Inflammation, chronic focal	22 (19%)	67 (27%)
Inflammation, chronic diffuse	34 (29%)	80 (32%)
Fibrosis, focal		1 (0%)
Fibrosis, multifocal		1 (0%)
#Cardiac valve	(117)	(250)
Inflammation, chronic focal	1 (1%)	
#Liver	(118)	(250)
Thrombosis, NOS		2 (1%)
Thrombus, organized	1 (1%)	
#Stomach	(118)	(250)
Periarteritis		1 (0%)
*Mesentery	(118)	(250)
Periarteritis		1 (0%)
#Uterus	(116)	(248)
Thrombosis, NOS		3 (1%)
#Pituitary	(116)	(247)
Thrombosis, NOS		1 (0%)
#Adrenal	(118)	(250)
Thrombosis, NOS		1 (0%)
DIGESTIVE SYSTEM		
*Tongue	(118)	(250)
Acanthosis		1 (0%)
#Salivary gland	(117)	(248)
Mineralization		1 (0%)
Inflammation, acute focal	1 (1%)	
Inflammation, acute diffuse	2 (2%)	
Inflammation, chronic	1 (1%)	3 (1%)
Inflammation, chronic focal	1 (1%)	
Inflammation, chronic diffuse		1 (0%)
Fibrosis		1 (0%)
Fibrosis, diffuse		2 (1%)
Atrophy, NOS	1 (1%)	
Atrophy, focal	1 (1%)	2 (1%)
#Parotid gland	(117)	(248)
Inflammation, chronic diffuse		1 (0%)

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
DIGESTIVE SYSTEM (Continued)		
#Liver	(118)	(250)
Congestion, NOS		2 (1%)
Hemorrhage		1 (0%)
Inflammation, chronic		1 (0%)
Inflammation, chronic focal		1 (0%)
Granuloma, NOS	25 (21%)	39 (16%)
Fibrosis, focal	1 (1%)	1 (0%)
Hepatitis, toxic	20 (17%)	56 (22%)
Degeneration, NOS		2 (1%)
Necrosis, NOS		1 (0%)
Necrosis, focal	15 (13%)	38 (15%)
Metamorphosis, fatty	43 (36%)	58 (23%)
Pigmentation, NOS	21 (18%)	55 (22%)
Hemosiderosis		1 (0%)
Focal cellular change	54 (46%)	109 (44%)
Angiectasis	4 (3%)	6 (2%)
#Hepatic capsule	(118)	(250)
Inflammation, acute focal	1 (1%)	
#Bile duct	(118)	(250)
Inflammation, chronic	3 (3%)	7 (3%)
Fibrosis		1 (0%)
Hyperplasia, NOS	6 (5%)	9 (4%)
#Pancreas	(118)	(249)
Ectopia	6 (5%)	6 (2%)
Hemorrhage		1 (0%)
Inflammation, chronic focal		2 (1%)
Necrosis, fat		1 (0%)
Pigmentation, NOS		1 (0%)
Atrophy, NOS	2 (2%)	
Atrophy, focal	3 (3%)	17 (7%)
Atrophy, diffuse	2 (2%)	4 (2%)
#Pancreatic acinus	(118)	(249)
Hyperplasia, focal	2 (2%)	9 (4%)
#Esophagus	(116)	(239)
Inflammation, chronic diffuse	1 (1%)	
Necrosis, diffuse	1 (1%)	
Hyperkeratosis	5 (4%)	3 (1%)
#Stomach	(118)	(250)
Mineralization	1 (1%)	
Cyst, NOS		1 (0%)
Edema, NOS	1 (1%)	
Inflammation, chronic	1 (1%)	2 (1%)
Inflammation, chronic focal	5 (4%)	10 (4%)
Inflammation, chronic diffuse	15 (13%)	34 (14%)
Ulcer, perforated	9 (8%)	17 (7%)
Necrosis, focal	23 (19%)	36 (14%)
Hyperplasia, epithelial	1 (1%)	1 (0%)
Hyperkeratosis	31 (26%)	28 (11%)
Acanthosis	28 (24%)	50 (20%)
#Duodenum	(118)	(250)
Inflammation, acute focal		1 (0%)
Inflammation, chronic focal		2 (1%)
Ulcer, perforated		1 (0%)
Necrosis, focal		1 (0%)
#Jejunum	(118)	(250)
Fibrosis, focal		1 (0%)
Necrosis, focal		1 (0%)
#Ileal mucosa	(118)	(250)
Hyperplasia, NOS		1 (0%)

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
DIGESTIVE SYSTEM (Continued)		
#Large intestine	(118)	(250)
Cyst, NOS		1 (0%)
Inflammation, chronic focal		1 (0%)
Parasitism	1 (1%)	8 (3%)
#Colon	(118)	(250)
Fibrosis, multifocal	1 (1%)	
Parasitism	8 (7%)	1 (0%)
Necrosis, focal	1 (1%)	
#Cecum	(118)	(250)
Congestion, NOS	1 (1%)	
Hemorrhage		3 (1%)
Inflammation, acute focal		1 (0%)
Inflammation, acute diffuse		1 (0%)
Inflammation, acute/chronic		1 (0%)
Inflammation, chronic focal		2 (1%)
Inflammation, chronic diffuse		1 (0%)
Fibrosis, focal		1 (0%)
Necrosis, focal	1 (1%)	2 (1%)
Hyperplasia, epithelial		2 (1%)
URINARY SYSTEM		
#Kidney	(117)	(250)
Mineralization	84 (72%)	208 (83%)
Hydronephrosis	1 (1%)	
Inflammation, acute focal	1 (1%)	
Inflammation, chronic	98 (84%)	28 (91%)
Inflammation, chronic diffuse		1 (0%)
Granuloma, NOS		1 (0%)
Fibrosis, focal	1 (1%)	
Necrosis, focal	1 (1%)	
Infarct, NOS	1 (1%)	
Infarct, healed	1 (1%)	
Calcification, NOS	7 (6%)	12 (5%)
Hyperplasia, tubular cell	2 (2%)	
#Kidney/capsule	(117)	(250)
Inflammation, chronic focal	1 (1%)	
#Kidney/cortex	(117)	(250)
Cyst, NOS	1 (1%)	2 (1%)
#Renal papilla	(117)	(250)
Abscess, NOS	1 (1%)	
#Kidney/tubule	(117)	(250)
Pigmentation, NOS	68 (58%)	179 (72%)
#Urinary bladder	(116)	(248)
Edema, NOS	1 (1%)	
Inflammation, chronic	1 (1%)	
Inflammation, chronic focal	1 (1%)	
Inflammation, chronic diffuse		1 (0%)
Hyperplasia, epithelial	3 (3%)	2 (1%)
Hyperplasia, papillary	1 (1%)	
Hyperkeratosis	1 (1%)	
Metaplasia, squamous	1 (1%)	
ENDOCRINE SYSTEM		
#Pituitary	(116)	(247)
Cyst, NOS	6 (5%)	15 (6%)
Hemorrhage	4 (3%)	1 (0%)
Hemorrhagic cyst	3 (3%)	5 (2%)
Necrosis, focal		1 (0%)
Pigmentation, NOS	1 (1%)	2 (1%)
Hyperplasia, focal	13 (11%)	17 (7%)
Angiectasis	13 (11%)	28 (11%)

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
ENDOCRINE SYSTEM (Continued)		
#Adrenal	(118)	(250)
Congestion, NOS	1 (1%)	
Hemorrhage	1 (1%)	
Metamorphosis, fatty	1 (1%)	3 (1%)
Pigmentation, NOS	1 (1%)	
Atrophy, NOS	1 (1%)	
Angiectasis	1 (1%)	2 (1%)
Metaplasia, osseous		1 (0%)
#Adrenal cortex	(118)	(250)
Congestion, NOS		3 (1%)
Degeneration, NOS	5 (4%)	12 (5%)
Necrosis, focal	2 (2%)	2 (1%)
Metamorphosis, fatty	35 (30%)	99 (40%)
Hypertrophy, focal	1 (1%)	
Hyperplasia, focal	12 (10%)	30 (12%)
Angiectasis	2 (2%)	12 (5%)
#Adrenal medulla	(118)	(250)
Hyperplasia, focal	19 (16%)	31 (12%)
#Thyroid	(117)	(250)
Cystic follicles		1 (0%)
Follicular cyst, NOS	7 (6%)	11 (4%)
Hemorrhagic cyst		1 (0%)
Hyperplasia, C-cell	15 (13%)	63 (25%)
Hyperplasia, follicular cell	1 (1%)	1 (0%)
#Parathyroid	(108)	(224)
Hyperplasia, NOS	8 (7%)	9 (4%)
#Pancreatic islets	(118)	(249)
Hyperplasia, focal		2 (1%)
REPRODUCTIVE SYSTEM		
*Mammary gland	(118)	(250)
Galactocele	8 (7%)	44 (18%)
Cyst, NOS	1 (1%)	1 (0%)
Cystic ducts	32 (27%)	88 (35%)
Inflammation, acute diffuse		1 (0%)
Abscess, NOS		4 (2%)
Hyperplasia, NOS	11 (9%)	28 (11%)
Hyperplasia, diffuse	2 (2%)	1 (0%)
*Preputial gland	(118)	(250)
Cystic ducts	3 (3%)	8 (3%)
Hemorrhage		1 (0%)
Inflammation, acute		1 (0%)
Inflammation, acute diffuse		2 (1%)
Abscess, NOS	1 (1%)	2 (1%)
Inflammation, acute/chronic	1 (1%)	
Inflammation, chronic diffuse	1 (1%)	2 (1%)
Necrosis, NOS		1 (0%)
Necrosis, focal	1 (1%)	
Necrosis, diffuse		1 (0%)
Hyperplasia, NOS		3 (1%)
Hyperplasia, diffuse	2 (2%)	
Hyperkeratosis	2 (2%)	2 (1%)
*Vagina	(118)	(250)
Acanthosis	1 (1%)	

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control	1% Crocidolite Asbestos
REPRODUCTIVE SYSTEM (Continued)		
#Uterus	(116)	(248)
Hydrometra	4 (3%)	8 (3%)
Cyst, NOS		1 (0%)
Hemorrhage		1 (0%)
Inflammation, acute focal		1 (0%)
Inflammation, acute/chronic	1 (1%)	
Inflammation, chronic diffuse	1 (1%)	1 (0%)
Hyperplasia, papillary		1 (0%)
#Cervix uteri	(116)	(248)
Cyst, NOS		1 (0%)
Abscess, NOS	1 (1%)	2 (1%)
Inflammation, chronic focal		1 (0%)
Fibrosis	1 (1%)	3 (1%)
Hyperkeratosis	1 (1%)	2 (1%)
Acanthosis		5 (2%)
#Uterus/endometrium	(116)	(248)
Cyst, NOS	4 (3%)	13 (5%)
#Ovary	(116)	(248)
Cyst, NOS	9 (8%)	10 (4%)
Follicular cyst, NOS		1 (0%)
Parovarian cyst	2 (2%)	3 (1%)
NERVOUS SYSTEM		
#Cerebrum	(118)	(248)
Hemorrhage	2 (2%)	3 (1%)
Inflammation, acute focal		1 (0%)
Necrosis, focal	1 (1%)	2 (1%)
Malacia	1 (1%)	
#Brain	(118)	(248)
Hemorrhage	2 (2%)	
#Cerebellum	(118)	(248)
Hemorrhage	1 (1%)	
Necrosis, focal		1 (0%)
Pigmentation, NOS		1 (0%)
SPECIAL SENSE ORGANS		
*Eye	(118)	(250)
Hemorrhage	5 (4%)	4 (2%)
Empyema	4 (3%)	
Inflammation, acute		1 (0%)
Synechia, anterior	1 (1%)	1 (0%)
Synechia, posterior	2 (2%)	2 (1%)
Cataract	21 (18%)	26 (10%)
Phthisis bulbi	2 (2%)	5 (2%)
*Eye/cornea	(118)	(250)
Inflammation, necrotizing		2 (1%)
Inflammation, acute diffuse	1 (1%)	
Inflammation, chronic focal	7 (6%)	2 (1%)
Inflammation, chronic diffuse	5 (4%)	12 (5%)
*Eye/retina	(118)	(250)
Degeneration, NOS	38 (32%)	78 (31%)
*Eyelid	(118)	(250)
Abscess, NOS		1 (0%)
*Harderian gland	(118)	(250)
Abscess, NOS		1 (0%)
Inflammation, chronic focal		1 (0%)
Inflammation, chronic diffuse		1 (0%)
Inflammation, pyogranulomatous		1 (0%)
Atrophy, NOS		2 (1%)
Hyperplasia, diffuse	1 (1%)	

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS (Continued)

	Untreated Control		1% Crocidolite Asbestos	
SPECIAL SENSE ORGANS (Continued)				
*Zymbal gland	(118)		(250)	
Cystic ducts	13	(11%)	24	(10%)
Inflammation, chronic			1	(0%)
Inflammation, chronic focal			1	(0%)
Hyperplasia, focal			1	(0%)
Hyperkeratosis	2	(2%)	4	(2%)
Acanthosis	1	(1%)		
MUSCULOSKELETAL SYSTEM				
*Skull	(118)		(250)	
Osteopetrosis	2	(2%)	4	(2%)
*Sternum	(118)		(250)	
Osteopetrosis	4	(3%)	18	(7%)
Hypoplasia, NOS	2	(2%)		
*Rib	(118)		(250)	
Degeneration, NOS			1	(0%)
BODY CAVITIES				
*Abdominal cavity	(118)		(250)	
Embryonal rest			1	(0%)
Inflammation, chronic focal	1	(1%)		
Inflammation, chronic diffuse	1	(1%)		
Necrosis, fat	4	(3%)	11	(4%)
*Mesentery	(118)		(250)	
Inflammation, acute focal			1	(0%)
Inflammation, chronic			1	(0%)
Inflammation, chronic focal	1	(1%)		
ALL OTHER SYSTEMS				
*Multiple organs	(118)		(250)	
Osteopetrosis	1	(1%)		
Mineralization			1	(0%)
Cyst, NOS	3	(3%)		
Inflammation, chronic	9	(8%)	5	(2%)
Pigmentation, NOS	2	(2%)	1	(0%)
Hyperplasia, NOS	1	(1%)	1	(0%)
Diaphragm				
Hernia, NOS	1		1	
Inflammation, acute focal			1	
Adipose tissue				
Hamartoma	1			
Inflammation, acute focal	1		1	
SPECIAL MORPHOLOGY SUMMARY				
None				

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

APPENDIX C

PATHOGEN BURDEN SURVEY

TABLE C1. INITIAL MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F_0 RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

Animal/Specimen Number (a)	Micro-organisms Identified (b)
165/3782	1 + Coliform; 1 + *Proteus vulgaris*
166/3783	3 + Coliform; 3 + *Proteus vulgaris*
167/3784	1 + Coliform; 1 + *Proteus vulgaris*
168/3785	1 + Coliform; 1 + *Proteus vulgaris*
169/3786	1 + Coliform; 1 + *Proteus vulgaris*
170/3787	1 + Coliform; 1 + *Proteus vulgaris*
171/3788	1 + Coliform; 1 + *Proteus vulgaris*
172/3789	1 + Coliform; 1 + *Proteus vulgaris*
173/3790	1 + Coliform
174/3791	No growth
175/3792	2 + Coliform
176/3793	2 + Coliform; 1 + *Proteus vulgaris*
177/3794	1 + Coliform
178/3795	No growth
179/3796	No growth
180/3797	3 + Coliform; 1 + *Proteus vulgaris*

(a) Date of specimen: 11/16/77
(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 F_0 RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

Sample Number	Complement Fixation	
	Sendai	LCM
3782	–	–
3784	–	–
3785	–	–
3786	–	–
3788	–	–
3789	–	–
3790	–	–
3792	–	–
3793	–	–
3795	–	–
3796	–	–
3797	–	–
Significant titer	10	10

TABLE C3. INITIAL INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F_0 RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

	Male								Female							
Animal Number:	1 6 5	1 6 6	1 6 7	1 6 8	1 6 9	1 7 0	1 7 1	1 7 2	1 7 3	1 7 4	1 7 5	1 7 6	1 7 7	1 7 8	1 7 9	1 8 0
Organ and Lesion																
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	O
Lung															X	
Peribronchial lymphoid hyperplasia	2	1	1	1	2	1	1	2	2	2	2	2	2	2		1
Perivascular lymphoid hyperplasia		1	1									1				
Aspirated blood											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	X	X
Nonsuppurative pericholangitis			1													
Kidney	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Small intestine	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Large intestine	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Salivary gland	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urinary bladder	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	O
Harderian gland	X	X	X	X	X	X	X	X	X	X	O	X	X	X	X	O
Skin	X	X	X	X	O	X	X	X	X	X	O	X	X	O	X	O
Anus	O	X	O	X	X	X	X	O	X	X	X	X	X	X	X	X
Trachea	X	X	X	X	X	O	X	X	X	X	X	X	X	X	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
5 = Severe

Pathogen Burden Summary (F_0 Repeated)

Sections of brain, heart, lung, spleen, liver, kidney, small intestine, large intestine, salivary gland, urinary bladder, harderian gland, skin, anus, and cecum were examined from five rats of each sex in the parental generation killed for pathology burden.

Evidence of respiratory disease was noted in all rats. This was characterized by minimal to moderate peribronchial lymphoid hyperplasia in all 10 rats and a bronchial exudate in 6 rats. The respiratory disease was slightly more pronounced than that observed at a prior kill. Microbiologic examination did not reveal the presence of *Mycoplasma* sp., and serum titers were negative for Sendai virus.

Minimal to focal nonsuppurative myocarditis was noted in two males. Minimal to slight pigment deposition (presumably hemosiderin) was noted in sections of spleen from three rats.

In sections of liver, minimal nonsuppurative pericholangitis occurred in four males and two females, and scattered microgranulomas and vacuolated hepatocytes were each noted in single male rats.

In sections of kidney, minimal chronic interstitial nephritis occurred in all five males and in one female. Intratubular mineralization was noted at the corticomedullary junction in four females.

Porphyrin pigment was noted in the harderian gland of four rats.

The remaining tissues examined were not remarkable; no external or internal parasites were observed.

TABLE C4. REPEATED MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F_0 RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

Animal/Specimen Number (a)	Micro-organisms Identified (b)
287/4021	4+ Group D *Streptococcus*; 3+ Coliform, 3+ *Proteus vulgaris* 2+ *Pseudomonas aeruginosa*
288/4022	4+ Group D *Streptococcus*, 3+ *Micrococcus* sp.; 3+ Coliform; 2+ *Proteus vulgaris*; 2+ *Pseudomonas aeruginosa*
289/4023	4+ Group D *Streptococcus*; 4+ *Staphylococcus epidermis*; 4+ *Micrococcus* sp.; 1+ Coliform
290/4024	4+ Group D *Streptococcus*; 4+ *Micrococcus* sp.; 4+ Coliform; 1+ *Pseudomonas aeruginosa*
291/4025	4+ Group D *Streptococcus*; 4+ *Micrococcus* sp ; 4+ Coliform; 2+ *Pseudomonas aeruginosa*
292/4026	4+ Group D *Streptococcus*; 4+ *Micrococcus* sp , 4+ Coliform, 2+ *Pseudomonas aeruginosa*
293/4027	4+ Group D *Streptococcus*; 2+ *Micrococcus* sp , 2+ Coliform; 3+ *Proteus vulgaris*; 1+ *Pseudomonas aeruginosa*
294/4028	4+ Group D *Streptococcus*; 4+ *Micrococcus* sp.; 4+ Diphtheroids; 4+ Coliform, 4+ *Pseudomonas aeruginosa*
295/4029	4+ Group D *Streptococcus*; 4+ *Micrococcus* sp.; 4+ Coliform
296/4030	4+ Group D *Streptococcus*; 4+ *Micrococcus* sp.; 4+ Diphtheroids; 4+ Coliform, 4+ *Proteus vulgaris*

(a) Date of specimen 6/5/78
(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 C5. REPEATED MURINE VIRUS ANTIBODY DETERMINATION IN F_0 RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

Sample Number	Complement Fixation	
	Sendai	LCM
4021	—	—
4022	—	—
4023	—	—
4024	—	—
4025	—	—
4026	—	—
4027	—	—
4028	—	—
4029	—	—
4030	—	—
Significant titer	10	10

TABLE C6. REPEATED INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F_0 RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

Organ and Lesion	Animal Number:	Control					1% Crocidolite				
		Male		Female			Male		Female		
		2	2	2	2	2	2	2	2	2	2
		8	8	8	9	9	9	9	9	9	9
		7	8	9	0	1	2	3	4	5	6
Brain		X	X	X	X	X	X	X	X	X	X
Heart			X	X	X		X	X	X	X	X
Focal nonsuppurative myocarditis		1				1					
Lung											
Peribronchial lymphoid hyperplasia		1	2	2	3	3	2	1	1	2	2
Bronchial exudate			P	P	P	P				P	P
Spleen			X	X		X	X	X	X		X
Pigment deposition		1			2					2	
Liver							X		X		X
Micrognanulomas		P									
Vacuolated hepatocytes				P							
Nonsuppurative pericholangitis		1	1		1	1		1		1	
Kidney											
Chronic interstitial nephritis		1	1	1	1	1	1				
Foci of mineralization								P	P	P	P
Small intestine		X	X	X	X	X	X	X	X	X	X
Large intestine		X	X	X	X	X	X	X	X	X	X
Salivary gland		X	X	X	X	X	X	X	X	X	O
Urinary bladder		X	X	X	X	X	X	X	X	X	X
Harderian gland			X	O	X		O		O	O	
Porphyrin pigment		P				P		P			P
Skin		X	X	X	X	X	X	X	X	X	O
Anus		X	O	O	O	O	O	O	O	X	O
Cecum		X	X	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
5 = Severe

Pathogen Burden Summary (F_1)

Sections of brain, heart, lung, spleen, liver, kidney, small intestine, large intestine, salivary gland, urinary gland, harderian gland, skin, anus, and cecum were examined from eight male and eight female rats killed for pathology burden.

Evidence of early spontaneous respiratory disease was present in the lungs of all rats examined. This lesion consisted of minimal to slight peribronchial lymphoid hyperplasia. Microbiologic examination did not reveal the presence of *Mycoplasma* sp., and serum titers were negative for Sendai virus.

In sections of kidney, foci of intratubular mineralization were noted at the corticomedullary junction in two males and six females.

The remaining tissues examined were not remarkable; no external or internal parasites were observed.

TABLE C7. MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F_1 RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

Animal/Specimen Number (a)	Micro-organisms Identified (b)
245/3951	4+ Group D *Streptococcus*; 1+ *Staphylococcus aureus;* 3+ Coliform; 3+ *Pseudomonas aeruginosa*
246/3952	4+ Group D *Streptococcus*; 1+ *Proteus morganii;* 1+ *Pseudomonas aeruginosa*
247/3953	4+ Group D *Streptococcus*; 3+ Coliform; 1+ *Proteus vulgaris*
248/3954	4+ Group D *Streptococcus*; 1+ *Staphylococcus aureus;* 2+ Coliform; 2+ *Pseudomonas aeruginosa*
249/3955	4+ Group D *Streptococcus*; 3+ *Staphylococcus epidermis;* 4+ *Pseudomonas aeruginosa*
250/3956	4+ Group D *Streptococcus*; 1+ *Bacillus* sp.; 1+ Coliform
251/3957	4+ Group D *Streptococcus*; 1+ *Staphylococcus aureus;* 3+ Coliform
252/3958	4+ Group D *Streptococcus*; 3+ Coliform; 2+ *Proteus vulgaris*; 1+ *Pseudomonas aeruginosa*
253/3959	4+ Group D *Streptococcus*; 1+ *Micrococcus* sp.; 3+ Coliform
254/3960	1+ *Bacillus* sp.; 4+ Group D *Streptococcus*; 1+ Coliform
255/3961	4+ Group D *Streptococcus*; 1+ *Bacillus* sp.
256/3962	4+ Group D *Streptococcus*; 4+ Coliform
257/3963	4+ Group D *Streptococcus*; 1+ Coliform
258/3964	4+ Group D *Streptococcus*; 3+ Coliform; 1+ *Pseudomonas aeruginosa*
259/3965	4+ Group D *Streptococcus*; 3+ Coliform; 1+ *Pseudomonas aeruginosa*; 2+ *Proteus vulgaris*
260/3966	4+ Group D *Streptococcus*; 2+ *Staphylococcus aureus;* 1+ *Pseudomonas aeruginosa*

(a) Date of specimen: 4/24/78
(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. MURINE VIRUS ANTIBODY DETERMINATION IN F_1 RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

Sample Number	Complement Fixation	
	Sendai	LCM
3951	–	–
3952	–	–
3953	–	–
3954	–	–
3955	–	–
3957	–	–
3958	–	–
3959	–	–
3960	–	–
3961	–	–
3962	–	–
3963	–	–
3964	–	–
3966	–	–
Significant titer	10	10

TABLE C9. INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F_1 RATS IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

	Control						1% Crocidolite									
	Male			Female			Male					Female				
Animal Number:	2 4 5	2 4 6	2 4 7	2 4 8	2 4 9	2 5 0	2 5 1	2 5 2	2 5 3	2 5 4	2 5 5	2 5 6	2 5 7	2 5 8	2 5 9	2 6 0
Organ and Lesion																
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	2	2	2	2	2	1	2	1	1	2	1	1	2	2	1
Spleen	X	X	X	O	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	X	X	X
Kidney		X	X				X	X	X	X		X	X			
Focal mineralization	P			P	P	P					P			P	P	P
Small intestine	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Large intestine	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Salivary gland	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	O
Urinary bladder	X	X	X	X	X	X	X	X	X	X	X	O	X	X	X	X
Harderian gland	X	X	X	O	O	O	X	X	X	X	X	X	X	X	X	O
Skin	X	O	X	X	X	X	X	O	X	X	X	X	X	X	X	X
Anus	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Cecum	O	X	X	X	X	X	X	X	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
5 = Severe

APPENDIX D

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

TABLE D1. ANALYSIS OF BEDDING SAMPLES AT HAZLETON LABORATORIES

Collection Date	Desired Level (ppm)	Determined Level of Pentachlorophenol (ppm)	Determined Level of 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 CROCIDOLITE ASBESTOS

APPENDIX E. WATER ANALYSIS

Samples of drinking water were submitted to the Water Supply Research Laboratory, U.S. Environmental Protection Agency, Cincinnati, Ohio, 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 CROCIDOLITE ASBESTOS

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 one room. 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, Pennsylvania), 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 CROCIDOLITE 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	0.0	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		0.00		
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	0.00
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 CROCIDOLITE 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					
1/79	0.07		0.13	0.17	0.04
2/80	0.048	0.048	0.048	0.24	
7/80		0.26	0.03	0.20	0.03
			Asbestos Fiber Concentration (no./cc of air)		
6/78					
1/79	0.04		0.04	0.04	0.00
2/80	0.048	0.048	0.00	0.14	
7/80		0.20	0.03	0.09	0
			>5 μm (no./cc of air)		
6/78					
1/79	0		0	0	0
2/80	0	0	0	0	
7/80		0.06	0	0	0
			>1 μm (no./cc of air)		
6/78					
1/79	0		0	0.04	0
2/80	0	0	0	0.05	
7/80		0.14	0	0.06	0

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

(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 PRIOR TO MORIBUND KILL IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS

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

	Weeks 83-87		Weeks 88-92		Weeks 93-97		Weeks 98-102	
	Male	Female	Male	Female	Male	Female	Male	Female
Number of animals killed in moribund condition	2	4	5	2	3	10	5	4
No clinical signs observed		1	1	1	2	4	1	
Pale		1		1		4		3
Thin		2	1	1		2		2
Hunched		1		1				
Head tilt	1							
Opaque eyes	1							
Pale eyes			2		1			
Bloody crust around nose and/or eyes		1						
Wheezing	1							
Labored respiration						2		
Depressed		1	3		1	3		1
Inactive							1	
Abdomen distended and/or dark			1					
Palpable mass in abdomen	1	2	1		2	4		2
Tissue mass leg, chest, side of body, head, inguinal, lower midline, or abdomen			2	2		1	3	2
Cyanotic						1		
Wet stains on abdomen				1				
Urine stains		1		1				
Soft feces			1					
Loss of equilibrium and/or righting reflex			1				1	
Unable to stand			1					
Swollen and abscessed area around ear	1							
Firm swelling of throat			1					

	Weeks 103-107		Weeks 108-112	
	Male	Female	Male	Female
Number of animals killed in moribund condition	6	6	7	3
No clinical signs observed	1			
Pale	2		4	1
Thin	1	4		
Head tilt	1	1		
Pale eyes	1			
Bloody crust around nose and/or eyes			1	
Wheezing			1	
Labored respiration				1
Depressed	2	3	3	1
Inactive	1			
Abdomen distended and/or dark	1		1	
Abdomen firm			1	
Palpable mass in abdomen	3	1		1
Tissue mass leg, chest, side of body, head, inguinal, lower midline, or abdomen		1	2	1
Unkempt	1	2		
Cyanotic			1	1
Yellowish feces	1			
Loss of equilibrium and/or righting reflex	1	4		
Paralysis in hindlegs		1		
Testes enlarged	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 G2. SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF CROCIDOLITE ASBESTOS: 1% (a)

	Weeks 83-87		Weeks 88-92		Weeks 93-97		Weeks 98-102	
	Male	Female	Male	Female	Male	Female	Male	Female
Number of animals killed in moribund condition	2	2	4	3	5	1	6	8
Pale	1	2			2		3	6
Thin	1	2	1		2		2	1
Bloody crust around nose and/or eyes	1							
Pale eyes	1		1	1	1			1
Malocclusion								1
Hunched		1						
Depressed	1	2	1	1	1		3	3
Labored respiration				1				
Wheezing			1					
Abdomen firm and/or distended				1				
Palpable mass in abdomen		2		1				3
Tissue mass--hindleg, neck, chest, back, eye, head, axilla, hip, inguinal, midline, or perineal	1	1	4	1	1	1	2	2
Loss of pain perception		1						
Unable to stand							1	
Lack of coordination					1			
Loss of equilibrium or righting reflex							2	1
Rough haircoat			2					
Flaccid muscle tone	1							
Yellow extremities		1		1				
Cold to touch		2			1			
Prostrate in cage					1			
Paralysis in hindlegs					1			1
Red discharge from penis					1			
Urine stains								1

	Weeks 103-107		Weeks 108-112	
	Male	Female	Male	Female
Number of animals killed in moribund condition	13	12	12	15
Pale	4	10	6	6
Thin	7	5	3	8
Cloudy eyes				2
Pale eyes	2	1	2	4
Salivating	1			
Hunched				1
Depressed	7	4	4	2
Labored respiration	1			1
Rapid respiration	1			
Wheezing	1			
Cyanotic	1			
Abdomen firm and/or distended			1	
Palpable mass in abdomen	8	8	8	5
Tissue mass--hindleg, neck, chest, back, eye, head, axilla, hip, inguinal, midline, or perineal	5	5	3	6
Nodule	1		1	
Side of head swollen				1
Unkempt	2		2	
Loss of equilibrium or righting reflex				1
Prostrate in cage	1		1	1
Paralysis in hindlegs		1		1
Urine discoloration (red, bright yellow)	2			

(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 CROCIDOLITE ASBESTOS

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

	Control		1% Crocidolite Asbestos			
Week	Grams Feed/ Day (a)	Body Weight (grams)	Grams Feed/ Day (a)	Body Weight (grams)	1%/Control (b)	Dose/Day (c)
17	17	312	17	244	1.0	697
27	17	359	16	317	0.9	505
37	18	408	17	351	0.9	484
47	18	411	17	366	0.9	464
57	17	443	17	392	1.0	434
67	18	466	17	413	0.9	412
77	16	471	16	427	1.0	375
87	17	417	16	429	0.9	373
97	16	464	15	424	0.9	354
107	17	460	15	419	0.9	358
117	15	424	15	399	1.0	376
127	18	401	16	373	0.9	429
137	15	361	18	332	1.2	542
Mean	16.8	415	16.3	376	1.0	446
SD (d)	1.1		0.9		0.1	96
CV(e)	6.5		5.5		10.0	21.5

(a) Grams of feed removed from the feeder per animal per day; not corrected for scatter.
(b) Grams of feed per day for the dosed group divided by that for the controls
(c) Estimated milligrams of crocidolite asbestos consumed per day per kilogram of body weight
(d) Standard deviation
(e) Coefficient of variation = (standard deviation/mean) × 100

TABLE H2. FEED AND COMPOUND CONSUMPTION BY FEMALE RATS FOR REPRESENTATIVE WEEKS IN THE LIFETIME FEED STUDY OF CROCIDOLITE ASBESTOS

	Control		1% Crocidolite Asbestos			
Week	Grams Feed/ Day (a)	Body Weight (grams)	Grams Feed/ Day (a)	Body Weight (grams)	1%/Control (b)	Dose/Day (c)
17	12	188	12	163	1.0	736
27	12	203	11	186	0.9	591
37	13	224	12	200	0.9	600
47	13	228	13	220	1.0	591
57	13	251	12	235	0.9	511
67	14	282	13	259	0.9	502
77	13	303	12	280	0.9	429
87	15	317	13	292	0.9	445
97	14	328	12	294	0.9	408
107	15	334	13	302	0.9	430
117	14	324	13	295	0.9	441
127	15	314	14	275	0.9	509
137	13	295	13	253	1.0	514
Mean	13.5	276	12.5	250	0.9	516
SD (d)	1.1		0.8		0.0	93
CV(e)	8.1		6.4		0.0	18.0

(a) Grams of feed removed from the feeder per animal per day; not corrected for scatter.
(b) Grams of feed per day for the dosed group divided by that for the controls
(c) Estimated milligrams of crocidolite asbestos consumed per day per kilogram of body weight
(d) Standard deviation
(e) Coefficient of variation = (standard deviation/mean) × 100

APPENDIX I

AUDIT SUMMARY

APPENDIX I. AUDIT SUMMARY

The experimental data, documents, pathology materials, and draft Technical Report for the lifetime toxicology and carcinogenesis studies of crocidolite asbestos in F344/N rats were audited for accuracy, consistency, and completeness. The laboratory experiments were conducted for the NTP at Hazleton Laboratories (Vienna, Virginia) under a subcontract with Tracor Jitco, Inc., from the National Cancer Institute. The exposure portion of the studies was begun in January 1978 and ended in December 1980, before the time (October 1981) the NTP implemented the requirement that studies be conducted in compliance with the Good Laboratory Practice (GLP) regulations of the Food and Drug Administration. The retrospective audit was conducted for the NIEHS at the NTP Archives from June to July 1985 by Dynamac Corporation (F. Cavender, Ph.D., Principal Investigator). A separate audit for the chemistry data for all NTP asbestos studies was conducted by Argus Research Laboratories (P. Wennerberg, D.V.M., Principal Investigator) in October 1986. The other individuals who conducted the audit are listed in the full audit report, which is on file at the NIEHS. The audit included a review of:

(1) All records concerning animal receipt, quarantine, randomization, and disposition prior to study start.
(2) Chemistry records for fiber characterization and chemical/vehicle analyses.
(3) Body weight and clinical observation data for a random 10% sample of the study animals.
(4) Feed consumption for approximately 10% of the animals.
(5) Inlife records concerning environmental conditions, palpable masses, and mortality.
(6) All postmortem records for individual animals concerning identification, disposition and condition codes, and correlation between gross observations and microscopic diagnoses.
(7) Wet tissues from a random 10% sample of the study animals to verify animal identification and to examine for untrimmed potential lesions.
(8) Blocks and slides of tissues from 50% of the control and exposed groups to examine for inventory and correspondence.
(9) Tabulated pathology diagnoses for a random 10% of study animals to verify computer data entry.

The audit indicated that records were not available for environmental conditions for the control animals or gestation and litter data following breeding of the F_0 to produce the F_1 generation. A Daily Animal Observation Record was not available for control animals, and therefore the primary mortality records for these animals were the Individual Animal Data Records. Other inlife records were generally complete and consistent.

The records documenting the identification and characterization of the various mineral fibers were complete and adequate. Recalculated values for formulated diets containing crocidolite asbestos were in agreement with the values recorded.

Wet tissues were present for all animals except three exposed male rats. Of the 74 rats examined at random for ear tag identification, 2 control males, 2 exposed males, and 1 exposed female had no ear tags in the tissue bags; all others were properly identified. Audit examination for gross to microscopic noncorrelation indicated four nonneoplastic lesions for the gastrointestinal tract (one exposed male, three exposed females) and eight potentially neoplastic lesions in "nontarget" organs (two control males, two exposed males, two control females, two exposed females). The NTP pathology review of these findings indicated that they would in no way change or affect the conclusions drawn in the study.

The retrospective audit indicated that the records and specimens for the lifetime studies of crocidolite asbestos support the data and results presented in the NTP Technical Report.