

**NATIONAL TOXICOLOGY PROGRAM**  
**Technical Report Series**  
**No. 246**



**LIFETIME CARCINOGENESIS STUDIES**

**OF**

**CHRYBOTILE ASBESTOS**

**(CAS NO. 12001-29-5)**

**IN SYRIAN GOLDEN HAMSTERS**

**(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 chemically induced disease. By bringing together the relevant programs, staff, and resources from the U.S. Public Health Service, DHHS, the National Toxicology Program has centralized and strengthened activities relating to toxicology research, testing and test development/validation efforts, and the dissemination of toxicological information to the public and scientific communities and to the research and regulatory agencies.

The NTP is comprised of four charter DHHS agencies: the National Cancer Institute, National Institutes of Health; the National Institute of Environmental Health Sciences, National Institutes of Health; the National Center for Toxicological Research, Food and Drug Administration; and the National Institute for Occupational Safety and Health, Centers for Disease Control. In 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 Counselor's Technical Reports Review Subcommittee on June 23, 1981 [see page 10]. Thereafter, the NTP adopted the policy that the experimental data and laboratory records from all NTP toxicology and carcinogenesis studies not yet printed and distributed would be audited. The audit report was reviewed by NTP staff, who determined that none of the discrepancies influenced the final interpretation of the results of these studies. All errors detected in the audit of the draft report were corrected in this final Technical Report. The audit report is on file at the NIEHS/NTP Quality Assurance Office and is available for review.

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

**NTP TECHNICAL REPORT  
ON THE  
LIFETIME CARCINOGENESIS STUDIES  
OF  
CHRYSTILE ASBESTOS  
(CAS NO. 12001-29-5)  
IN SYRIAN GOLDEN HAMSTERS  
(FEED STUDIES)**



**NATIONAL TOXICOLOGY PROGRAM  
Research Triangle Park  
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North Carolina 27709**

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

## NOTE TO THE READER

This is one in a series of experiments designed to determine whether selected chemicals produce cancer in animals. Chemicals selected for testing in the NTP carcinogenesis program are chosen primarily on the bases of human exposure, level of production, and chemical structure. Selection per se is not an indicator of a chemical's carcinogenic potential. Negative results, in which the test animals do not have a greater incidence of cancer than control animals, do not necessarily mean that a test chemical is not a carcinogen, inasmuch as the experiments are conducted under a limited set of conditions. Positive results demonstrate that a test chemical is carcinogenic for animals under the conditions of the test and indicate that exposure to the chemical has the potential for hazard to humans. The determination of the risk to humans from chemicals found to be carcinogenic in animals requires a wider analysis which extends beyond the purview of this study.

This study was designed and conducted at the National Institute of Environmental Health Sciences, National Toxicology Program.

Comments and questions about the National Toxicology Program Technical Reports on Carcinogenesis Studies should be directed to the National Toxicology Program, located at Research Triangle Park, North Carolina 27709 (919-541-3991) or at Room 835B, Westwood Towers, 5401 Westbard Ave., Bethesda, Maryland 20205 (301-496-1152).

Although every effort is made to prepare the Technical Reports as accurately as possible, mistakes may occur. Readers are requested to communicate any mistakes to the Deputy Director, NTP (P.O. Box 12233, Research Triangle Park, NC 27709), so that corrective action may be taken. Further, anyone who is aware of related ongoing or published studies not mentioned in this report is encouraged to make this information known to the NTP.

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Single copies of this carcinogenesis studies technical report are available without charge (while supplies last) for the NTP Public Information Office, National Toxicity Program, P.O. Box 12233, Research Triangle Park, NC 27709.

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## CARCINOGENESIS STUDIES OF CHRYSOTILE ASBESTOS

### ABSTRACT

Carcinogenesis studies of short range (SR), intermediate range (IR), or intermediate range chrysotile asbestos in combination with the intestinal carcinogen 1,2-dimethylhydrazine dihydrochloride (DMH) were conducted with male and female Syrian golden hamsters. Both forms of chrysotile asbestos were administered at the concentration of 1% in pelleted diet for the entire lifetime of the hamsters starting with mothers of the test animals. Group sizes varied from 125 to 253. Starting at 6 weeks of age, male and female hamsters in the intermediate range chrysotile/DMH study were given oral doses of DMH (4 mg/kg) every other week for a total of 5 doses. There was no adverse effect on body weight gain or survival by either form of asbestos or by asbestos in combination with DMH.

A significant increase ( $P < 0.05$ ) in adrenal cortical adenomas was observed in male hamsters exposed to SR and IR chrysotile asbestos and in females treated with IR chrysotile asbestos when compared to the pooled control groups (males: pooled controls, 25/466, 5%; SR chrysotile, 26/229, 11%; IR chrysotile, 24/244, 10%; females: pooled controls, 15/468, 3%; IR chrysotile, 18/234, 8%). However, statistical significance was lost when these dosed groups were compared with concurrent control groups (males: SR control, 7/115, 6%; IR control, 7/115, 6%; females: SR control, 4/112, 4%; IR control, 6/118, 5%).

The results of the combination study (IR chrysotile plus DMH) did not yield a significant increase in tumors above the background level observed in the DMH group alone or in the untreated control group. The DMH failed to yield a background level of intestinal tumors high enough to provide a valid test of the cocarcinogenic potential of chrysotile asbestos. For this reason, the cocarcinogenic potential of orally administered asbestos should be considered untested.

Under the conditions of these studies, neither short range chrysotile nor intermediate range chrysotile asbestos was carcinogenic when ingested at 1% levels in the diet by male and female Syrian golden hamsters. While there were increases in the rates of adrenal cortical adenomas in male and female hamsters exposed to intermediate range chrysotile asbestos compared with pooled control groups, these incidence rates were not different when compared with the concurrent control groups. Additionally, the biologic importance of adrenal tumors in the absence of target organ (gastrointestinal tract) neoplasia is questionable. The cocarcinogenesis studies using IR chrysotile asbestos and 1,2-dimethylhydrazine dihydrochloride were considered inadequate because there was no increase in intestinal neoplasia in the DMH group.

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## SUMMARY OF PEER REVIEW COMMENTS

On June 23, 1981, this technical report on the carcinogenesis studies of chrysotile asbestos underwent peer review and was approved by the National Toxicology Program Board of Scientific Counselors' Technical Report Review Subcommittee and associated Panel of Experts at an open meeting held in Building 101, National Toxicology Program, Research Triangle Park, North Carolina.

Dr. Swenberg, as a principal reviewer, agreed with the conclusions that the ingestion via the diet of short range (SR) or intermediate range (IR) chrysotile asbestos was not carcinogenic in male and female Syrian golden hamsters. The asbestos was made available in pelleted diet, 1%, for the lifetime of the hamsters. While there were significant increases in the rates of adrenal cortical adenomas in male (SR or IR) and female (IR) hamsters exposed to chrysotile asbestos compared to pooled control groups, they were no longer significant when contrasted to the concurrent control groups. Additionally, the biologic importance of adrenal tumors in the absence of intestinal or mesothelial neoplasia is questionable. Combination studies using IR chrysotile and 1,2-dimethylhydrazine (DMH) were considered inadequate because of the lack of an increase in intestinal neoplasia in the DMH group.

Dr. Swenberg said that several aspects of the study conduct and reporting could use more attention: missexed animals; fluctuations in animal body weights; information on the DMH experiment; non-tumor pathology; and more detailed review of the clinical records for autolyzed or cannibalized animals.

As a second principal reviewer, Dr. Mirer emphasized the variations in duration of exposure in the absence of terminal sacrifice, which differs from past or standard experimental design. He noted there were large differences in median fiber length for both SR and IR as measured by electron microscopy versus light microscopy; this difference may relate to the distribution of fiber sizes found in the diet samples. He reiterated the inadequacy of the DMH studies in that a literature report indicated a higher incidence of hemangiomas and hemangiosarcomas in DMH-treated hamsters than were seen in the current study. Dr. Mirer asked for available references to studies in hamsters of asbestos exposure by other routes of administration. He emphasized again that the nature of the test material is most important before meaningful conclusions can be made.

Dr. Williams suggested that the DMH studies may have been inadequate because the DMH was not appropriately buffered to prevent decomposition. He asked that summary data be included from an EPA report showing various forms of asbestos to be inactive genetically (Reiss et al., 1979). Dr. Mirer elaborated further on experiments not done which might have aided interpretation of the results. One had to do with uptake and translocation of asbestos fibers in the body, while the other related to whether asbestos pelleted in diet is available to be absorbed and/or translocated in the same way that asbestos suspended in drinking water would be.

Dr. Moore, NTP, said there was disagreement between the original pathologist and the Pathology Working Group for both this report and the amosite asbestos report. Dr. Swenberg felt that this was handled well in the reports. He said that the quality assurance review findings should also be included in the report or there should at least be a statement to the effect that the findings are available on request.

Dr. Swenberg moved that the technical report on the carcinogenesis studies of chrysotile asbestos be approved following the insertion of the minor revisions indicated. Dr. Mirer seconded the motion and the technical report was approved unanimously by the Peer Review Panel.

## **I. INTRODUCTION**

## I. INTRODUCTION

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The term asbestos has a commercial/industrial derivation limited to naturally occurring fibrous minerals of the serpentine or amphibole series. Chrysotile is the only asbestos in the serpentine series, whereas the amphibole series is represented by actinolite, amosite, anthophyllite, crocidolite, and tremolite. The essential characteristic of asbestos minerals is their fibrous nature. The gross fibers which are visible to the naked eye are actually bundles of much finer fibrils that are submicroscopic in size.

Studies during the past 25 years have clearly established an association between occupational exposure to asbestos and increased risk of cancer. Human studies have shown that increased tumor risk is associated with chrysotile, amosite, and anthophyllite exposure; animal studies also implicate crocidolite.

Excellent reviews of the carcinogenic and public health effects associated with asbestos are those by Selikoff (1980), the Environmental Protection Agency (1980), Selikoff and Hammond (1979), and the International Agency for Research on Cancer (1977).

Lung cancer and mesothelioma are neoplasms most frequently observed in people exposed to asbestos, with the latter tumor perhaps unique in its association with these fibers. A modest increase in the incidence of gastrointestinal tumors has also been observed among asbestos insulation workers, miners, and factory workers. The increased incidence of gastrointestinal cancer and possible peritoneal mesothelioma in occupationally exposed populations may be a consequence of direct fiber ingestion or ingestion of inhaled fibers cleared from the nasal or tracheobronchus portions of the respiratory system by mucociliary processes.

Large portions of the population ingest asbestos through consumption of food and water. Analysis of water samples from 365 cities found 45% to have detectable levels of asbestos (Millette, 1979). Forty-one cities had asbestos concentrations in water that exceeded 10 million fibers per liter. Asbestos or asbestos-like fibers may gain access to water supplies as a result of mining (Lake Superior), presence of natural serpentine or amphibole deposits in water sheds (Seattle, Washington, and San Francisco, California), or, under certain conditions, through the use of asbestos-cement pipe by municipal water supplies (EPA, 1980). In the latter instance erosion of fibers is associated with the "aggressiveness" of the water, a term representing a

mathematical expression of pH, alkalinity, and calcium content. Approximately 69% of U.S. water systems utilize water that is potentially capable of eroding asbestos-cement pipe (EPA, 1980).

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

Furthermore, beers and wines could contain asbestos, possibly as a consequence of the use of asbestos filters in the preparation of these products (Cunningham and Pontefract, 1971). The ingestion of rice treated with talc that contains asbestos has been hypothesized to be associated with an increased incidence of stomach cancer (Merliss, 1971a and 1971b).

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

Studies in animals have shown that the inhalation of asbestos can produce lung carcinoma and mesothelioma in the pleural cavity. Intrapleural, intratracheal, and intraperitoneal injection of asbestos will also produce neoplasia in several species of laboratory animals. A review of these studies is given by Levine (1978).

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

## I. INTRODUCTION

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liver. Asbestos was also found to be cytotoxic to Syrian hamster peritoneal macrophages (Bey and Harrington, 1971).

Using the HGPRT locus/resistance to 6-thioguanine assay system, Reiss et al. (1979) showed that the above three forms of asbestos were not mutagenic. In addition, no mutagenic activity was demonstrated using chrysotile, amosite, or crocidolite asbestos in *Escherichia coli* or *Salmonella typhimurium* systems (Chamberlain and Tarmy, 1977). From these data, asbestos is not likely to be genotoxic, but rather a carcinogen of the solid state type (Weisburger and Williams, 1979).

In 1973 the National Institute of Environmental Health Sciences and the Environmental Protection Agency cosponsored a symposium on the possible biological effects of ingested asbestos (EHP, 1974). This conference concluded that a paucity of data existed concerning the effects of ingested asbestos and that specific research was needed.

A Subcommittee of the DHEW Committee to Coordinate Toxicology and Related Programs subsequently reviewed existing data and pre-

pared a draft research protocol that the Committee felt was responsive to the major public health consensus. The protocol was widely distributed for comment within and outside the government. On the basis of the comments received, a revised protocol was developed which required long-term animal toxicology and carcinogenesis studies to evaluate the ingestion of several forms of asbestos for carcinogenic effect. The forms of asbestos to be studied included chrysotile (a serpentine asbestos) (NTP TR 246), amosite (NTP TR 249 for studies in Syrian golden hamsters and TR 279 for studies in F344/N rats) and crocidolite (representative of amphibole asbestos) (NTP TR 280), and a nonfibrous tremolite (NTP TR 267), which contained low levels of asbestiform fibers.

All materials were to be tested in the Fischer 344 strain of rat, whereas two forms of asbestos were to be tested in hamsters. All studies were to encompass the lifetime of the animal, defined as the period from which the animal commences eating solid food until death.

This technical report presents the results of those studies undertaken to determine the effects of short range and intermediate range chrysotile asbestos in the diet fed to male and female Syrian golden hamsters.



## **II. MATERIALS AND METHODS**

**TEST MATERIALS**

**TEST DIETS**

**SOURCE AND SPECIFICATIONS OF TEST ANIMALS**

**ANIMAL MAINTENANCE**

**CLINICAL EXAMINATIONS AND PATHOLOGY**

**DATA RECORDING AND STATISTICAL METHODS**

**PILOT STUDY FOR DOSE SETTING OF INTESTINAL CARCINOGEN**

## II. MATERIALS AND METHODS: TEST MATERIALS

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### TEST MATERIALS

Asbestos is a general term applied to certain natural mineral silicates when they appear in a fibrous form. Chrysotile is the fibrous member of the serpentine mineral group; its chemical structure is  $Mg_3Si_2O_5(OH)_4$ . Two chrysotile test materials were selected for testing and are referred to as short range (SR) and intermediate range (IR) chrysotile. Intermediate range chrysotile differs from short range chrysotile in that the former contains fibers extending into relatively large sizes both with respect to length and diameter.

The short range chrysotile was purchased from the Union Carbide Corporation, Niagara Falls, New York, which referred to the material as COF-25. The chrysotile was mined from the New Idria serpentine mass located in the southern part of the Diablo Range in the southwestern San Benito and western Fresno counties of California.

The intermediate range chrysotile was purchased from the Johns Manville Company, which referred to the material as Plastobest-20. This is a particularly clean grade of chrysotile used in the plastics industry. The chrysotile was obtained from the Jeffrey Mine, Asbestos, Quebec, Canada.

The two chrysotile test materials were each purchased in quantities of about 1,000 pounds. Each material was packaged in new fiberboard

drums in quantities of 25 (short range) or 50 pounds (intermediate range) and stored with other forms of asbestos in a special warehouse room at Research Triangle Park, North Carolina. Each drum received a color marking unique to the specific asbestos type.

The homogeneity of the samples and the physical and chemical properties of the materials were extensively characterized by the Bureau of Mines, U.S. Department of the Interior (Supt. of Documents No. I 28.23:8452) and by the Fine Particle Laboratories, Illinois Institute of Technology Research Institute, Chicago, Illinois (Special Report and Addendum on project L6085, contract NO1-ES-5-3157). Copies of these reports are available upon request from the National Toxicology Program.

Selected chemical and physical properties which define differences between the two chrysotile samples are given below and in Table 1.

Short range chrysotile was detected at greater than 96% by volume; minor amounts of calcite, brucite, talc, feldspar, quartz, and opaques were present.

Intermediate range chrysotile was detected at greater than 96% by volume; minor amounts of platy serpentine, calcite, brucite, pyroxene, talc, magnetite, and other opaques were present.

### TEST DIETS

The feed used was NIH-31 open formula rodent diet prepared by Zeigler Brothers Inc., Gardners, PA. The appropriate chrysotile asbestos was incorporated to a level of 1% by weight into the test diet. Pilot studies determined that homogeneous mixing of asbestos and feed would occur when a 55 cu. ft. Patterson Kelly "V" blender was loaded by alternate layering of feed and asbestos. All feed was pelleted with a

Sprout-Waldron pelleter; the pellets were of oval configuration, 3/8" by 3/4" in size. Pelleted feed was packaged in 25 pound aliquots in standard paper feed bags which were color coded to minimize the occurrence of feeding errors at the test laboratory. Each lot of blended feed was analyzed for asbestos concentration; the results of these analyses are given in Appendix A.

**TABLE 1. FIBER CHARACTERISTICS AND CHEMICAL-INSTRUMENTAL ANALYSES OF CHRYSOTILE ASBESTOS (a)**

	Short Range	Intermediate Range
<b>Fiber Characteristics</b>		
Surface area (m <sup>2</sup> /g)	54.3 ± 3.9 (b)	20.2 ± 0.1 (b)
	54.2 ± 0.9 (c)	24.9 ± 2.2 (c)
Density (g/cm <sup>3</sup> )	2.577 ± .022SD	2.607 ± .016 SD
Measurement, transmission electron microscopy		
fiber count/gram	.6081 x 10 <sup>13</sup>	.1291 x 10 <sup>12</sup>
median length (μm)	0.66	0.82
range of length (μm) (d)	0.088 - 51.1	0.104 - 783.4
median diameter (μm)	0.059	0.089
range of diameter (μm)	0.019 - 1.67	0.019 - 11.5
median fiber aspect ratio (l/d)	11.1698	8.435
<b>Chemical Instrument Analyses (expressed as weight percent)</b>		
Al <sub>2</sub> O <sub>3</sub>	0.66	1.47
CaO	0.32	0.05
FeO	Not Detected	Not Detected
Fe <sub>2</sub> O <sub>3</sub>	2.02	2.93
MgO	40.62	40.26
K <sub>2</sub> O	Not Detected	0.08
SiO <sub>2</sub>	39.77	39.90
Na <sub>2</sub> O	0.01	0.04
TiO <sub>2</sub>	0.03	0.04
MnO	0.07	0.06
Cr <sub>2</sub> O <sub>3</sub>	0.17	0.06
NiO	0.17	0.06
Co <sub>2</sub> O <sub>3</sub>	0.01	Not Detected
CO <sub>2</sub>	0.78	0.51
H <sub>2</sub> O <sup>-</sup>	1.54	1.17
H <sub>2</sub> O <sup>+</sup>	12.69	12.81
Benzene extracted organics	0.026	0.011

(a) Measurements by transmission electron microscopy were performed at the Illinois Institute of Technology Research Institute; all other analyses were performed by the Bureau of Mines.

(b) As measured with the Quantachrome surface area instrument on 15-30 independent samples.

(c) As measured with the Perkin-Elmer surface area instrument on 15-30 independent samples.

(d) SR is comprised of short fibers, with 98% < 10 μm. IR consists of 65% > 10 μm, with a significant number of fibers (~14%) longer than 100 μm.

## II. MATERIALS AND METHODS: SOURCE AND SPECIFICATIONS OF TEST ANIMALS

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### SOURCE AND SPECIFICATIONS OF TEST ANIMALS

Disease free, mated female outbred Syrian golden hamsters were obtained over a period of 20 weeks in 1977 from Charles River Lakeview

Laboratories, Wilmington, MA. The hamsters had been mated 6 days prior to shipping.

### ANIMAL MAINTENANCE

Upon arrival, the mated female hamsters were weighed and sorted into weight ranges. They were then distributed randomly between control and treatment groups, which were housed in separate rooms. The first shipment of mated females was assigned to the short range (SR) chrysotile study, the second to the intermediate range (IR) chrysotile study, the third shipment to the IR chrysotile plus DMH study, the fourth group to the amosite study and their respective control groups. Each dam was placed in an individual cage with filter top in its respective room. Control or formulated diets were provided *ad libitum* in feed jars on the floor of each cage. Water was provided *ad libitum* via bottles. The hamsters were not handled except when the cages were changed just before the litters were due to be born. Once the litters were born, they were left undisturbed until they were approximately 10 days of age. Then, the cages were changed weekly until the offspring were 4 weeks of age, at which time they were weaned. Details of animal maintenance are presented in Table 2.

At weaning, the offspring were individually weighed and separated by sex. The test groups were randomly placed into groups of 3 males or 3 females and housed in polycarbonate cages for the remainder of the lifetime study. The dams were killed at this time. Twenty male and 20 female offspring were removed from the study for endo- and ectoparasite examination (Appendix B) to confirm that the test groups were of a desired health status. Extra hamsters were not discarded at this time, in case animals had been missexed. Approximately 6 weeks after weaning, all missexed hamsters were killed along with their cage mates and were replaced with these alternates which had received maintenance identical to that received by the original hamsters. The remaining hamsters were killed. The experimental design insured that ingestion of asbestos spanned the entire phase of solid food consump-

tion during the lifetime of the animal. Food consumption was not determined because of the hamster's habit of sequestering its feed in the bedding. Control hamsters were housed in separate rooms. The number of animals in the study is shown in Table 3.

Starting at 6 weeks of age, male and female hamsters in the intermediate range chrysotile/1,2-dimethylhydrazine dihydrochloride (DMH) study (Table 3) were given oral doses of DMH (4 mg/kg) every other week for a total of 5 doses. The dose of DMH used in this study was based on the results of a pilot study carried out previously in the same facility (see Pilot Study section for details). The latter was conducted in a manner similar to that reported in rats (McConnell et al., 1980). The DMH (Aldrich Chemical Co., Milwaukee, WI) was used as received and was dissolved in 0.9% saline to give a concentration of 2.00 mg/ml. The solutions were made up within one hour prior to the dosing of the hamsters. All dosing was completed in less than 3 hours. The DMH was analyzed after each dosing (Appendix C).

During the test period, the room temperature was maintained at  $22^{\circ}\text{C} \pm 2^{\circ}\text{C}$  and the relative humidity ranged from 40% to 80%. To minimize contamination of room air with asbestos, each cage was totally enclosed. Incoming air to the cages was passed through fiberglass filters, while exit air was passed through a fiberglass roughing filter followed by a bag housing filter. The cage air pressure was negative relative to the room and the room was maintained at a slightly negative pressure in relation to corridor air. Air flow within the animal rooms was maintained with a minimum of 20 air changes per hour. Fluorescent lighting was provided 12 hours per day.

**TABLE 2. MATERIALS AND METHODS FOR ANIMAL MAINTENANCE**

<b>Item</b>	<b>Manufacturer</b>	<b>Specifications</b>	<b>Frequency of Change or Cleaning</b>
Cages	Maryland Plastics New York, NY	Econo-Cage Polycarbonate 19" x 10-1/2" x 8"	Weekly
Racks	Bussy Products	Stainless Steel 20 cages/rack	Weekly
Bedding	Ab-sorb-Dri, Inc. Rochelle Park, NJ	Hardwood 50 lb/bag	Weekly
Cage tops	Able Molded Plastics, Inc. Chicago, IL	GE Lexan Polycarbonate	Weekly
Cage Filter	Associated Air Filter Co. Rosemont, IL	3" Diameter cut from FG50 Filter Mats	Weekly
Metal Holder for Cage Filter	C.D. Cash Manufacturing Chicago, IL	Outer shell with screen and baffle Inner shell with screen	Weekly
Snap Ring for Holder	Keats-Lorenz Spring Co. Chicago, IL	Phosphor Bronz Spring tempered	Weekly
Feed dish with Metal Lips	W. Braun Company Chicago, IL	16 oz. Opal or clear glass jars	Weekly
Feed Follower	Unifab Corp. Kalamazoo, MI	Stainless Steel with 7 holes	Weekly
Water Bottles	Continental Glass Co. Chicago, IL	Pint Flint glass	Weekly
Watering Tube	Wahmann Mfg. Co. Timonium, MD	Stainless Steel 5/16" OD, 7-1/2" length with 120° bend 1-1/2" from bottle	Weekly
Feed	Ziegler Brothers Gardners, PA	NIH-31 Diet 25- or 50-lb bags	Weekly
Cage & Bottle Washer	Blakeslee Cicero, IL	Tunnel Wash	Daily check Monthly maintenance
Autoclaves	American Sterilizer	Models 1) Medallion 2) RSP (Vacumatic S)	Bimonthly maintenance
Washing Compounds	Economics Labs, Inc. St. Paul, MN	Spearhead Lime Away	
Room Air Filters (Exhaust)	(Roughing Filters) Air Filter Equip. Corp. Chicago, IL  (Bag Housing) Pure Air Filter Chicago, IL	Amer-Glass Filters Type G filters  Dri Pak 2100 H Class II  Absolute Filters Am. Air Filter Astrocel	
Rack Washer	Metal Wash Machinery Elizabeth, NJ	Mark V	Daily check Monthly maintenance

TABLE 3. DISPOSITION OF HAMSTERS FROM THE CHRYSOTILE ASBESTOS FEED STUDY

Group	Sex	On Test	Histopathologic Evaluation	Missing	Cannibalized	Autolyzed	Missexed
SR Chrysotile	M	126	115	0	3	6	2
Control	F	126	114	1	1	6	5
IR Chrysotile	M	126	116	0	0	8	2
Control	F	126	119	0	0	4	3
DMH and IR Chrysotile	M	125	119	0	0	3	3
Control	F	128	120	1	0	2	5
Amosite	M	127	122	0	0	4	1
Control	F	126	119	1	0	1	5
SR Chrysotile	M	253	233	0	1	10	9
	F	252	228	1	0	17	6
IR Chrysotile	M	251	245	0	0	3	3
	F	252	244	1	0	3	4
DMH	M	127	127	0	0	0	0
	F	126	122	0	0	1	3
DMH and IR Chrysotile	M	176	173	0	0	2	1
	F	173	161	3	0	6	4

## CLINICAL EXAMINATIONS AND PATHOLOGY

All hamsters were observed daily for signs of toxicity. Body weights of individual animals were recorded weekly for the duration of the study. All animals were allowed to die or were killed with pentobarbital sodium when moribund. A complete post-mortem examination was performed on all animals not severely cannibalized or autolyzed. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and does not necessarily represent the number of animals that were placed on study in each group (Table 3).

The gastrointestinal tract, chosen as one of the target organs prior to the study, was handled in a manner slightly different than in standard rodent lifetime studies. Prior to placement 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 2 portions of jejunum were placed unopened in fixative. The remaining small intestine was opened, washed gently with saline, and then carefully examined. Suspected lesions were processed separately and identified

individually as to location. Likewise, the entire colon with anus was opened, examined, and pinned to cardboard prior to 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 prior to embedding, the colon was "carpet-rolled" starting at the posterior end, with the mucosal surface inward.

All tissues were fixed in 10% neutral buffered formalin, sectioned, and stained with hematoxylin and eosin. Tissues/organs examined microscopically were: tissue masses, the above-mentioned portions of gastrointestinal tract, mesenteric and bronchial lymph nodes, salivary gland, bone marrow (sternum), larynx, trachea, lungs and bronchi, heart, thyroid, parathyroid, liver, gallbladder, pancreas, spleen, kidneys, adrenal glands, urinary bladder, seminal vesicles/prostate/ testes, ovaries/uterus, brain and pituitary gland. Mammary gland, thigh muscle, nasal cavity with turbinates, eyes, and spinal cord were examined grossly.

The findings of the contracting pathologist were subjected to a quality assurance review by an independent pathology contractor. This

## II. MATERIALS AND METHODS: ANIMAL MAINTENANCE

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review consisted of an examination of all tumors diagnosed by the original pathologist, target organs (gastrointestinal tract) from all animals, and all organs from 10% randomly selected hamsters, and of a tissue count on all animals. Sections from all tumors and from any other organ in which a discrepancy existed between the original and reviewing pathologists were submitted to the NTP Pathology Working Group (NTP/

PWG) for subsequent review. When there was a discrepancy in tumor diagnosis between the original pathologist and the NTP/PWG, all slides in question were returned to the original pathologist for reevaluation. The tables in this report represent the original pathologist's final diagnosis. Cases in which the original pathologist did not agree with the NTP/PWG are reported separately.

### DATA RECORDING AND STATISTICAL METHODS

The individual animal pathology data from this experiment were recorded in the Carcinogenesis Bioassay Data System. The data elements include descriptive information on the chemicals, animals, experimental design, clinical observations, survival, and individual pathologic results.

Probabilities of survival were estimated by the product-limit procedure of Kaplan and Meier (1958) and are presented in this report in the form of graphs. Animals were statistically censored as of the time that they died of other than natural causes or were found to be missing; animals dying from natural causes were not statistically censored. Differences in survival were evaluated by Cox's (1972) life table method.

As noted earlier, concurrent studies were conducted in this laboratory with another form of asbestos (amosite) with exactly the same protocol (NTP, 1983). Although the results of these studies are not given in this report, the amosite controls were included with the chrysotile control groups for statistical purposes as part of the pooled controls.

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 (numerator) to the number of animals in which that site was examined (denominator). In most instances, the denominators included only those animals for which that site was examined histologically. However, when macroscopic examination was required to detect lesions (e.g., skin or mammary tumors) prior to histologic sampling, or when lesions could have appeared at multiple sites (e.g., lymphomas), the denominators consist of the numbers of animals necropsied.

For the statistical analysis of tumor incidence data, two different methods of adjusting for

intercurrent mortality were employed. Each used the classical methods for combining contingency tables developed by Mantel and Haenszel (1959).

The first method of analysis assumed that all tumors of a given type 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 treated 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 were then combined by the Mantel-Haenszel methods to obtain an overall probability (P) value. This method of adjusting for intercurrent mortality is Cox's life table method (1972).

The second method of analysis assumed that all tumors of a given type were "incidental," i.e., they were merely observed at autopsy in animals dying of an unrelated cause. According to this approach, the proportions of animals found to have tumors in treated and control groups were compared in each of five time intervals. For male hamsters these time intervals were 0-52 weeks, 53-78 weeks, 79-92 weeks, 93-103 weeks, and beyond 103 weeks. For female hamsters whose median survival was considerably less than that of the males, the time intervals were 0-44 weeks, 45-52 weeks, 53-60 weeks, 61-68 weeks, and beyond 68 weeks. The denominators of these proportions were the number of animals actually autopsied during the time interval. The individual time interval comparisons were then combined by the previously described methods to obtain a single overall result. (See Peto et al., 1980.)

In addition to these tests, one other set of statistical analyses was carried out for each primary tumor: the Fisher exact test based on

## II. MATERIALS AND METHODS: DATA RECORDING AND STATISTICAL METHODS

the overall proportion of tumor-bearing animals (Gart et al., 1979). All reported P values are one

sided. Except where noted, the three alternative analyses gave similar results.

### PILOT STUDY FOR DOSE SETTING OF INTESTINAL CARCINOGEN

This pilot study was designed to determine the dose of a known intestinal carcinogen that would produce a low incidence ( $10\% \pm 5\%$ ) of intestinal cancer and relatively little toxicity or neoplasia at other sites in the body. This experiment was conducted in a manner similar to that reported in rats (McConnell et al., 1980). The chemicals chosen were methylazoxymethanol acetate (MAM) and 1,2-dimethylhydrazine dihydrochloride (DMH) (Aldrich Chemical Co., Milwaukee, WI). The chemical which most nearly met these two criteria would be used in the cocarcinogenesis studies.

MAM or DMH was used as received and dissolved in 0.9% saline to a concentration of 1.5% (15 mg/ml), then diluted with saline to give the appropriate concentration for dosing. The solutions were made up within one hour prior to dosing the animals. To obviate decomposition of the chemical, all dosing was completed in less than 3 hours following preparation of the solutions.

While in the rooms, personnel wore full protective clothing and activated charcoal respirators during the actual dosing and for an additional 2 weeks following the last dose. After this time, normal safety precautions were used.

Four-week-old male and female Syrian golden hamsters were obtained from A.R. Schmidt Co. (Madison, WI) for this pilot study. The animals were acclimatized to their environment for 2 weeks; during this period, 2 males and 2 females were chosen randomly for qualitative disease diagnosis as described earlier. Caging, bedding, and feeding were also handled as described earlier (Table 1). At 6 weeks of age, hamsters were sorted by weight and assigned randomly to the dose groups prior to compound administration. DMH or MAM solutions were administered by gastric intubation, 0.2 ml/kg body weight every other week for 10 weeks (5 doses). Dose levels and group sizes are shown in Table 4. The unbalanced group sizes were selected so that the largest numbers of animals would be included in dosage groups in which the desired effects were most likely to be observed. The study was terminated 9 months following the last dose of the carcinogen.

TABLE 4. DOSE LEVELS AND GROUP SIZES OF HAMSTERS USED IN THE PILOT STUDIES OF METHYL-AZOXYMETHANOL (MAM) AND 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH)

Dose Level (mg/kg b.w.)	Group Size		
	Males	Females	Total
0 (0.9% saline control)	30	30	60
0.2	30	30	60
1	27	27	54
4	27	27	54
7.5	27	27	54
15	21	21	42
30	18	18	36

All hamsters were observed daily and weighed once per week. (Statistical analyses were not done on body weight gain.) Clinical signs were not recorded unless considered pertinent to pathological observations. Fecal samples were collected and analyzed for the presence of occult blood (clinitest tablets) at 3 months after the dosing regimen started (blood in the feces is often associated with the presence of intestinal neoplasms). A slight positive reaction is normally observed, due to the presence of undigested myoglobin in the feed. Any increase in intensity was considered to be a qualitative indication of occult blood.

All hamsters were subjected to a complete post-mortem examination as described earlier. While all hamsters were necropsied, not all animals were submitted for histopathological evaluation. Tissues from animals selected for histology were taken predominantly from the control groups of hamsters, from animals showing macroscopic tumors, and from those hamsters treated with lower doses of DMH, since it was obvious early in the study that DMH produced less hepatic toxicity than MAM (see below). Tissues routinely selected for histopathologic examination included representative portions of the entire gastrointestinal tract, liver, kidneys, mesenteric and colo-rectal lymph nodes, and any macroscopically visible or suspect lesions. Methods used for the handling of

## II. MATERIALS AND METHODS: PILOT STUDY FOR INTESTINAL CARCINOGEN

these tissues were identical to those described previously.

Only the highest dose (30 mg/kg) of either MAM or DMH caused a marked effect on body weight gain. Females were more affected than males. The 30 mg/kg and 15 mg/kg doses of either MAM or DMH markedly decreased the survival rate, with females again being more affected than males at the same dose. Many of these hamsters died early in the study due to hepatic toxicity. (Note: body weight and survival data are not given.)

Of those animals receiving the two higher doses (30 and 15 mg/kg) of either compound, the majority that did not die early in the study due to toxic hepatitis had macroscopically visible masses in the colon and/or cecum; the colonic masses often adhered to the abdominal wall and in many instances contained large abscesses (Table 5). However, because animals died early in the study due to toxic hepatitis, the relationship between the dose administered and the tumor incidence in these groups could not be determined.

**TABLE 5. INTESTINAL TUMOR INCIDENCE IN HAMSTERS GIVEN 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH) BY GAVAGE (a)**

Dosage Group	Effective Number of Animals (b)	Number of Animals Examined Histopathologically	TBA (c)	% TBA (d)	Total No. of Tumors	
					Benign	Malignant
<b>Males</b>						
Saline control	29	9	2	7%	2	0
0.2 mg/kg	27	14	6	22%	9	0
1 mg/kg	27	14	6	22%	18	2
4 mg/kg	27	7	4	15%	5	0
7.5 mg/kg	27	10	7	26%	14	25
<b>Females</b>						
Saline control	29	18	2	7%	2	0
0.2 mg/kg	27	11	3	11%	3	0
1 mg/kg	27	13	3	11%	4	0
4 mg/kg	27	11	3	11%	2	5
7.5 mg/kg	26	13	13	50%	29	114

(a) DMH was administered once per week every other week for 10 weeks (5 doses).

(b) Effective Number of Animals = original number in group minus animals lost to autolysis.

(c) Based on histopathological evaluation = intestinal tumor-bearing animals.

(d) 
$$\% \text{ TBA} = \frac{\text{TBA}}{\text{Effective No. Animals}} \times 100$$

The effective number of animals was used in the denominator because these lesions are seen at necropsy and are examined microscopically for confirmation and differentiation.

## II. MATERIALS AND METHODS: PILOT STUDY FOR INTESTINAL CARCINOGEN

Tumors of the colon were comparable morphologically to those described in the similar study in Fischer 344 rats given DMH (McConnell et al., 1980) and in a single-dose study of MAM (Ward, 1975). These neoplasms varied from adenomatous polyps to tubular or mucinous adenocarcinomas with invasion through the muscle wall and local metastases to regional lymph nodes (Table 6). Cystic epithelial hyperplasia of the cecum was commonly observed, but was probably not related to carcinogen exposure.

In addition to effects on the gastrointestinal tract, marked hepatic toxicity (dose related) was observed both at necropsy and histopathologically and was present to a greater extent in hamsters given MAM than in those given DMH. Affected livers had a diffuse nodular appearance and a coarse, granular surface. Some livers contained large sac-like structures filled with blood; at times, these replaced most of the affected lobe. Microscopically, the liver lesions encompassed a variety of changes, including focal necrosis with blood-filled spaces, hepatocellular vacuolization, cellular and nuclear pleomorphism, and focal nodular hyperplasia. Hepatotoxicity in hamsters administered DMH was judged to be

minimal at doses of 7.5 and 4 mg/kg and was not observed below the latter dose. Lesions in the liver that were not related to chemical administration included periportal amyloidosis, bile-duct proliferation, and intrahepatic biliary cysts. These changes were found in almost every hamster.

In those hamsters that survived the hepatic toxicity there was increasing mortality, apparently due to severe nephropathy. This appeared in all dose groups and in the controls. The kidneys from these animals were pale and granular and had a thin cortex. Most of these animals were emaciated, and the liver often had a granular appearance. Microscopically, the kidneys were characterized by diffuse and often massive accumulations of amyloid. The glomerulus seemed to be primarily affected, but involvement of the entire cortex, and to a lesser extent of the medulla, was also observed. Inflammation was conspicuously absent.

In conclusion, both chemicals induced dose-related intestinal tumors, but DMH had fewer toxic side effects than MAM; for this reason, DMH was chosen for the cocarcinogenesis studies. The dose selection for females was relatively

TABLE 6. NUMBERS AND TYPES OF INTESTINAL TRACT TUMORS IN HAMSTERS GIVEN 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH) BY GAVAGE

Group	Number of Animals Examined Histopathically	Tumor-Bearing Animals	Number of Tumors					Location
			Adenomatous Polyp	Adenoma, Sessile	Adeno CA (Sessile)	Adeno CA (in situ)	Mucinous Adeno CA	
<b>Males</b>								
Saline (DMH)	9	2	2	0	0	0	0	Colon
DMH, 0.2 mg/kg	14	6	9	0	0	0	0	Colon, Cecum
DMH, 1 mg/kg	14	6	11	7	0	1	1	Colon, Cecum
DMH, 4 mg/kg	7	4	4	1	0	0	0	Colon, Cecum
DMH, 7.5 mg/kg	10	7	14	0	13	12	0	Colon, Cecum
<b>Females</b>								
Saline (DMH)	18	2	2	0	0	0	0	Colon
DMH, 0.2 mg/kg	11	3	3	0	0	0	0	Colon
DMH, 1 mg/kg	13	3	1	3	0	0	0	Colon
DMH, 4 mg/kg	11	3	2	0	0	5	0	Colon
DMH, 7.5 mg/kg	13	13	29	0	28	86	0	Colon, Cecum

## II. MATERIALS AND METHODS: PILOT STUDY FOR INTESTINAL CARCINOGEN

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straightforward: 4 mg/kg produced the desired incidence (11%) of tumors of the large intestine (benign and malignant), while 7.5 mg/kg caused a high incidence (50%) of intestinal tumors, and 1 mg/kg caused no malignant tumors (Tables 4-6). The data for males were more difficult to interpret because of the lack of a clear dose-response. Four mg/kg was also chosen for these

cocarcinogenesis studies because 7.5 mg/kg caused too high an incidence of malignant tumors. Even though malignant tumors were not observed at the 4 mg/kg dose, they were observed at a low incidence in the 1 mg/kg dose group; as interpreted, these data suggested that 4 mg/kg should produce a higher yield of intestinal tumors in the subsequent study.



### **III. RESULTS**

**ESTABLISHMENT OF TEST GROUPS**

**BODY WEIGHTS AND CLINICAL SIGNS**

**SURVIVAL**

**PATHOLOGY AND STATISTICAL ANALYSES OF RESULTS**

### III. RESULTS: ESTABLISHMENT OF TEST GROUPS

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#### ESTABLISHMENT OF TEST GROUPS

The experiments were designed to evaluate the effects of orally ingested chrysotile asbestos during the entire life of the animal, starting from the time it was able to eat. For this reason, the mated female hamsters were placed on the test diets for approximately 2 weeks before the first litters were born. Ten to 15 percent of the females were either not pregnant or aborted, or their litters died immediately after birth. Several more dams died after showing a prolapsed rectum in the week following birth. The incidences of infertility and neonatal deaths were unrelated to the test diet. To minimize the chance that the mothers would reject or cannibalize their young, the litters were not handled during lactation. Many of the pups which died during the nursing period were cannibalized by their mothers. In those pups in which a postmortem examination was possible, the stomachs were typically without food (milk), suggesting maternal rejection or

inability to compete with litter mates. None of these observations were compound related.

Approximately 2% of the offspring in all groups died between weaning and 14 weeks of age due to cage fighting or an enteritis of undetermined origin. Histologically, the disease was compatible with the acute form of proliferative ileitis ("wet tail"), a common disease of hamsters. Combinations of cage fighting and enteritis were also observed. These deaths were not compound related, although cage fighting was more severe in the SR chrysotile and its concurrent control groups than in the other two portions of the study. Replacement hamsters were incorporated into the groups (in additional cages) to maintain group sizes until the animals were 12 weeks of age; from this time on, no additional hamsters were added to the experimental groups. The extra hamsters were killed (Figure 1).

Figure 1. Schedule of Major Events in the Chrysotile Asbestos Study

Weeks	Events
- 1	Pregnant dams obtained: —SR Chrysotile - 9 Feb 77 —IR Chrysotile - 29 March 77 —IR Chrysotile + DMH - 26 April 77 —Amosite - 6 July 77
	Start test diet
0	Birth
+ 4	Weaned Weighed Sexed Randomly grouped 3/cage Ecto + endoparasite exam
+10	Missexed hamsters discarded Alternates added Remaining extra hamsters discarded
Lifetime	Natural death or moribund sacrifice

### III. RESULTS: BODY WEIGHTS AND CLINICAL SIGNS

#### BODY WEIGHTS AND CLINICAL SIGNS

Body weight gain was not adversely affected in any dose group, including the group given 1,2-dimethylhydrazine dihydrochloride (DMH) (Figures 2-7). In fact, hamsters eating diets containing chrysotile asbestos appeared to have increased body weights in most of the dosed groups. The inordinately sharp rise in weight gain of male and female hamsters in the SR chrysotile study at week 29 and sharp decrease in

male and female IR chrysotile-exposed animals at week 18 could not be explained, but was felt to be a spurious observation. No compound-related clinical signs were observed during the entire study. Occasional skin lesions and bite wounds were observed in both sexes, but were more apparent in males; these became less of a problem after the hamsters were 20 weeks of age.

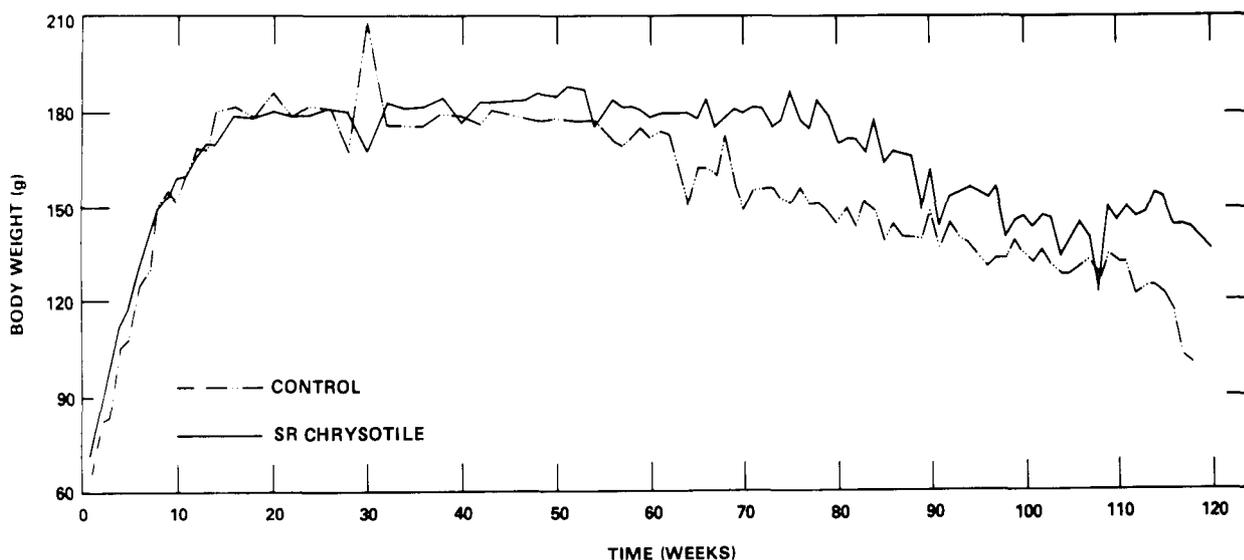


Figure 2. Growth Curves for Male Hamsters Administered Short Range (SR) Chrysotile Asbestos in the Diet

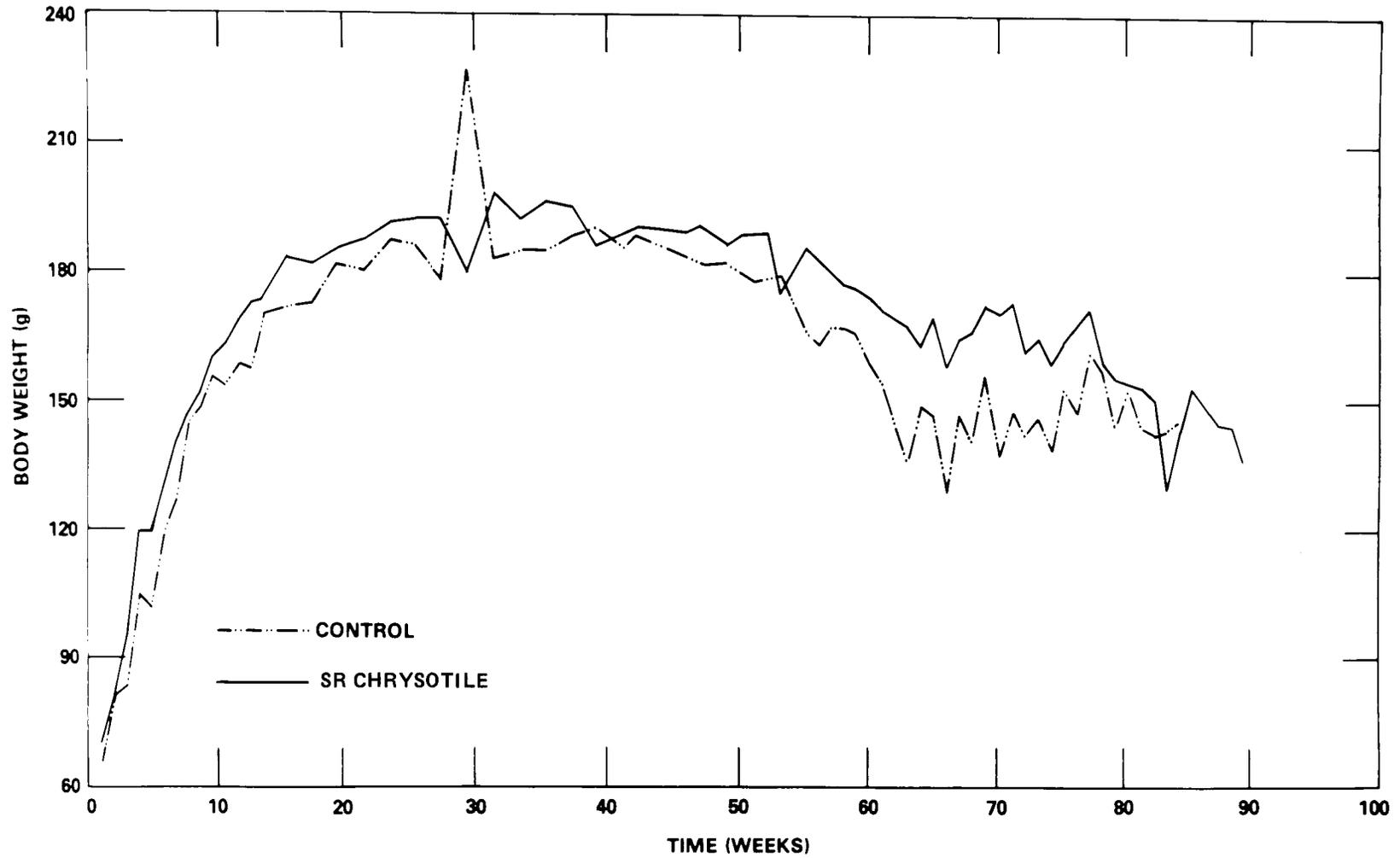


Figure 3. Growth Curves for Female Hamsters Administered Short Range (SR) Chrysotile Asbestos in the Diet

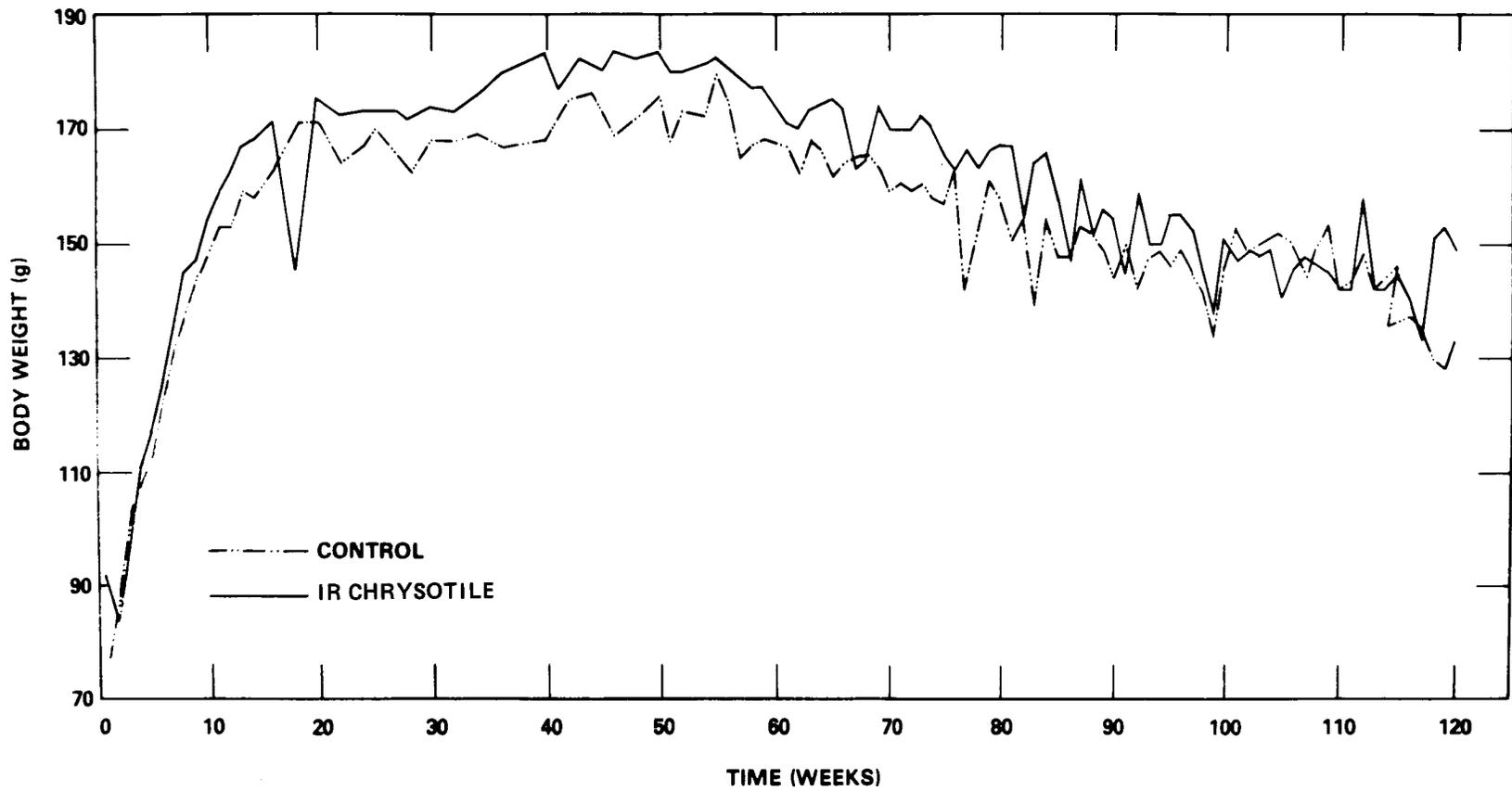


Figure 4. Growth Curves for Male Hamsters Administered Intermediate Range (IR) Chrysotile Asbestos in the Diet

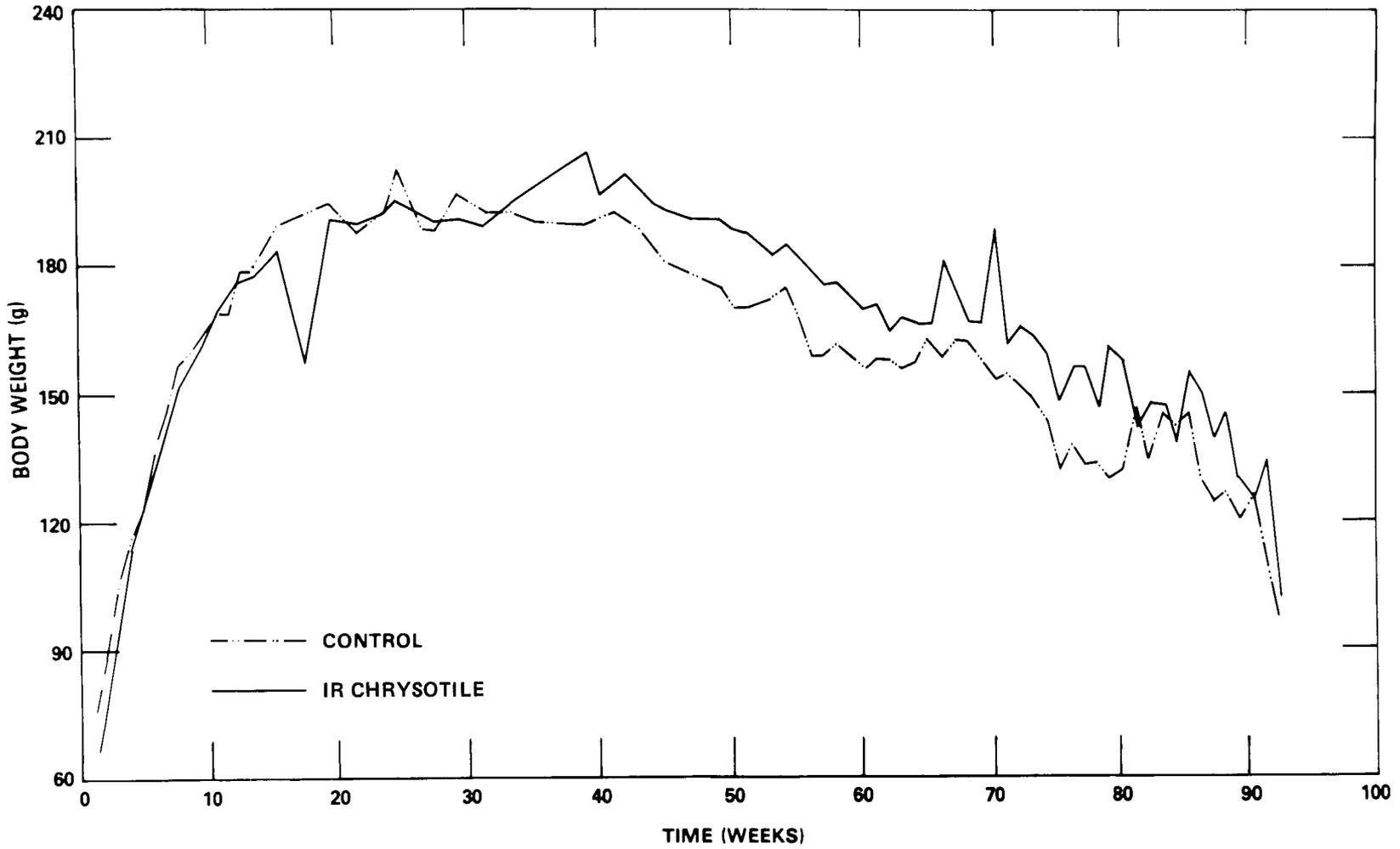


Figure 5. Growth Curves for Female Hamsters Administered Intermediate Range (IR) Chrysotile Asbestos in the Diet

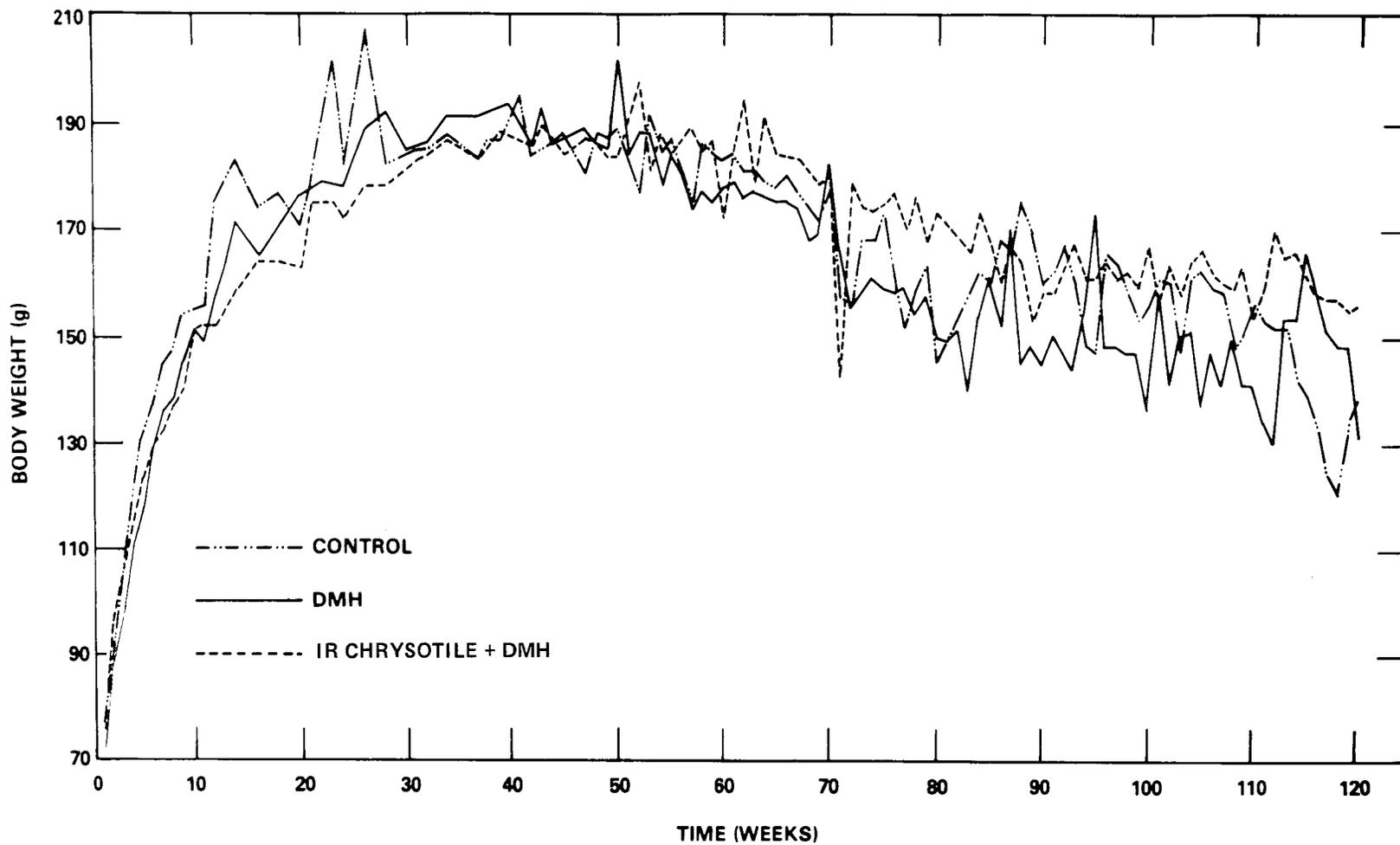


Figure 6. Growth Curves for Male Hamsters Administered 1,2-Dimethylhydrazine Dihydrochloride (DMH) by Gavage or 1,2-Dimethylhydrazine Dihydrochloride (DMH) Plus Intermediate Range (IR) Chrysotile Asbestos in the Diet

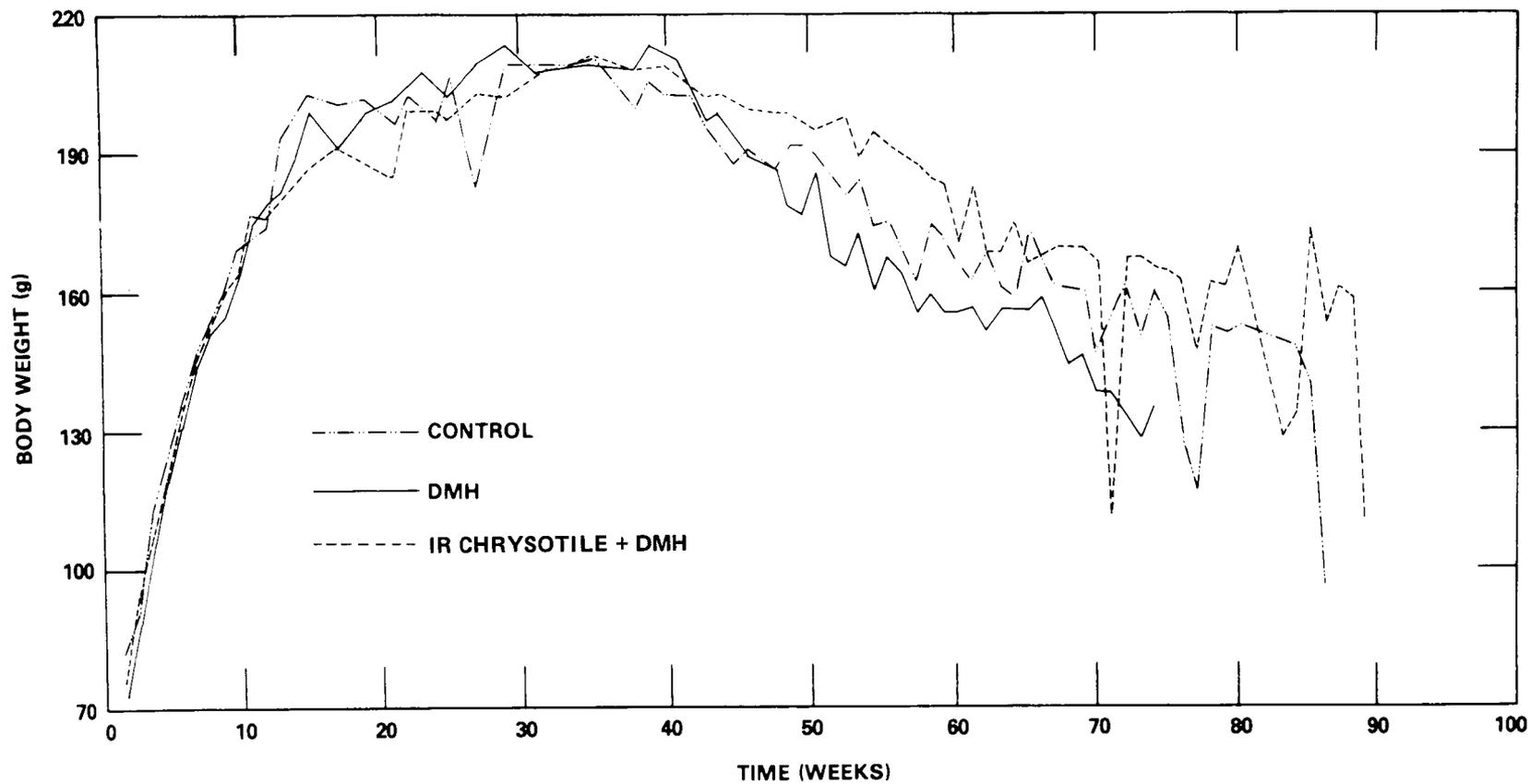


Figure 7. Growth Curves for Female Hamsters Administered 1,2-Dimethylhydrazine Dihydrochloride (DMH) by Gavage or 1,2-Dimethylhydrazine Dihydrochloride (DMH) Plus Intermediate Range (IR) Chrysotile Asbestos in the Diet

### III. RESULTS: SURVIVAL

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#### SURVIVAL

Survival was not adversely affected by any of the test diets (Figures 8-13) with the possible exception of DMH-treated female hamsters (Figure 13). Survival rates were higher in the SR and IR chrysotile groups relative to the concurrent controls. The median life spans of females

(control and treated) were shorter than those of corresponding groups of males (Table 7). The median survival of control female groups was 57-61 weeks, compared to 77-83 weeks for control male hamsters (Figures 8-13 and Table 7).

**TABLE 7. MEDIAN LIFE SPANS OF HAMSTERS RECEIVING 1% CHRYSOTILE ASBESTOS IN THE DIET FOR THEIR LIFETIME**

Group	Sex	Median Life Span (Weeks)
IR Chrysotile Control	M	84
	F	62
IR Chrysotile	M	87
	F	60
.....		
SR Chrysotile Control	M	78
	F	57
SR Chrysotile	M	87
	F	63 (a)
.....		
DMH and IR Chrysotile Control	M	81
	F	56
DMH	M	82
	F	54 (b)
IR Chrysotile and DMH	M	90
	F	62 (a)

(a) Significantly ( $P < 0.05$ ) improved overall survival relative to controls (life table analysis).

(b) Significantly ( $P < 0.05$ ) reduced overall survival relative to controls (life table analysis).

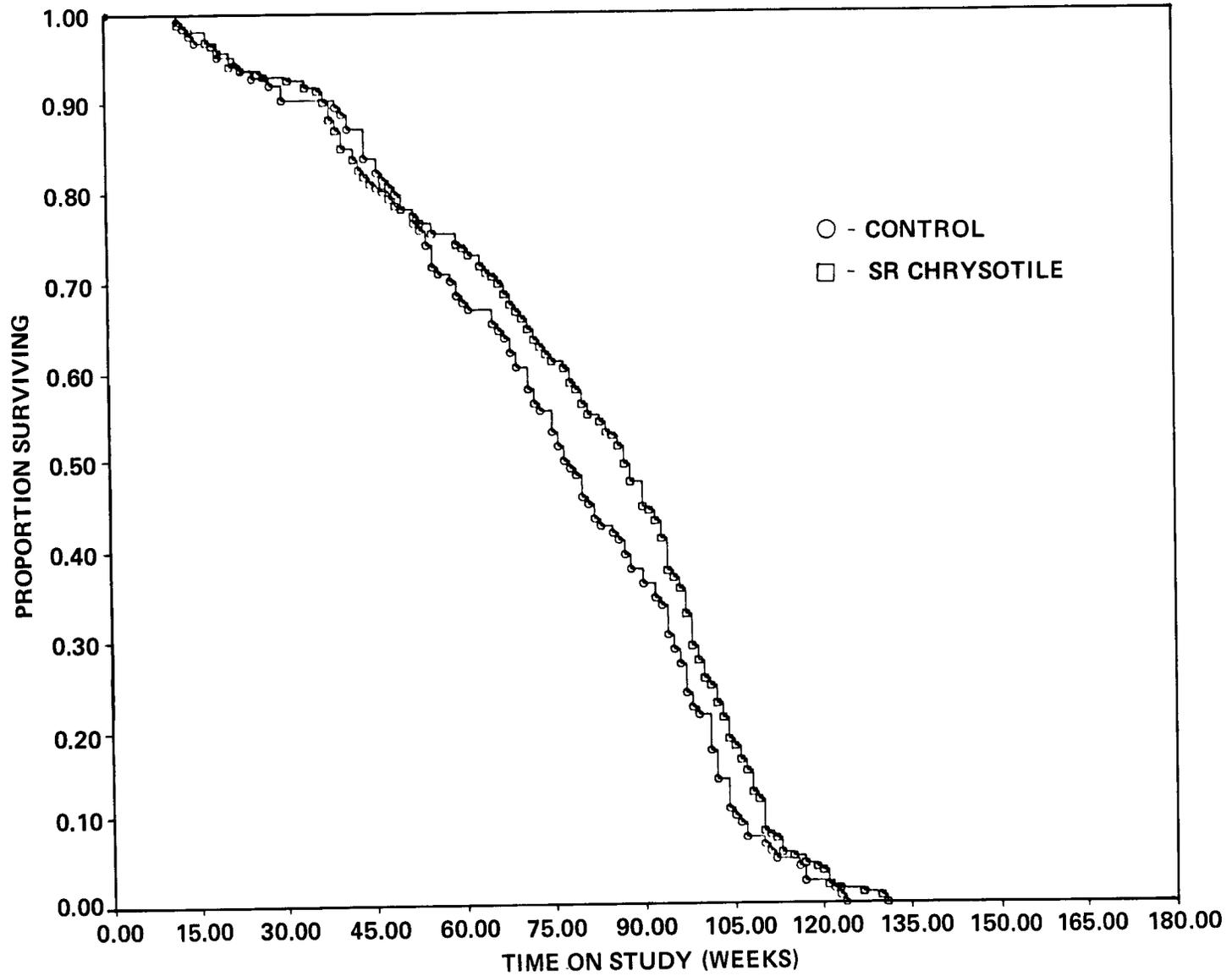


Figure 8. Survival Curves for Male Hamsters Receiving Short Range (SR) Chrysotile Asbestos in the Diet

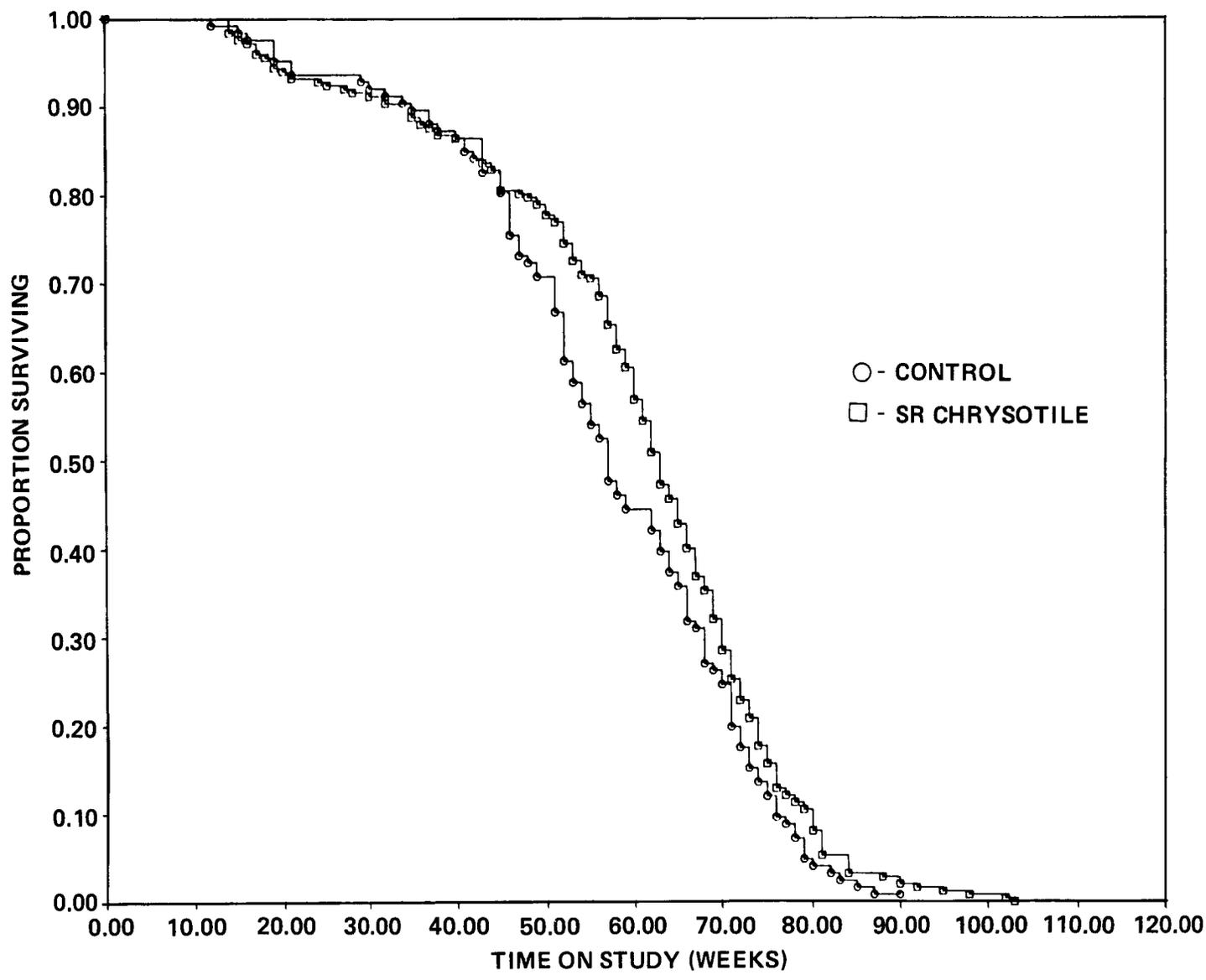


Figure 9. Survival Curves for Female Hamsters Receiving Short Range (SR) Chrysotile Asbestos in the Diet

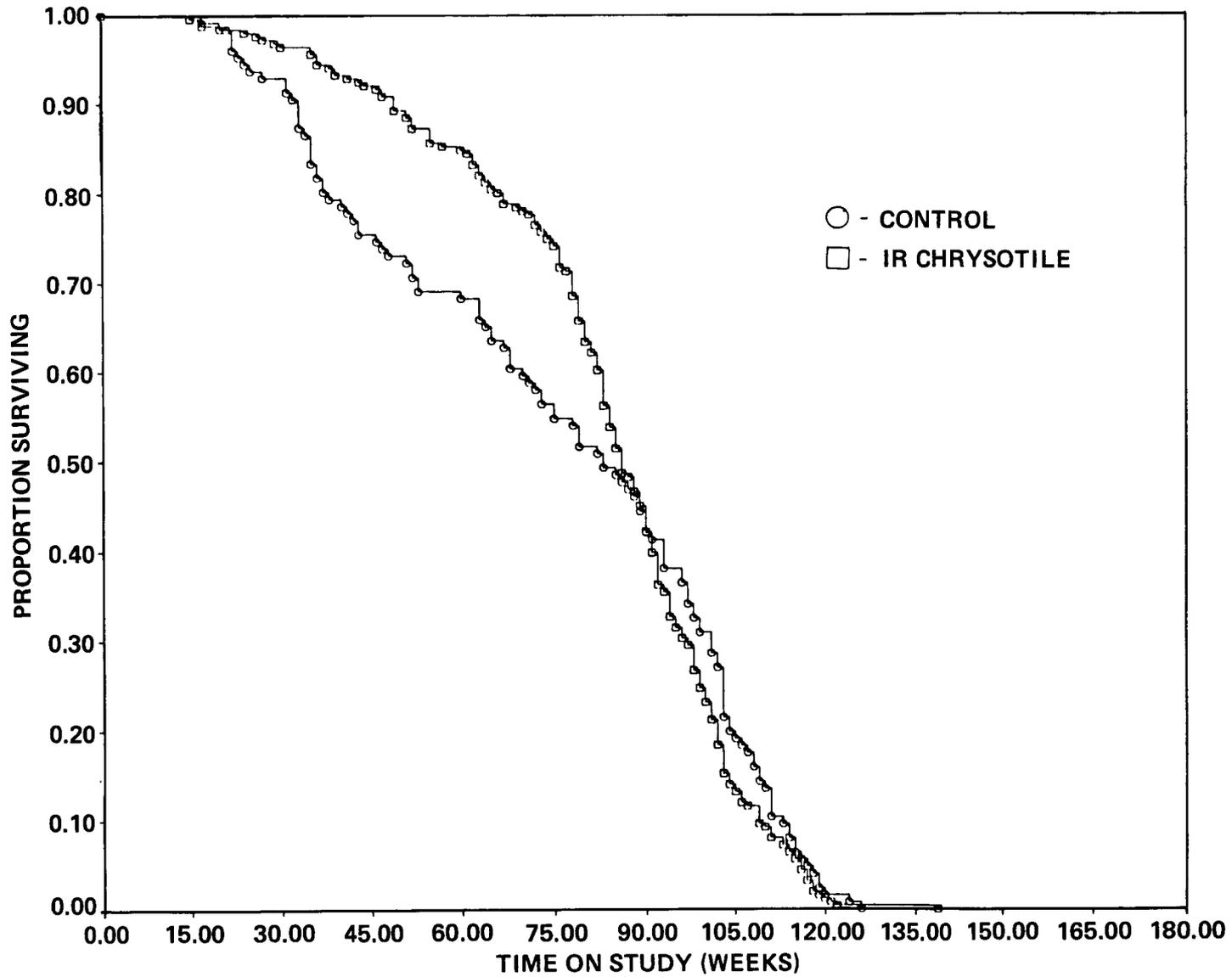


Figure 10. Survival Curves for Male Hamsters Receiving Intermediate Range (IR) Chrysotile Asbestos in the Diet

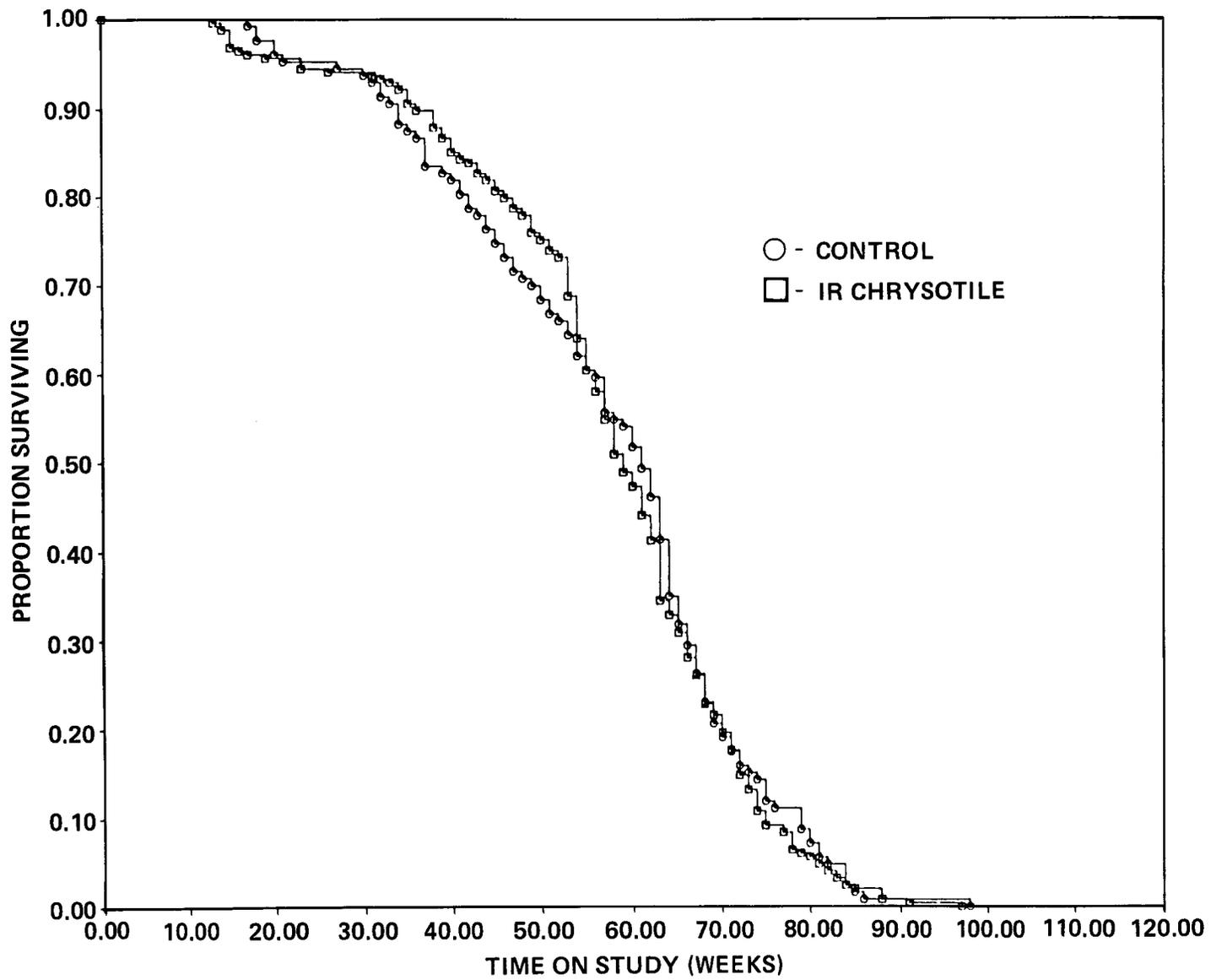


Figure 11. Survival Curves for Female Hamsters Receiving Intermediate Range (IR) Chrysotile Asbestos in the Diet

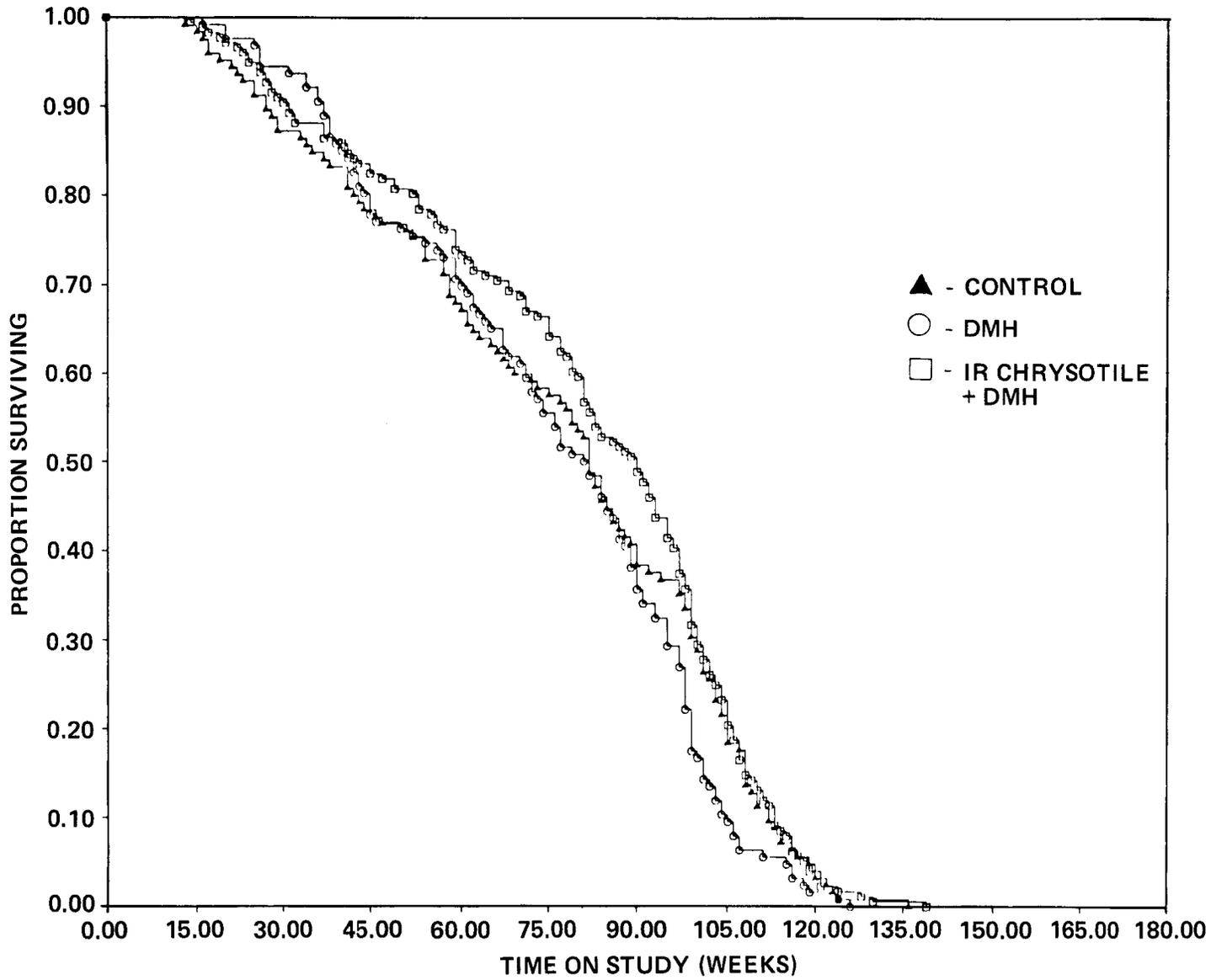


Figure 12. Survival Curves for Male Hamsters Receiving 1,2-Dimethylhydrazine Dihydrochloride (DMH) by Gavage or DMH plus Intermediate Range (IR) Chrysotile Asbestos in the Diet

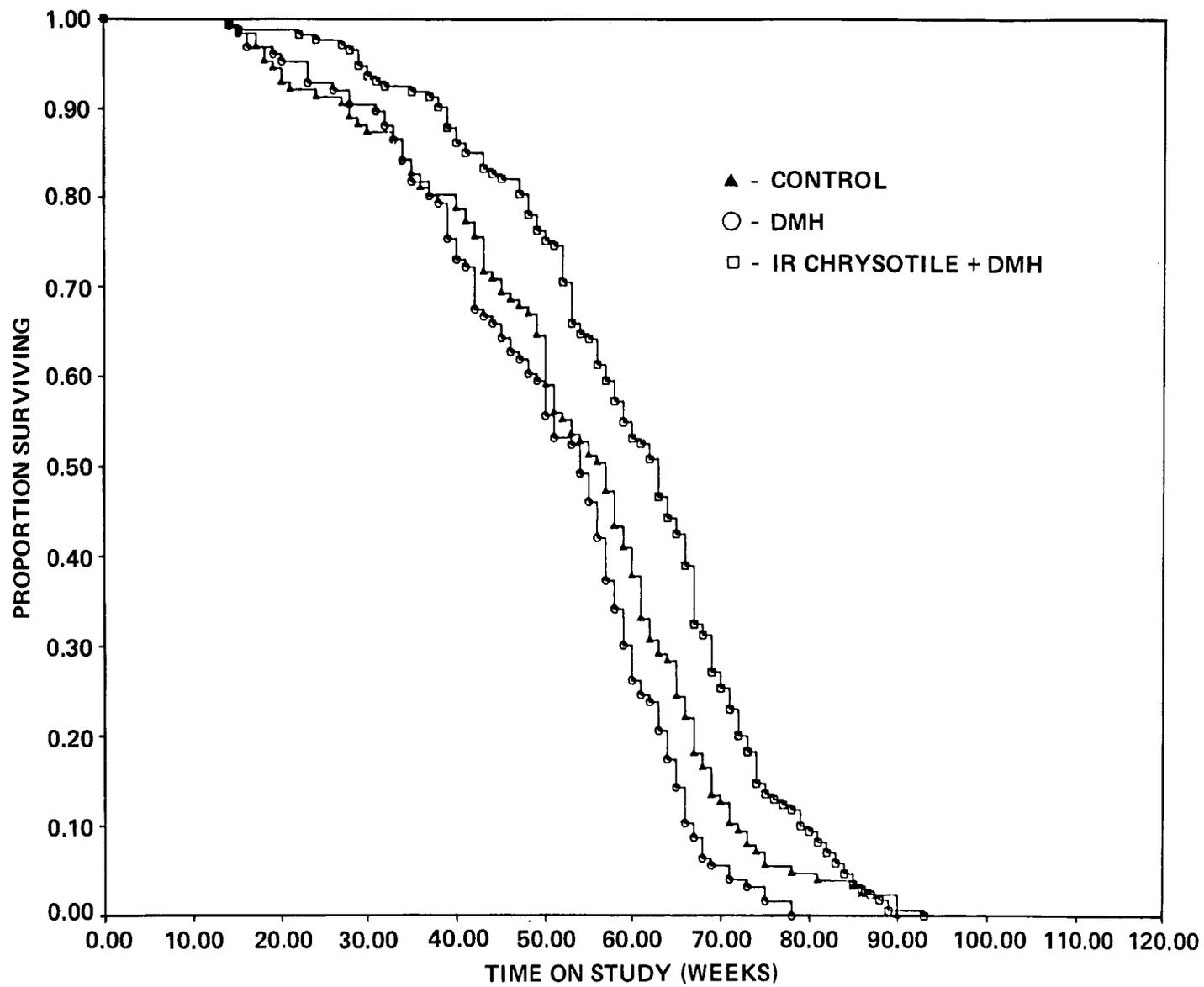


Figure 13. Survival Curves for Female Hamsters Receiving 1,2-Dimethylhydrazine Dihydrochloride (DMH) by Gavage or DMH plus Intermediate Range (IR) Chrysotile Asbestos in the Diet

### III. RESULTS: PATHOLOGY AND STATISTICAL ANALYSES OF RESULTS

#### PATHOLOGY AND STATISTICAL ANALYSES OF RESULTS

The number of hamsters available for histopathologic examination is shown in Table 3. Most animals not examined pathologically were excluded because of autolysis or cannibalization. Review of the clinical records of hamsters lost to autolysis or cannibalization gave no indication that these animals had neoplasia.

A variety of neoplasms were observed in control (Tables 8 and 9) and chrysotile-exposed

hamsters (Tables 10-15). The proportions of control male or female hamsters bearing primary tumors were not statistically different among the 4 control groups. Thus, statistical comparisons were made with pooled controls as well as with temporal controls. Overall, the male hamsters had a slightly higher rate of neoplasia than the females. This response was also seen in the amosite studies (NTP, 1983).

TABLE 8. INCIDENCES OF PRIMARY TUMORS IN MALE HAMSTER CONTROL GROUPS

	Short Range Chrysotile Control	Intermediate Range Chrysotile Control	DMH & Intermediate Range Chrysotile Control	Amosite Control
Animals with primary tumors	21/115 (18%)	26/116 (22%)	27/119 (23%)	21/122 (17%)
Skin or sub. tissue: All tumors	0/115 (0%)	1/116 (1%)	1/119 (1%)	0/122 (0%)
Lung or trachea: All tumors	0/115 (0%)	0/116 (0%)	0/119 (0%)	0/120 (0%)
Adrenal:				
Cortical adenoma	7/115 (6%)	7/115 (6%)	3/117 (3%)	8/119 (7%)
Cortical carcinoma	3/115 (3%)	3/115 (3%)	4/117 (3%)	3/119 (3%)
Pheochromocytoma	2/115 (2%)	5/115 (4%)	3/117 (3%)	3/119 (3%)
Other tumors	0/115 (0%)	3/115 (3%)	2/117 (2%)	1/119 (1%)
Pancreas:				
Islet-cell adenoma	2/111 (2%)	7/110 (6%)	8/110 (7%)	3/114 (3%)
Islet-cell carcinoma	1/111 (1%)	0/110 (0%)	0/110 (0%)	0/114 (0%)
Thyroid:				
C-cell adenoma	3/109 (3%)	3/106 (3%)	0/107 (0%)	1/106 (1%)
C-cell carcinoma	1/109 (1%)	1/106 (1%)	0/107 (0%)	1/106 (1%)
Other tumors	0/109 (0%)	0/106 (0%)	1/107 (1%)	0/106 (0%)
Parathyroid: Adenoma	0/72 (0%)	1/71 (1%)	1/64 (2%)	0/64 (0%)
G.I. Tract: All tumors	2/115 (2%)	1/116 (1%)	2/119 (2%)	1/122 (1%)
Pituitary: All tumors	0/84 (0%)	0/77 (0%)	0/80 (0%)	0/81 (0%)
Kidney: All tumors	0/115 (0%)	2/116 (2%)	1/119 (1%)	1/120 (1%)
Liver: All tumors	0/115 (0%)	0/116 (0%)	0/119 (0%)	0/120 (0%)
Leukemia or malignant lymphoma	2/115 (2%)	1/116 (1%)	4/119 (3%)	1/122 (1%)
Hemangioma or hemangiosarcoma	0/115 (0%)	0/116 (0%)	3/119 (3%)	2/122 (2%)
All other tumors	1/115 (1%)	0/116 (0%)	3/119 (3%)	1/122 (1%)

**TABLE 9. INCIDENCES OF PRIMARY TUMORS IN FEMALE HAMSTER CONTROL GROUPS**

	<b>Short Range Chrysotile Control</b>	<b>Intermediate Range Chrysotile Control</b>	<b>DMH &amp; Intermediate Range Chrysotile Control</b>	<b>Amosite Control</b>
Animals with primary tumors	19/114 (17%)	17/119 (14%)	15/120 (12%)	15/119 (13%)
Skin or sub. tissue: All tumors	0/114 (0%)	0/119 (0%)	0/120 (0%)	0/119 (0%)
Lung or trachea: All tumors	0/114 (0%)	0/119 (0%)	0/119 (0%)	0/119 (0%)
Adrenal:				
Cortical adenoma	4/112 (4%)	6/118 (5%)	3/120 (2%)	2/118 (2%)
Cortical carcinoma	0/112 (0%)	0/118 (0%)	0/120 (0%)	0/118 (0%)
Pheochromocytoma	0/112 (0%)	0/118 (0%)	0/120 (0%)	0/118 (0%)
Other tumors	0/112 (0%)	0/118 (0%)	0/120 (0%)	0/118 (0%)
Pancreas:				
Islet-cell adenoma	2/109 (2%)	5/116 (4%)	5/116 (4%)	3/115 (3%)
Islet-cell carcinoma	1/109 (1%)	0/116 (0%)	0/116 (0%)	0/115 (0%)
Thyroid:				
C-cell adenoma	2/107 (2%)	3/115 (3%)	0/112 (0%)	1/106 (1%)
C-cell carcinoma	0/107 (0%)	0/115 (0%)	1/112 (1%)	0/106 (0%)
Other tumors	2/107 (2%)	0/115 (0%)	0/112 (0%)	0/106 (0%)
Parathyroid: Adenoma	3/68 (4%)	1/77 (1%)	1/74 (1%)	1/61 (1%)
G.I. Tract: All tumors	1/114 (1%)	2/119 (2%)	1/120 (1%)	1/119 (1%)
Pituitary: All tumors	0/77 (0%)	2/67 (3%)	0/62 (0%)	0/79 (0%)
Kidney: All tumors	0/114 (0%)	1/119 (1%)	0/120 (0%)	0/119 (0%)
Liver: All tumors	0/114 (0%)	0/119 (0%)	0/119 (0%)	0/118 (0%)
Leukemia or malignant lymphoma	2/114 (2%)	0/119 (0%)	3/120 (2%)	2/119 (2%)
Hemangioma or hemangiosarcoma	0/114 (0%)	0/119 (0%)	1/120 (1%)	1/119 (1%)
Uterus: All tumors	3/113 (3%)	1/119 (1%)	2/120 (2%)	2/119 (2%)
All other tumors	3/114 (3%)	0/119 (0%)	1/120 (1%)	2/119 (2%)

**TABLE 10. INCIDENCES OF PRIMARY TUMORS IN MALE HAMSTERS ADMINISTERED 1% SHORT RANGE CHRYSOTILE IN THE DIET**

	Pooled Controls	Short Range Chrysotile Controls	Short Range Chrysotile
Animals with primary tumors	95/472 (20%)	21/115 (18%)	64/233 (27%) (a)
Skin or sub. tissue: All tumors	2/472 (<1%)	0/115 (0%)	0/233 (0%)
Lung or trachea: All tumors	0/470 (0%)	0/115 (0%)	0/231 (0%)
Adrenal:			
Cortical adenoma	25/466 (5%)	7/115 (6%)	26/229 (11%) (b)
Cortical carcinoma	13/466 (3%)	3/115 (3%)	8/229 (3%)
Pheochromocytoma	13/466 (3%)	2/115 (2%)	4/229 (2%)
Other tumors	6/466 (1%)	0/115 (0%)	1/229 (<1%)
Pancreas:			
Islet-cell adenoma	20/445 (4%)	2/111 (2%)	15/218 (7%)
Islet-cell carcinoma	1/445 (<1%)	1/111 (1%)	0/218 (0%)
Thyroid:			
C-cell adenoma	7/428 (2%)	3/109 (3%)	3/207 (1%)
C-cell carcinoma	3/428 (1%)	1/109 (1%)	1/207 (<1%)
Other tumors	1/428 (<1%)	0/109 (0%)	0/207 (0%)
Parathyroid: Adenoma	2/271 (1%)	0/72 (0%)	3/132 (2%)
G.I. Tract: All tumors	6/472 (1%)	2/115 (2%)	0/233 (0%)
Pituitary: All tumors	0/322 (0%)	0/84 (0%)	0/159 (0%)
Kidney: All tumors	4/470 (1%)	0/115 (0%)	3/232 (1%)
Liver: All tumors	0/470 (0%)	0/115 (0%)	0/232 (0%)
Leukemia or malignant lymphoma	8/472 (2%)	2/115 (2%)	3/233 (1%)
Hemangioma or hemangiosarcoma	5/472 (1%)	0/115 (0%)	4/233 (2%)
All other tumors	5/472 (1%)	1/115 (1%)	3/233 (1%)

(a) P = 0.152 (life table); P = 0.065 (incidental tumor test) and P = 0.019 (Fisher's exact test) vs. pooled controls.

(b) P < 0.05 vs. pooled controls.

**TABLE 11. INCIDENCES OF PRIMARY TUMORS IN FEMALE HAMSTERS ADMINISTERED 1% SHORT RANGE CHRYSOTILE IN THE DIET**

	Pooled Controls	Short Range Chrysotile Controls	Short Range Chrysotile
Animals with primary tumors	66/472 (14%)	19/114 (17%)	28/228 (12%)
Skin or sub. tissue: All tumors	0/472 (0%)	0/114 (0%)	3/228 (1%)
Lung or trachea: All tumors	0/471 (0%)	0/114 (0%)	0/228 (0%)
Adrenal:			
Cortical adenoma	15/468 (3%)	4/112 (4%)	8/226 (4%)
Cortical carcinoma	0/468 (0%)	0/112 (0%)	0/226 (0%)
Pheochromocytoma	0/468 (0%)	0/112 (0%)	3/226 (1%)
Other tumors	0/468 (0%)	0/112 (0%)	1/226 (<1%)
Pancreas:			
Islet-cell adenoma	15/456 (3%)	2/109 (2%)	2/217 (1%) (a)
Islet-cell carcinoma	1/456 (<1%)	1/109 (1%)	0/217 (0%)
Thyroid:			
C-cell adenoma	6/440 (1%)	2/107 (2%)	0/214 (0%)
C-cell carcinoma	1/440 (<1%)	0/107 (0%)	0/214 (0%)
Other tumors	2/440 (<1%)	2/107 (2%)	0/214 (0%)
Parathyroid: Adenoma	6/280 (2%)	3/68 (4%)	3/139 (2%)
G.I. Tract: All tumors	5/472 (1%)	1/114 (1%)	1/228 (<1%)
Pituitary: All tumors	2/285 (1%)	0/77 (0%)	1/132 (1%)
Kidney: All tumors	1/472 (<1%)	0/114 (0%)	0/228 (0%)
Liver: All tumors	0/472 (0%)	0/114 (0%)	0/228 (0%)
Leukemia or malignant lymphoma	7/472 (1%)	2/114 (2%)	2/228 (1%)
Hemangioma or hemangiosarcoma	2/472 (<1%)	0/114 (0%)	1/228 (<1%)
Uterus: All tumors	8/471 (2%)	3/113 (3%)	5/226 (2%)
All other tumors	6/472 (1%)	3/114 (3%)	3/228 (1%)

(a) P < 0.05 decrease relative to pooled controls (life table and incidental tumor test).

**TABLE 12. INCIDENCES OF PRIMARY TUMORS IN MALE HAMSTERS ADMINISTERED 1% INTERMEDIATE RANGE CHRYSOTILE IN THE DIET**

	Pooled Controls	Intermediate Range Chrysotile Controls	Intermediate Range Chrysotile
Animals with primary tumors	95/472 (20%)	26/116 (22%)	78/245 (32%) (a,b)
Skin or sub. tissue: All tumors	2/472 (<1%)	1/116 (1%)	0/245 (0%)
Lung or trachea: All tumors	0/470 (0%)	0/116 (0%)	1/245 (<1%)
Adrenal:			
Cortical adenoma	25/466 (5%)	7/115 (6%)	24/244 (10%) (c)
Cortical carcinoma	13/466 (3%)	3/115 (3%)	7/244 (3%)
Pheochromocytoma	13/466 (3%)	5/115 (4%)	11/244 (5%)
Other tumors	6/466 (1%)	3/115 (3%)	1/244 (<1%)
Pancreas:			
Islet-cell adenoma	20/445 (4%)	7/110 (6%)	15/226 (7%)
Islet-cell carcinoma	1/445 (<1%)	0/110 (0%)	1/226 (<1%)
Thyroid:			
C-cell adenoma	7/428 (2%)	3/106 (3%)	5/216 (2%)
C-cell carcinoma	3/428 (1%)	1/106 (1%)	4/216 (2%)
Other tumors	1/428 (<1%)	0/106 (0%)	1/216 (<1%)
Parathyroid: Adenoma	2/271 (1%)	1/71 (1%)	4/138 (3%)
G.I. Tract: All tumors	6/472 (1%)	1/116 (1%)	3/245 (1%)
Pituitary: All tumors	0/322 (0%)	0/77 (0%)	0/182 (0%)
Kidney: All tumors	4/470 (1%)	2/116 (2%)	1/245 (<1%)
Liver: All tumors	0/470 (0%)	0/116 (0%)	0/244 (0%)
Leukemia or malignant lymphoma	8/472 (2%)	1/116 (1%)	10/245 (4%)
Hemangioma or hemangiosarcoma	5/472 (1%)	0/116 (0%)	1/245 (<1%)
All other tumors	5/472 (1%)	0/116 (0%)	2/245 (1%)

(a) P < 0.01 vs. pooled controls.

(b) P < 0.05 vs. intermediate range chrysotile controls.

(c) P < 0.05 vs. pooled controls.

**TABLE 13. INCIDENCES OF PRIMARY TUMORS IN FEMALE HAMSTERS ADMINISTERED 1% INTERMEDIATE RANGE CHRYSOTILE IN THE DIET**

	Pooled Controls	Intermediate Range Chrysotile Controls	Intermediate Range Chrysotile
Animals with primary tumors	66/472 (14%)	17/119 (14%)	39/244 (16%)
Skin or sub. tissue: All tumors	0/472 (0%)	0/119 (0%)	2/244 (1%)
Lung or trachea: All tumors	0/471 (0%)	0/119 (0%)	0/243 (0%)
Adrenal:			
Cortical adenoma	15/468 (3%)	6/118 (5%)	18/234 (8%) (a)
Cortical carcinoma	0/468 (0%)	0/118 (0%)	1/234 (<1%)
Pheochromocytoma	0/468 (0%)	0/118 (0%)	1/234 (<1%)
Other tumors	0/468 (0%)	0/118 (0%)	0/234 (0%)
Pancreas:			
Islet-cell adenoma	15/456 (3%)	5/116 (4%)	4/236 (2%)
Islet-cell carcinoma	1/456 (<1%)	0/116 (0%)	0/236 (0%)
Thyroid:			
C-cell adenoma	6/440 (1%)	3/115 (3%)	2/223 (1%)
C-cell carcinoma	1/440 (<1%)	0/115 (0%)	0/223 (0%)
Other tumors	2/440 (<1%)	0/115 (0%)	1/223 (<1%)
Parathyroid: Adenoma	6/280 (2%)	1/77 (1%)	1/148 (1%)
G.I. Tract: All tumors	5/472 (1%)	2/119 (2%)	1/244 (<1%)
Pituitary: All tumors	2/285 (1%)	2/67 (3%)	2/164 (1%)
Kidney: All tumors	1/472 (<1%)	1/119 (1%)	0/243 (0%)
Liver: All tumors	0/472 (0%)	0/119 (0%)	0/243 (0%)
Leukemia or malignant lymphoma	7/472 (1%)	0/119 (0%)	2/244 (1%)
Hemangioma or hemangiosarcoma	2/472 (<1%)	0/119 (0%)	1/244 (<1%)
Uterus: All tumors	8/471 (2%)	1/119 (1%)	7/240 (3%)
All other-tumors	6/472 (1%)	0/119 (0%)	2/244 (1%)

(a) P < 0.05 vs. pooled controls.

**TABLE 14. INCIDENCES OF THE PRIMARY TUMORS IN MALE HAMSTERS ADMINISTERED 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH) OR INTERMEDIATE RANGE CHRYSOTILE AND DMH (a)**

	Pooled Controls	DMH & Intermediate Range Chrysotile Controls	DMH	DMH & Intermediate Range Chrysotile
Animals with primary tumors	95/472 (20%)	27/119 (23%)	29/127 (23%)	51/173 (29%) (b)
Skin or sub. tissue: All tumors	2/472 (<1%)	1/119 (1%)	0/127 (0%)	1/173 (1%)
Lung or trachea: All tumors	0/470 (0%)	0/119 (0%)	0/126 (0%)	0/173 (0%)
Adrenal:				
Cortical adenoma	25/466 (5%)	3/117 (3%)	3/127 (2%)	8/171 (5%)
Cortical carcinoma	13/466 (3%)	4/117 (3%)	2/127 (2%)	7/171 (4%)
Pheochromocytoma	13/466 (3%)	3/117 (3%)	4/127 (3%)	6/171 (4%)
Other tumors	6/466 (1%)	2/117 (2%)	0/127 (0%)	1/171 (1%)
Pancreas:				
Islet-cell adenoma	20/445 (4%)	8/110 (7%)	6/114 (5%)	10/167 (6%)
Islet-cell carcinoma	1/445 (<1%)	0/110 (0%)	0/114 (0%)	1/167 (1%)
Thyroid:				
C-cell adenoma	7/428 (2%)	0/107 (0%)	2/118 (2%)	3/163 (2%)
C-cell carcinoma	3/428 (1%)	0/107 (0%)	0/118 (0%)	1/163 (1%)
Other tumors	1/428 (<1%)	1/107 (1%)	0/118 (0%)	0/163 (0%)
Parathyroid: Adenoma	2/271 (1%)	1/64 (2%)	0/81 (0%)	2/118 (2%)
G.I. Tract: All tumors	6/472 (1%)	2/119 (2%)	3/127 (2%)	4/173 (2%)
Pituitary: All tumors	0/322 (0%)	0/80 (0%)	1/87 (1%)	2/123 (2%)
Kidney: All tumors	4/470 (1%)	1/119 (1%)	0/127 (0%)	0/173 (0%)
Liver: All tumors	0/470 (0%)	0/119 (0%)	2/127 (2%)	1/173 (1%)
Leukemia or malignant lymphoma	8/472 (2%)	4/119 (4%)	7/127 (6%) (c)	8/173 (5%)
Hemangioma or hemangiosarcoma	5/472 (1%)	3/119 (3%)	2/127 (2%)	2/173 (1%)
All other tumors	5/472 (1%)	3/119 (3%)	1/127 (1%)	4/173 (2%)

(a) DMH was given by gastric intubation at 4 mg/kg b.w. once every other week for 10 weeks; chrysotile asbestos was offered in the diet at a 1% level.

(b) P = 0.257 (life table); P = 0.038 (incidental tumor test); P = 0.009 (Fisher's exact test) vs. pooled controls.

(c) P < 0.05 vs. pooled controls.

**TABLE 15. INCIDENCES OF PRIMARY TUMORS IN FEMALE HAMSTERS ADMINISTERED 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH) OR INTERMEDIATE RANGE CHRYSOTILE AND DMH (a)**

	Pooled Controls	DMH & Intermediate Range Chrysotile Controls	DMH	DMH & Intermediate Range Chrysotile
Animals with primary tumors	66/472 (14%)	15/120 (12%)	15/122 (12%)	19/161 (12%)
Skin or sub. tissue: All tumors	0/472 (0%)	0/120 (0%)	1/122 (1%)	0/161 (0%)
Lung or trachea: All tumors	0/471 (0%)	0/119 (0%)	0/122 (0%)	1/160 (1%)
Adrenal:				
Cortical adenoma	15/468 (3%)	3/120 (2%)	2/120 (2%)	6/158 (4%)
Cortical carcinoma	0/468 (0%)	0/120 (0%)	0/120 (0%)	2/158 (1%)
Pheochromocytoma	0/468 (0%)	0/120 (0%)	0/120 (0%)	0/158 (0%)
Other tumors	0/468 (0%)	0/120 (0%)	0/120 (0%)	0/158 (0%)
Pancreas:				
Islet-cell adenoma	15/456 (3%)	5/116 (4%)	2/119 (2%)	4/149 (3%)
Islet-cell carcinoma	1/456 (<1%)	0/116 (0%)	0/119 (0%)	0/149 (0%)
Thyroid:				
C-cell adenoma	6/440 (1%)	0/112 (0%)	0/108 (0%)	0/141 (0%)
C-cell carcinoma	1/440 (<1%)	1/112 (1%)	0/108 (0%)	0/141 (0%)
Other tumors	2/440 (<1%)	0/112 (0%)	0/108 (0%)	0/141 (0%)
Parathyroid: Adenoma	6/280 (2%)	1/74 (1%)	2/57 (4%)	0/91 (0%)
G.I. Tract: All tumors	5/472 (1%)	1/120 (1%)	2/122 (2%)	0/161 (0%)
Pituitary: All tumors	2/285 (1%)	0/62 (0%)	0/59 (0%)	0/109 (0%)
Kidney: All tumors	1/472 (<1%)	0/120 (0%)	0/122 (0%)	0/161 (0%)
Liver: All tumors	0/472 (0%)	0/119 (0%)	0/121 (0%)	0/161 (0%)
Leukemia or malignant lymphoma	7/472 (1%)	3/120 (2%)	2/122 (2%)	3/161 (2%)
Hemangioma or hemangiosarcoma	2/472 (<1%)	1/120 (1%)	0/122 (0%)	1/161 (1%)
Uterus: All tumors	8/471 (2%)	2/120 (2%)	2/116 (2%)	2/156 (1%)
All other tumors	6/472 (1%)	1/120 (1%)	2/122 (2%)	2/161 (1%)

(a) DMH was given by gastric intubation at 4 mg/kg b.w. once every other week for 10 weeks; chrysotile asbestos was offered in the diet at a 1% level.

### III. RESULTS: PATHOLOGY AND STATISTICAL ANALYSES OF RESULTS

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A greater than 4% incidence of neoplasia in dosed or control groups was observed in the adrenal gland, pancreas (Islets of Langerhans), parathyroid, and reticuloendothelial system. Of these, only the adrenal cortex showed an increased rate of neoplasia in chrysotile-exposed hamsters compared to the controls. In male hamsters, the incidence of cortical adenomas was significantly increased ( $P < 0.05$ ) in the SR and IR chrysotile groups compared with the pooled controls (Tables 10 and 12) but not in the DMH chrysotile group (Table 14). None of the chrysotile groups showed a significant ( $P < 0.05$ ) increase in cortical adenomas relative to their concurrent control groups. A similar increase in cortical adenomas was observed in the female IR chrysotile group compared with pooled controls, but this also ceased to be significant when compared with the concurrent control group (Tables 11 and 13). Combining male hamsters with either adenomas or carcinomas of the adrenal glands resulted in significantly ( $P < 0.05$ ) increased incidences in both the SR (34/229, 14.8%) and IR (31/244, 12.7%) groups compared with pooled controls. For females only the IR group (18/234, 7.7%) was different ( $P < 0.05$ ) from pooled controls. In every comparison significance was eliminated using concurrent controls.

Males and females administered DMH did not show a significant ( $P < 0.05$ ) increase in intestinal neoplasia. Nor did the intermediate range chrysotile produce a higher rate of intestinal neoplasia in DMH-dosed animals. A summary of all gastrointestinal tumors observed in this study is given in Table 16.

In only two other instances did specific tumor types show significant effects relative to pooled

or concurrent controls. Female hamsters administered SR chrysotile showed a significantly ( $P < 0.05$ ) decreased incidence of islet-cell adenoma of the pancreas relative to pooled controls (Table 11). Male hamsters administered DMH showed a significantly ( $P < 0.05$ ) increased incidence of leukemia or malignant lymphoma relative to pooled controls (Table 14).

The only group to show a significant ( $P < 0.05$ ) increase in overall primary tumors was the male IR chrysotile group (Table 14). This increase was due primarily to adrenal tumors. Male hamsters receiving SR chrysotile or DMH and IR chrysotile also showed an elevated incidence of primary tumors relative to pooled controls. However, when survival differences were taken into account by life table analyses, these differences were not statistically significant (Tables 10 and 14). Female chrysotile groups showed little evidence of an increased incidence of primary tumors relative to concurrent or pooled controls.

The diagnoses of the NTP Pathology Working Group differed from the original pathologist's interpretation, as shown in Table 17. The major diagnostic difference concerned the issue of whether certain adrenal tumors originated in the medulla or cortex. As shown in Table 17, the PWG diagnoses reduced the significance of adrenal cortical tumors in the male SR chrysotile group, but did not materially alter the results in other groups. To diagnose adrenal tumors, the NTP/PWG used the criteria reported by Homburger and Russfield (1970), Matsuyama and Suzuki (1970), and Murthy and Russfield (1966).

**TABLE 16. INCIDENCES OF GASTROINTESTINAL TRACT TUMORS IN HAMSTERS IN THE CHRYSOTILE ASBESTOS STUDIES**

	Pooled Controls		Short Range Chrysotile		Intermediate Range Chrysotile		DMH		DMH & Intermediate Range Chrysotile	
	M	F	M	F	M	F	M	F	M	F
Stomach (no. examined)	(464)	(468)	(222)	(224)	(244)	(242)	(127)	(118)	(170)	(160)
Squamous cell papilloma	3				1				2	
Carcinoma in-situ					1					
Papillary adenoma					1	1 (a)				
Small Intestine (no. examined)	(467)	(469)	(226)	(227)	(244)	(244)	(127)	(120)	(170)	(159)
Adenoma	1									
Adenocarcinoma	1									
Large Intestine (no. examined)	(464)	(468)	(222)	(226)	(241)	(243)	(126)	(118)	(170)	(159)
Papilloma									1	
Adenoma		1 (a)					1			
Papillary adenoma							1			
Adenocarcinoma		1		1						
Lipoma		1								
Adenomatous polyp								1 (a)		
Rectum (no. examined)	(472)	(472)	(233)	(228)	(245)	(244)	(127)	(122)	(173)	(161)
Adenoma	1	1 (a)								
Papillary adenoma									1 (a)	
Fibrosarcoma							1			
Squamous cell carcinoma								1		
Fibroma		1								

(a) These lesions were diagnosed by the original pathologist and were not confirmed by the NTP Pathology Working Group.

**TABLE 17. COMPARISON OF ADRENAL TUMOR INCIDENCE AS DETERMINED BY ORIGINAL PATHOLOGIST (OP) AND BY THE NTP PATHOLOGY WORKING GROUP (PWG)**

	Pooled Controls	SR Chrysotile Controls	SR Chrysotile	IR Chrysotile Controls	IR Chrysotile	DMH & IR Chrysotile Controls	DMH	DMH & IR Chrysotile
<b>Males (OP)</b>								
Cortical adenoma	25/466 (5%)	7/115 (6%)	26/229 (11%)(a)	7/115 (6%)	24/244 (10%)(a)	3/117 (3%)	3/127 (2%)	8/171 (5%)
Cortical carcinoma	13/466 (3%)	3/115 (3%)	8/229 (3%)	3/115 (3%)	7/244 (3%)	4/117 (3%)	2/127 (2%)	7/171 (4%)
Pheochromocytoma	13/466 (3%)	2/115 (2%)	4/229 (2%)	5/115 (4%)	11/244 (5%)	3/117 (3%)	4/127 (3%)	6/171 (4%)
Other	6/466 (1%)	0/115 (0%)	1/229 (<1%)	3/115 (3%)	1/244 (<1%)	2/117 (2%)	0/127 (0%)	1/171 (1%)
<b>Males (PWG)</b>								
Cortical adenoma	31/466 (7%)	7/115 (6%)	26/229 (11%)	9/115 (8%)	29/244 (12%)(a)	6/117 (5%)	5/127 (4%)	11/171 (6%)
Cortical carcinoma	14/466 (3%)	3/115 (3%)	9/229 (4%)	3/115 (3%)	7/244 (3%)	5/117 (4%)	4/127 (3%)	8/171 (5%)
Pheochromocytoma	7/466 (2%)	2/115 (2%)	2/229 (1%)	4/115 (3%)	7/244 (3%)	0/117 (0%)	2/127 (2%)	1/171 (1%)
Other	2/466 (<1%)	0/115 (0%)	1/229 (<1%)	1/115 (1%)	1/244 (<1%)	1/117 (1%)	0/127 (0%)	1/171 (1%)
<b>Females (OP)</b>								
Cortical adenoma	15/468 (3%)	4/112 (4%)	8/226 (4%)	6/118 (5%)	18/234 (8%) (a)	3/120 (2%)	2/120 (2%)	6/158 (4%)
Cortical carcinoma	0/468 (0%)	0/112 (0%)	0/226 (0%)	0/118 (0%)	1/234 (<1%)	0/120 (0%)	0/120 (0%)	2/158 (1%)
Pheochromocytoma	0/468 (0%)	0/112 (0%)	3/226 (1%)	0/118 (0%)	1/234 (<1%)	0/120 (0%)	0/120 (0%)	0/158 (0%)
Other	0/468 (0%)	0/112 (0%)	1/226 (<1%)	0/118 (0%)	0/234 (0%)	0/120 (0%)	0/120 (0%)	0/158 (0%)
<b>Females (PWG)</b>								
Cortical adenoma	19/468 (4%)	4/112 (4%)	9/226 (4%)	7/118 (6%)	23/234 (10%)(a)	4/120 (3%)	2/120 (2%)	7/158 (4%)
Cortical carcinoma	0/468 (0%)	0/112 (0%)	0/226 (0%)	0/118 (0%)	1/234 (<1%)	0/120 (0%)	0/120 (0%)	2/158 (1%)
Pheochromocytoma	0/468 (0%)	0/112 (0%)	2/226 (1%)	0/118 (0%)	1/234 (<1%)	0/120 (0%)	0/120 (0%)	0/158 (0%)
Other	0/468 (0%)	0/112 (0%)	1/226 (<1%)	0/118 (0%)	0/234 (0%)	0/120 (0%)	0/120 (0%)	0/158 (0%)

(a) P < 0.05 relative to pooled controls

### **III. RESULTS: PATHOLOGY AND STATISTICAL ANALYSES OF RESULTS**

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#### **Adrenal Cortex**

**Focal hyperplasia**—There was a proliferation of cells appearing normal and resembling those of the zona fasciculata. The cells were of uniform size and morphology, and mitotic figures were not observed. These lesions were invariably observed in adrenals showing severe amyloidosis. Another type of hyperplastic lesion encountered was the presence of extracapsular nodules of cortical tissue that had a normal appearance. These were completely encased in a connective tissue capsule.

**Cortical adenoma**—Two types were observed. One was composed of cells resembling the zona fasciculata; these cells were somewhat pheomorphic and were compressing the adjacent parenchyma. The second type contained cells similar to those of the first, except that admixed between them were spindle-shaped cells which resembled fibroblasts. Mitotic figures were rare. The border of both types of adenomas was well defined but no capsule was evident.

**Neurolemmoma**—This tumor was composed of delicate spindle cells arranged in parallel palisades. It was well circumscribed but nonencapsulated. No mitotic figures were observed. This type of tumor was of much lower incidence than the previously described adenomas.

**Cortical carcinoma**—Carcinomas were composed of cells resembling both types of the adenomas described above. They were differentiated from adenomas on the basis of pleomorphism, nuclear atypia, increased numbers of mitotic figures, and invasive growth through the capsule and/or into adjacent blood vessels. Areas of necrosis and hemorrhage were common.

#### **Adrenal Medulla**

**Hyperplasia**—This lesion was characterized by proliferation of cells that appeared normal, although an increase in basophilia was sometimes noted. The normal architecture was preserved, and the lesion was usually diffuse.

**Pheochromocytoma**—This lesion consisted of a focal nodular proliferation of uniform cells that appeared fairly normal, although they were often smaller than normal. Mitotic figures were not observed. Growth was by expansion. The borders were distinct, and there appeared to be a delicate capsule.

**Malignant pheochromocytoma**—The major distinguishing characteristics of this neoplasm were nuclear atypia and invasive growth.

The major difference in terminology between the original pathologist and the NTP/PWG was in regard to the adrenal tumors (benign and malignant) composed of a mixture of spindle-shaped cells and eosinophilic hepatoid-like cells. The original pathologist diagnosed these as pheochromocytomas or malignant pheochromocytomas, while the PWG called them cortical adenomas or carcinomas.

While this study was not designed to evaluate nonneoplastic disease, noteworthy lesions were observed. None appeared to be dosage related; rather, they were consistent with lesions that are normally found in aging hamsters. The pathologist opined that the most important lesion, responsible for many deaths, was generalized amyloidosis. The kidneys were particularly affected by diffuse accumulation of amyloid, which replaced glomeruli and infiltrated tubular interstitium to a point where the normal cortical architecture was obliterated. Other organs which showed significant accumulations of amyloid were the adrenal gland, liver, spleen, and the epithelium of the small intestine. Amyloid was observed within the walls of blood vessels in many tissues.

Many of the livers were cirrhotic, infiltrated with amyloid, and contained large cystic structures filled with a lightly staining proteinaceous fluid. These structures were interpreted as cystic bile ducts and are consistent with what others have termed "retention cysts." At times, these cysts were so large and/or numerous that less than half of the livers remained.

Other nonneoplastic lesions that were observed in more than 5% of the hamsters in any of the experimental groups were:

1. Skin—chronic dermatitis
2. Lung—interstitial pneumonitis
3. Spleen—lymphoid atrophy
4. Lymph node—hyperplasia
5. Heart—atrial thrombosis
6. Gallbladder—edema and calculi
7. Stomach (nonglandular)—hyperkeratosis or acanthosis
8. Colon—intussusception, inflammation
9. Urinary bladder—chronic inflammation, hyperplasia
10. Adrenal gland—cortical and medullary hyperplasia
11. Thyroid gland—follicular atrophy
12. Pituitary gland—degeneration

### **III. RESULTS: PATHOLOGY AND STATISTICAL ANALYSES OF RESULTS**

13. Ovary—atrophy

14. Uterus—inflammation, endometrial hyperplasia.

15. Vagina—acute inflammation, squamous metaplasia

None of these lesions were dose related.

#### **IV. SUMMARY, COMMENTS, AND CONCLUSIONS**

#### IV. SUMMARY, COMMENTS, AND CONCLUSIONS

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The clinicopathologic results in this study showed that chronic ingestion of 1% chrysotile [short range (SR) or intermediate range (IR) fiber lengths] asbestos in the diet did not have any adverse effect on body weight gain and survival. In fact, both weight gain and survival seemed to be enhanced. An explanation for these observations is not apparent.

The only organ which showed a statistically significant ( $P < 0.05$ ) increased rate of neoplasia was the adrenal cortex in male and female hamsters exposed to IR chrysotile asbestos and males exposed to SR chrysotile asbestos when compared with pooled controls. However, statistical significance was lost when these groups were compared to their concurrent controls. Also, the increased incidence in SR males was not statistically significant when the diagnoses of the NTP/PWG were used. The increase in body weight may have been a factor in adrenal cortical tumorigenesis, but this is speculative. It is difficult to imagine how orally administered asbestos, even though it is known to be absorbed through the gastrointestinal tract (Cook and Olson, 1979), could cause an increased tumor rate in the adrenal cortex without causing similar increases in tumors in other abdominal organs and tissues, i.e., gastrointestinal tract and peritoneum. For these reasons, the biologic importance of adrenal tumors in this study is doubtful. The overall increase in total primary tumors in male IR chrysotile hamsters can be explained primarily on the basis of an increased incidence of adrenal tumors in this group. The enhanced survival of animals in the chrysotile groups also contributed to the elevated incidence of primary tumors observed in these groups compared with controls. Similar increases were not observed in the amosite asbestos studies (NTP, 1983).

The only other instance of an increased rate of neoplasia was a significant ( $P < 0.05$ ) increase in leukemia or malignant lymphoma in male hamsters exposed to DMH when compared to pooled controls. Again, statistical significance was lost when this group was compared to its concurrent control group. This finding also loses importance because it was not observed in the DMH plus IR chrysotile group.

Other such studies involving the long-term ingestion of asbestos are few. Donham et al., (1980) reported equivocal results in F344 rats which were fed a diet containing 10% chrysotile for their lifetime. While they did not observe a statistically significant ( $P < 0.05$ ) increase in the number of tumors in exposed animals, the

authors believed that there was a trend toward increased colon lesions in general, evidence of penetration of asbestos into the colonic mucosa and possible cytotoxicity to colonic tissues and they suggested a possible relationship to peritoneal mesothelioma. Another equivocal study is that reported by Gibel et al. (1976), who described an increase in malignant tumors in the lung, kidney, liver, and reticuloendothelial system, but no increase in intestinal neoplasia in Wistar rats fed asbestos filter material (20 mg/day) for a period of 8-14 months. Cunningham et al. (1977) reported 2 studies in male Wistar rats administered 1% chrysotile in the diet, one study of 24 months and one of 30 months. No intestinal tumors were found in the control rats. Negative results were reported by Gross et al., (1974), who fed rats a diet containing 5% chrysotile asbestos for a period of 21 months with no evidence of intestinal neoplasia.

The only other oral asbestos study in hamsters was reported by Smith et al. (1980). They exposed groups of 30 male and 30 female hamsters via drinking water for lifetime to amosite asbestos, mine tailings, beach rock, and Lake Superior drinking water. They did not observe adverse effects on body weight or survival time in any of the groups. A peritoneal mesothelioma, one pulmonary carcinoma, and two early squamous cell carcinomas of the nonglandular stomach were found in the hamsters exposed to amosite, but the incidence was not statistically significant ( $P > 0.05$ ). They concluded that these studies were essentially negative.

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

The results of the combination study (IR chrysotile plus DMH) did not yield a significant increase in tumors above the background level observed in the DMH group alone or in the untreated control group. The DMH failed to yield a background level of intestinal tumors high enough to provide a valid test of the cocarcinogenic potential of chrysotile asbestos. For this reason, the cocarcinogenic potential of orally administered asbestos should be considered untested. However, the DMH plus chrysotile group provides an additional IR chrysotile group for comparative purposes.

#### IV. SUMMARY, COMMENTS, AND CONCLUSIONS

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Why the DMH dosed group of hamsters failed to show an increased incidence of intestinal neoplasia remains unclear. The results from the pilot study indicated that the dose of DMH used should have caused an incidence of approximately 10% to 15%. DMH solutions rapidly decompose if they are at room temperature or if they are not properly buffered. For these studies, however, precautions were taken to prevent decomposition.

The only long-term study designed to determine the cocarcinogenic potential of asbestos was reported by Ward et al. (1980). They administered 1 mg amosite asbestos in saline by gavage to 6-week-old F344 rats 3 times per week for 10 weeks. Once per week during this same period, half of the rats received subcutaneous injections of 7.4 mg/kg azoxymethane (AOM), a known intestinal carcinogen in animals. All surviving rats were killed at 94-95 weeks of age. Ward et al. reported an intestinal tumor incidence of 66.7% for AOM alone, 77.1% for amosite plus AOM, and 32.6% for amosite alone. The authors concluded that while amosite did not significantly add to the incidence of AOM-induced intestinal neoplasia, amosite alone caused a relatively high rate of intestinal neoplasia. However, there was no untreated control group with which to compare the treated groups. These authors also reported a 14% incidence of Zymbal gland tumors in the rats exposed to amosite alone. The historical rate of Zymbal gland tumors in the Program is 0.34%, indicating that this neoplasm is an extremely rare spontaneous tumor. However, AOM is known to induce Zymbal gland tumors with a single dose of 5.1 mg/kg in male F344 rats producing a 14% incidence of tumors in this organ (Ward, 1975); in this study 5.1 mg/kg AOM also caused a 24% incidence of

intestinal neoplasia. An appropriate explanation for the high incidence of Zymbal gland tumors in the amosite group would be that those animals were inadvertently exposed to AOM. If this occurred, animals would also be expected to show a high incidence of intestinal neoplasia.

This investigation of the carcinogenic and cocarcinogenic potential of ingested asbestos is a two-animal-species effort by the National Institute of Environmental Health Sciences/National Toxicology Program. While the results in the hamster appear to be negative, carcinogenesis studies involving more types of asbestos but using essentially the same protocol (1% diet) in rats are currently being evaluated. The concurrent study (NTP, 1983) using 1% amosite in the diet of hamsters did not show any significant increase in tumor incidence compared to pooled or concurrent control groups.

*Conclusions: Under the conditions of these studies, neither short range chrysotile nor intermediate range chrysotile asbestos was carcinogenic when ingested at 1% levels in the diet by male and female Syrian golden hamsters. While there were increases in the rates of adrenal cortical adenomas in male and female hamsters exposed to intermediate range chrysotile asbestos compared with pooled control groups, these incidence rates were not different when compared with the concurrent control groups. Additionally, the biologic importance of adrenal tumors in the absence of target organ (gastrointestinal tract) neoplasia is questionable. The cocarcinogenesis studies using IR chrysotile asbestos and 1,2-dimethylhydrazine dihydrochloride were considered inadequate because there was no increase in intestinal neoplasia in the DMH group.*



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## V. REFERENCES

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**APPENDIX A**  
**ANALYSIS OF FEED**

## APPENDIX A

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Five pellets from the asbestos dosed and seven pellets from the control diet were individually crushed, transferred to a tared crucible, and weighed. The sample sizes used for the assays were 350 to 500 mg of asbestos-containing diet and 1,000 to 1,500 mg of control diet. The crucibles containing the diet were placed in a muffle furnace and ashed overnight at 550°C. After cooling, the ashed samples were quantitatively transferred to 100-ml beakers. Twenty ml of a 1:1:2 solution of nitric and hydrochloric acid in distilled water were added to each beaker and the samples were gently boiled for 8 hours. The digested sample was quantitatively transferred to a volumetric flask and a sufficient quantity of a stock solution containing potassium, lanthanum, and hydrochloric acid was added to provide a final concentration of 100 mg/l of K<sup>+</sup> and 30 mg/l of La<sup>++</sup> at a pH below 3. The quantity of asbestos was determined by measuring the magnesium content by atomic absorption spectroscopy.

Results of the analyses are presented in Tables A1 and A2.

**TABLE A1. CALCULATED VALUES OF SHORT RANGE CHRYSOTILE ASBESTOS IN INDIVIDUAL LOTS OF FEED AS DETERMINED BY MAGNESIUM CONTENT**

Feed Preparation Date	Calculated Asbestos Content (%)
03/23/77	1.05 ± 0.07
03/14/77	0.96 ± 0.07
05/20/77	0.89 ± 0.38
06/23/77	1.29 ± 1.96
06/23/77	0.94 ± 0.07
09/21/77	0.96 ± 0.13
12/07/77	1.00 ± 0.06
02/01/78	0.94 ± 0.06
09/78	0.93 ± 0.06
10/79	0.97 ± 0.07
<hr/>	
Mean = 0.98 ± 0.22	

**TABLE A2. CALCULATED VALUES OF INTERMEDIATE RANGE  
CHRYSTILE ASBESTOS IN INDIVIDUAL LOTS OF  
FEED AS DETERMINED BY MAGNESIUM CONTENT**

<b>Feed Preparation Date</b>	<b>Calculated Asbestos Content (%)</b>
03/14/77	1.02 ± 0.04
05/20/77	1.00 ± 0.11
06/23/77	1.64 ± 1.49
06/23/77	1.09 ± 0.39
06/23/77	0.94
06/23/77	0.89 ± 0.06
09/21/77	0.89
09/21/77	0.85
12/07/77	1.02 ± 0.05
02/01/78	1.03 ± 0.13
02/01/78	1.02 ± 0.17
07/11/78	0.97 ± 0.02
10/27/78	0.92 ± 0.07
10/79	1.00
<hr/>	
<b>Mean = 0.96 ± 0.12</b>	
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**APPENDIX B**

**DISEASE STATUS OF HAMSTERS EXPOSED  
IN THE CHRYSOTILE ASBESTOS STUDIES**



## **APPENDIX C**

### **ANALYSES OF 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE**

**TABLE C1. ANALYSIS OF 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE SOLUTIONS**

Date Prepared and Used	Theoretical Concentration	Actual Concentration
6/22/77	2.00 mg/ml	2.004 ± 0.03 mg/ml
7/6/77	2.00 mg/ml	1.75 ± 0.04 mg/ml
7/20/77	2.00 mg/ml	2.51 ± 0.08 mg/ml
8/3/77	2.00 mg/ml	1.92 ± 0.06 mg/ml
8/17/77	2.00 mg/ml	1.68 ± 0.14 mg/ml

The concentration of 1,2-dimethylhydrazine dihydrochloride was determined by the pentacyanoamino ferrate colorimetric method. Quantity modifications were made to avoid the small and fraction milliliter quantities and to make possible the use of standard laboratory ware.

All solutions and solid reagents in use or storage were kept cold, at about ice temperatures in a *cold* refrigerator.

#### REAGENTS

1. Trisodium salt of pentacyanoamino ferrate; concentration 20 mg/ml dissolved in cold borate buffer.
2. Stock 1,2-DMH•2HCl solution; approximately 40 mg/200 ml; dissolved in cold acetate buffer; concentration, approximately 200 µg/ml.
3. 0.05 M Borate buffer:
  - 0.05 M H<sub>3</sub>BO<sub>3</sub>:3.08 g/l
  - 0.5 M Na<sub>3</sub>B<sub>4</sub>O<sub>7</sub>•10 H<sub>2</sub>O:19.06 g/l
  - Add the salt to boric acid until pH 8.5.
4. 0.2 M acetate buffer
  - 0.2 M HOAc:11.4 ml conc glacial acetic acid per liter. Conc HOAc=17.6M
  - 0.2 M NaOAc:27.2 g/liter of NaOAc•3H<sub>2</sub>O
  - Add HOAc to the salt solution until pH 5.
5. 1-1 HCl solution.
6. Color development reagent (combined reagent) 12.0 ml (by pipette) of pentacyanoamino ferrate reagent diluted to 250 ml with cold borate buffer. Keep cold.

#### EQUIPMENT

Beckman spectrophotometer; 1 cm cells. Wavelength 536 nm.

#### CALIBRATION CURVE

No attempt was made to weigh 40.0 mg of the symmetrical DMH•2HCl because of its unstable nature at room temperature and its tendency to pick up water. 40 mg or more were quickly weighed and immediately dissolved in cold acetate buffer and diluted to 200 ml in a volumetric flask.

To prepare the calibration curve, 6 standard solutions were prepared from which 5 ml aliquots were taken to obtain each absorbance value.

Std Solution		If Stock is 210 $\mu\text{g/ml}$	
ml Stock	ml OAc <sup>-</sup> Buffer	Std Sol $\mu\text{g/ml}$	Calib. Sol. $\mu\text{g/ml}$
4	36	21	3.44
8	32	42	6.88
10	30	52.5	8.61
12	28	63	10.3
16	24	84	13.8
20	20	105	17.2

The calibration curve points were obtained by 5 aliquots of 5 ml each diluted with 25 ml color reagent and 0.5 ml of 1-1 HCl solution or a total of 30.5 ml. Concentration in  $\mu\text{g/ml}$  for each of these calibration points is  $(5 \text{ ml} \times \text{conc each std } \mu\text{g/ml}) \div 30.5 \text{ ml}$  and is included in the above table. The blank consists of 5 ml OAc<sup>-</sup> buffer with 25 ml indicator and 0.5 ml 1-1 acid.

The color develops and fades very rapidly, even when cold. To obtain reasonably consistent values for 5 aliquots, the acid was measured with a fast pipette, and a dry cuvette was filled and read immediately. If any motion is delayed, this is reflected in a bad reading. A typical calibration curve and a copy of a data sheet are attached.

A new calibration curve was prepared for each sample analyzed. Because these curves were prepared from somewhat different concentrations (plotted according to ml), two curves prepared from two different concentrations two weeks apart were converted to equivalent concentrations and plotted. The two curves were nearly identical.

#### SAMPLE ANALYSES

For sample analyses, samples were received as a solution; three separate aliquots were taken from the original sample. These were diluted to 50 ml; then, a 10 ml sample was taken from each and diluted to 50 ml. From the latter, 5 separate samples were taken, each diluted to 30.5 ml, and the absorbance values were averaged to determine the concentration. The 5 absorbance values were averaged to give the concentration of each aliquot.



## **APPENDIX D**

### **SUMMARY OF THE INCIDENCE OF NEOPLASMS IN HAMSTERS ADMINISTERED CHRYSOTILE ASBESTOS IN THE DIET**

TABLE D1.

**SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE HAMSTERS ADMINISTERED  
SHORT RANGE (SR) CHRYSOTILE ASBESTOS IN THE DIET**

	CONTROL	SR CHRYSOTILE
ANIMALS INITIALLY IN STUDY	126	253
ANIMALS NECROPSIED	115	233
ANIMALS EXAMINED HISTOPATHOLOGICALLY	115	233
-----		
INTEGUMENTARY SYSTEM		
NONE		
-----		
RESPIRATORY SYSTEM		
#PERITRACHEAL TISSUE SARCOMA, NOS, METASTATIC	(115)	(228) 1 (0%)
#LUNG PARANGLIOMA, METASTATIC SARCOMA, NOS, METASTATIC	(115)	(231) 1 (0%) 1 (0%)
-----		
HEMATOPOIETIC SYSTEM		
*MULTIPLE ORGANS MALIG.LYMPHOMA, LYMPHOCYTIC TYPE MALIG.LYMPHOMA, HISTIOCYTIC TYPE GRANULOCYTTIC LEUKEMIA	(115) 1 (1%) 1 (1%)	(233) 2 (1%) 1 (0%)
#LYMPH NODE C-CELL CARCINOMA, METASTATIC	(114)	(230) 1 (0%)
#THYMUS PARANGLIOMA, METASTATIC	(90)	(137) 1 (1%)
-----		
CIRCULATORY SYSTEM		
#SPLEEN HEMANGIOSARCOMA	(112)	(229) 1 (0%)
#HEART PARANGLIOMA, MALIGNANT	(114)	(230) 1 (0%)
#LIVER HEMANGIOSARCOMA	(115)	(232) 2 (1%)
#TESTIS HEMANGIOMA	(112)	(229) 1 (0%)
-----		
DIGESTIVE SYSTEM		
#LIVER OSTEOSARCOMA, METASTATIC	(115)	(232) 1 (0%)
#CARDIAC STOMACH SQUAMOUS CELL PAPILLOMA	(113) 1 (1%)	(222)
#DUODENUM ADENOMA, NOS	(114) 1 (1%)	(226)
-----		
URINARY SYSTEM		
#KIDNEY TUBULAR-CELL ADENOMA	(115)	(232) 2 (1%)
#KIDNEY/CORTEX ADENOMA, NOS	(115)	(232) 1 (0%)

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

**TABLE D1. MALE HAMSTERS: NEOPLASMS (CONTINUED)**

	CONTROL	SR CHRYSOTILE
<b>ENDOCRINE SYSTEM</b>		
#ADRENAL	(115)	(229)
CORTICAL ADENOMA	7 (6%)	26 (11%)
CORTICAL CARCINOMA	3 (3%)	8 (3%)
PHEOCHROMOCYTOMA	2 (2%)	4 (2%)
NEURILEMOMA		1 (0%)
#THYROID	(109)	(207)
C-CELL ADENOMA	3 (3%)	3 (1%)
C-CELL CARCINOMA	1 (1%)	1 (0%)
#PARATHYROID	(72)	(132)
ADENOMA, NOS		3 (2%)
#PANCREATIC ISLETS	(111)	(218)
ISLET-CELL ADENOMA	2 (2%)	15 (7%)
ISLET-CELL CARCINOMA	1 (1%)	
-----		
<b>REPRODUCTIVE SYSTEM</b>		
NONE		
-----		
<b>NERVOUS SYSTEM</b>		
#BRAIN	(114)	(223)
ASTROCYTOMA	1 (1%)	
-----		
<b>SPECIAL SENSE ORGANS</b>		
NONE		
-----		
<b>MUSCULOSKELETAL SYSTEM</b>		
*SKELETAL MUSCLE	(115)	(233)
FIBROSARCOMA		1 (0%)
-----		
<b>BODY CAVITIES</b>		
*THORACIC CAVITY	(115)	(233)
OSTEOSARCOMA		1 (0%)
-----		
<b>ALL OTHER SYSTEMS</b>		
NONE		
-----		
<b>ANIMAL DISPOSITION SUMMARY</b>		
ANIMALS INITIALLY IN STUDY	126	253
NATURAL DEATHS	112	221
MORIBUND SACRIFICE	11	29
SCHEDULED SACRIFICE		
ACCIDENTALLY KILLED		2
TERMINAL SACRIFICE		
ANIMAL MISSING		

<sup>a</sup> INCLUDES AUTOLYZED ANIMALS

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

**TABLE D1. MALE HAMSTERS: NEOPLASMS (CONTINUED)**

	<b>CONTROL</b>	<b>SR CHRYSOTILE</b>
TUMOR SUMMARY		
TOTAL ANIMALS WITH PRIMARY TUMORS*	21	64
TOTAL PRIMARY TUMORS	24	74
TOTAL ANIMALS WITH BENIGN TUMORS	15	48
TOTAL BENIGN TUMORS	16	56
TOTAL ANIMALS WITH MALIGNANT TUMORS	8	18
TOTAL MALIGNANT TUMORS	8	18
TOTAL ANIMALS WITH SECONDARY TUMORS#		4
TOTAL SECONDARY TUMORS		6
TOTAL ANIMALS WITH TUMORS UNCERTAIN- BENIGN OR MALIGNANT		
TOTAL UNCERTAIN TUMORS		
TOTAL ANIMALS WITH TUMORS UNCERTAIN- PRIMARY OR METASTATIC		
TOTAL UNCERTAIN TUMORS		

\* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS

# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE D2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE HAMSTERS ADMINISTERED  
SHORT RANGE (SR) CHRYSOTILE ASBESTOS IN THE DIET

	CONTROL	SR CHRYSOTILE
ANIMALS INITIALLY IN STUDY	126	252
ANIMALS MISSING	1	1
ANIMALS NECROPSIED	114	228
ANIMALS EXAMINED HISTOPATHOLOGICALLY	114	228
-----		
INTEGUMENTARY SYSTEM		
*SUBCUT TISSUE	(114)	(228)
SARCOMA, NOS		1 (0%)
FIBROSARCOMA		1 (0%)
LIPOMA		1 (0%)
-----		
RESPIRATORY SYSTEM		
#LUNG	(114)	(228)
SARCOMA, NOS, METASTATIC		2 (1%)
-----		
HEMATOPOIETIC SYSTEM		
*MULTIPLE ORGANS	(114)	(228)
MALIGNANT LYMPHOMA, NOS	1 (1%)	
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE		2 (1%)
#LYMPH NODE	(114)	(227)
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE	1 (1%)	
-----		
CIRCULATORY SYSTEM		
#SPLEEN	(112)	(226)
HEMANGIOMA		1 (0%)
-----		
DIGESTIVE SYSTEM		
#COLON	(114)	(226)
ADENOCARCINOMA, NOS	1 (1%)	1 (0%)
-----		
URINARY SYSTEM		
NONE		
-----		
ENDOCRINE SYSTEM		
#PITUITARY	(77)	(132)
CHROMOPHOBE ADENOMA		1 (1%)
#ADRENAL	(112)	(226)
CORTICAL ADENOMA	4 (4%)	8 (4%)
PHEOCHROMOCYTOMA		3 (1%)
NEURILEMOMA		1 (0%)
#THYROID	(107)	(214)
FOLLICULAR-CELL ADENOMA	2 (2%)	
C-CELL ADENOMA	2 (2%)	
#PARATHYROID	(68)	(139)
ADENOMA, NOS	3 (4%)	3 (2%)
#PANCREATIC ISLETS	(109)	(217)
ISLET-CELL ADENOMA	2 (2%)	2 (1%)
ISLET-CELL CARCINOMA	1 (1%)	

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

**TABLE D2. FEMALE HAMSTERS: NEOPLASMS (CONTINUED)**

	CONTROL	SR CHRYSOTILE
<b>REPRODUCTIVE SYSTEM</b>		
*VAGINA	(114)	(228)
PAPILLARY ADENOMA	1 (1%)	
#UTERUS	(113)	(226)
PAPILLOMA, NOS		1 (0%)
PAPILLARY CARCINOMA		1 (0%)
ADENOMA, NOS		1 (0%)
PAPILLARY ADENOMA		1 (0%)
LEIOMYOMA	2 (2%)	1 (0%)
ENDOMETRIAL STROMAL POLYP	1 (1%)	
#OVARY	(112)	(222)
FIBROMA		1 (0%)
-----		
<b>NERVOUS SYSTEM</b>		
NONE		
-----		
<b>SPECIAL SENSE ORGANS</b>		
NONE		
-----		
<b>MUSCULOSKELETAL SYSTEM</b>		
NONE		
-----		
<b>BODY CAVITIES</b>		
*THORACIC CAVITY	(114)	(228)
OSTEOSARCOMA	1 (1%)	
-----		
<b>ALL OTHER SYSTEMS</b>		
PERINEUM		
PAPILLOMA, NOS	1	
SITE UNKNOWN		
SARCOMA, NOS		1
OSTEOSARCOMA		1
-----		
<b>ANIMAL DISPOSITION SUMMARY</b>		
ANIMALS INITIALLY IN STUDY	126	252
NATURAL DEATH <sup>a</sup>	112	231
MORIBUND SACRIFICE	13	19
SCHEDULED SACRIFICE		
ACCIDENTALLY KILLED		
TERMINAL SACRIFICE		
ANIMAL MISSING	1	1

<sup>a</sup> INCLUDES AUTOLYZED ANIMALS

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

**TABLE D2. FEMALE HAMSTERS: NEOPLASMS (CONTINUED)**

	CONTROL	SR CHRYSOTILE
TUMOR SUMMARY		
TOTAL ANIMALS WITH PRIMARY TUMORS*	19	28
TOTAL PRIMARY TUMORS	23	33
TOTAL ANIMALS WITH BENIGN TUMORS	16	24
TOTAL BENIGN TUMORS	18	25
TOTAL ANIMALS WITH MALIGNANT TUMORS	5	7
TOTAL MALIGNANT TUMORS	5	8
TOTAL ANIMALS WITH SECONDARY TUMORS#		2
TOTAL SECONDARY TUMORS		2
TOTAL ANIMALS WITH TUMORS UNCERTAIN- BENIGN OR MALIGNANT		
TOTAL UNCERTAIN TUMORS		
TOTAL ANIMALS WITH TUMORS UNCERTAIN- PRIMARY OR METASTATIC		
TOTAL UNCERTAIN TUMORS		

\* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS

# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE D3.

**SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE HAMSTERS ADMINISTERED  
INTERMEDIATE RANGE (IR) CHRYSOTILE ASBESTOS IN THE DIET**

	CONTROL	IR CHRYSOTILE
ANIMALS INITIALLY IN STUDY	126	251
ANIMALS NECROPSIED	116	245
ANIMALS EXAMINED HISTOPATHOLOGICALLY	116	245
-----		
INTEGUMENTARY SYSTEM		
*SUBCUT TISSUE SARCOMA, NOS	(116) 1 (1%)	(245)
-----		
RESPIRATORY SYSTEM		
#TRACHEA CARCINOMA, NOS	(116)	(244) 1 (0%)
-----		
HEMATOPOIETIC SYSTEM		
*MULTIPLE ORGANS MALIG. LYMPHOMA, LYMPHOCYTIC TYPE	(116)	(245) 8 (3%)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE	1 (1%)	1 (0%)
#CERVICAL LYMPH NODE CARCINOMA, NOS	(116)	(244) 1 (0%)
C-CELL CARCINOMA, METASTATIC		1 (0%)
#LYMPH NODE OF THORAX SARCOMA, NOS, METASTATIC	(116)	(244) 1 (0%)
#MEDIASTINAL L. NODE ADENOCARCINOMA, NOS, METASTATIC	(116) 1 (1%)	(244)
#PANCREATIC L. NODE ADENOCARCINOMA, NOS, METASTATIC	(116) 1 (1%)	(244)
#MESENTERIC L. NODE MALIG. LYMPHOMA, HISTIOCYTIC TYPE	(116)	(244) 1 (0%)
-----		
CIRCULATORY SYSTEM		
#SPLENIC CAPSULE HEMANGIOMA	(112)	(242) 1 (0%)
-----		
DIGESTIVE SYSTEM		
#LIVER ADENOCARCINOMA, NOS, METASTATIC	(116) 1 (1%)	(244)
#CARDIAC STOMACH SQUAMOUS CELL PAPILOMA	(115)	(244) 1 (0%)
PAPILLARY ADENOMA		1 (0%)
#GASTRIC FUNDUS CARCINOMA-IN-SITU, NOS	(115)	(244) 1 (0%)
#JEJUNUM ADENOCARCINOMA, NOS	(116) 1 (1%)	(244)
-----		
URINARY SYSTEM		
#KIDNEY ADENOCARCINOMA, NOS	(115) 1 (1%)	(245)
TUBULAR-CELL ADENOCARCINOMA		1 (0%)
#KIDNEY/CORTEX ADENOCARCINOMA, NOS	(115) 1 (1%)	(245)
-----		
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY		
* NUMBER OF ANIMALS NECROPSIED		

**TABLE D3. MALE HAMSTERS: NEOPLASMS (CONTINUED)**

	CONTROL	IR CHRYSOTILE
<b>ENDOCRINE SYSTEM</b>		
#ADRENAL	(115)	(244)
CORTICAL ADENOMA	7 (6%)	24 (10%)
CORTICAL CARCINOMA	3 (3%)	7 (3%)
PHEOCHROMOCYTOMA	5 (4%)	9 (4%)
PHEOCHROMOCYTOMA, MALIGNANT		2 (1%)
GANGLIONEUROMA	1 (1%)	
NEUROBLASTOMA	2 (2%)	1 (0%)
#THYROID	(106)	(216)
ADENOMA, NOS		1 (0%)
C-CELL ADENOMA	3 (3%)	5 (2%)
C-CELL CARCINOMA	1 (1%)	4 (2%)
#PARATHYROID	(71)	(138)
ADENOMA, NOS	1 (1%)	4 (3%)
#PANCREATIC ISLETS	(110)	(226)
ISLET-CELL ADENOMA	7 (6%)	15 (7%)
ISLET-CELL CARCINOMA		1 (0%)
-----		
<b>REPRODUCTIVE SYSTEM</b>		
NONE		
-----		
<b>NERVOUS SYSTEM</b>		
NONE		
-----		
<b>SPECIAL SENSE ORGANS</b>		
NONE		
-----		
<b>MUSCULOSKELETAL SYSTEM</b>		
NONE		
-----		
<b>BODY CAVITIES</b>		
NONE		
-----		
<b>ALL OTHER SYSTEMS</b>		
*MULTIPLE ORGANS	(116)	(245)
CARCINOMA, NOS, METASTATIC		1 (0%)
FIBROSARCOMA		1 (0%)
-----		
<b>ANIMAL DISPOSITION SUMMARY</b>		
ANIMALS INITIALLY IN STUDY	126	251
NATURAL DEATH	102	218
MORBUND SACRIFICE	24	33
SCHEDULED SACRIFICE		
ACCIDENTALLY KILLED		
TERMINAL SACRIFICE		
ANIMAL MISSING		

∞ INCLUDES AUTOLYZED ANIMALS

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

\* NUMBER OF ANIMALS NECROPSIED

**TABLE D3. MALE HAMSTERS: NEOPLASMS (CONTINUED)**

	<b>CONTROL</b>	<b>IR CHRYSOTILE</b>
<b>TUMOR SUMMARY</b>		
TOTAL ANIMALS WITH PRIMARY TUMORS*	26	78
TOTAL PRIMARY TUMORS	35	91
TOTAL ANIMALS WITH BENIGN TUMORS	19	55
TOTAL BENIGN TUMORS	24	61
TOTAL ANIMALS WITH MALIGNANT TUMORS	10	30
TOTAL MALIGNANT TUMORS	11	30
TOTAL ANIMALS WITH SECONDARY TUMORS#	1	3
TOTAL SECONDARY TUMORS	3	3
TOTAL ANIMALS WITH TUMORS UNCERTAIN- BENIGN OR MALIGNANT		
TOTAL UNCERTAIN TUMORS		
TOTAL ANIMALS WITH TUMORS UNCERTAIN- PRIMARY OR METASTATIC		
TOTAL UNCERTAIN TUMORS		

\* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS

# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE D4.

**SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE HAMSTERS ADMINISTERED  
INTERMEDIATE RANGE (IR) CHRYSOTILE ASBESTOS IN THE DIET**

	CONTROL	IR CHRYSOTILE
ANIMALS INITIALLY IN STUDY	126	252
ANIMALS MISSING		1
ANIMALS NECROPSIED	119	244
ANIMALS EXAMINED HISTOPATHOLOGICALLY	119	244
-----		
INTEGUMENTARY SYSTEM		
*SKIN	(119)	(244)
MALIGNANT MELANOMA		1 (0%)
*SUBCUT TISSUE	(119)	(244)
SARCOMA, NOS		1 (0%)
-----		
RESPIRATORY SYSTEM		
NONE		
-----		
HEMATOPOIETIC SYSTEM		
*MULTIPLE ORGANS	(119)	(244)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (0%)
#LYMPH NODE	(119)	(243)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (0%)
-----		
CIRCULATORY SYSTEM		
#SPLEEN	(118)	(241)
HEMANGIOMA		1 (0%)
-----		
DIGESTIVE SYSTEM		
#GASTRIC FUNDUS	(118)	(242)
PAPILLARY ADENOMA		1 (0%)
#COLON	(118)	(243)
ADENOMA, NOS	1 (1%)	
-----		
*ANUS	(119)	(244)
FIBROMA	1 (1%)	
-----		
URINARY SYSTEM		
#KIDNEY/CORTEX	(119)	(243)
ADENOCARCINOMA, NOS	1 (1%)	
-----		
ENDOCRINE SYSTEM		
#PITUITARY	(67)	(164)
ADENOMA, NOS	1 (1%)	1 (1%)
CHROMOPHOBE ADENOMA	1 (1%)	
CHROMOPHOBE CARCINOMA		1 (1%)
#ADRENAL	(118)	(234)
CORTICAL ADENOMA	6 (5%)	18 (8%)
CORTICAL CARCINOMA		1 (0%)
PHEOCHROMOCYTOMA		1 (0%)
#THYROID	(115)	(223)
FOLLICULAR-CELL ADENOMA		1 (0%)
C-CELL ADENOMA	3 (3%)	2 (1%)
#PARATHYROID	(77)	(148)
ADENOMA, NOS	1 (1%)	1 (1%)
#PANCREATIC ISLETS	(116)	(236)
ISLET-CELL ADENOMA	5 (4%)	4 (2%)

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

**TABLE D4. FEMALE HAMSTERS: NEOPLASMS (CONTINUED)**

	CONTROL	IR CHRYSOTILE
<b>REPRODUCTIVE SYSTEM</b>		
#UTERUS	(119)	(240)
PAPILLOMA, NOS		1 (0%)
ADENOMA, NOS		1 (0%)
ADENOCARCINOMA, NOS		1 (0%)
PAPILLARY ADENOMA		2 (1%)
LEIOMYOMA	1 (1%)	2 (1%)
<hr/>		
<b>NERVOUS SYSTEM</b>		
NONE		
<hr/>		
<b>SPECIAL SENSE ORGANS</b>		
NONE		
<hr/>		
<b>MUSCULOSKELETAL SYSTEM</b>		
*THORACIC VERTEBRA SARCOMA, NOS	(119)	(244) 1 (0%)
<hr/>		
<b>BODY CAVITIES</b>		
*MESENTERY OSTEOMA	(119)	(244) 1 (0%)
<hr/>		
<b>ALL OTHER SYSTEMS</b>		
NONE		
<hr/>		
<b>ANIMAL DISPOSITION SUMMARY</b>		
ANIMALS INITIALLY IN STUDY	126	252
NATURAL DEATH	114	235
MORIBUND SACRIFICE	12	16
SCHEDULED SACRIFICE		
ACCIDENTALLY KILLED		
TERMINAL SACRIFICE		
ANIMAL MISSING		1
<hr/>		
a INCLUDES AUTOLYZED ANIMALS		
<hr/>		
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY		
* NUMBER OF ANIMALS NECROPSIED		
<hr/>		
<b>TUMOR SUMMARY</b>		
TOTAL ANIMALS WITH PRIMARY TUMORS*	17	39
TOTAL PRIMARY TUMORS	21	45
TOTAL ANIMALS WITH BENIGN TUMORS	16	33
TOTAL BENIGN TUMORS	20	37
TOTAL ANIMALS WITH MALIGNANT TUMORS	1	8
TOTAL MALIGNANT TUMORS	1	8
TOTAL ANIMALS WITH SECONDARY TUMORS#		
TOTAL SECONDARY TUMORS		
TOTAL ANIMALS WITH TUMORS UNCERTAIN- BENIGN OR MALIGNANT		
TOTAL UNCERTAIN TUMORS		
TOTAL ANIMALS WITH TUMORS UNCERTAIN- PRIMARY OR METASTATIC		
TOTAL UNCERTAIN TUMORS		
<hr/>		
* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS		
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN		

TABLE D5.

**SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE HAMSTERS ADMINISTERED  
1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH) PLUS INTERMEDIATE RANGE (IR)  
CHRYSTOLE ASBESTOS IN THE DIET**

	CONTROL	DMH	IR CHRYSTOLE PLUS DMH
ANIMALS INITIALLY IN STUDY	125	127	176
ANIMALS NECROPSIED	119	127	173
ANIMALS EXAMINED HISTOPATHOLOGICALLY	119	127	173
-----			
INTEGUMENTARY SYSTEM			
*SKIN	(119)	(127)	(173)
SARCOMA, NOS	1 (1%)		
*SUBCUT TISSUE	(119)	(127)	(173)
FIBROSARCOMA			1 (1%)
-----			
RESPIRATORY SYSTEM			
#LUNG	(119)	(126)	(173)
UNDIFFERENTIATED CARCINOMA METAS		3 (2%)	3 (2%)
SARCOMA, NOS, METASTATIC	1 (1%)		
-----			
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(119)	(127)	(173)
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE	2 (2%)	2 (2%)	3 (2%)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE	1 (1%)	5 (4%)	5 (3%)
GRANULOCYTIC LEUKEMIA	1 (1%)		
#LYMPH NODE OF THORAX	(118)	(127)	(173)
C-CELL CARCINOMA, METASTATIC			1 (1%)
#COLO-RECTAL L. NODE	(118)	(127)	(173)
FIBROSARCOMA, METASTATIC			1 (1%)
-----			
CIRCULATORY SYSTEM			
#LIVER	(119)	(127)	(173)
HEMANGIOMA	1 (1%)	2 (2%)	1 (1%)
HEMANGIOSARCOMA	1 (1%)		1 (1%)
#CECUM	(116)	(126)	(170)
HEMANGIOMA	1 (1%)		
-----			
DIGESTIVE SYSTEM			
#LIVER	(119)	(127)	(173)
HEPATOCELLULAR ADENOMA		2 (2%)	
SARCOMA, NOS			1 (1%)
#PANCREAS	(110)	(114)	(167)
MESOTHELIOMA, METASTATIC	1 (1%)		
#CARDIAC STOMACH	(116)	(127)	(170)
SQUAMOUS CELL PAPILLOMA	1 (1%)		2 (1%)
#COLON	(116)	(126)	(170)
ADENOMA, NOS		1 (1%)	
FIBROSARCOMA, METASTATIC			1 (1%)
#CECUM	(116)	(126)	(170)
PAPILLOMA, NOS			1 (1%)
PAPILLARY ADENOMA		1 (1%)	
*RECTUM	(119)	(127)	(173)
ADENOMA, NOS	1 (1%)		
PAPILLARY ADENOMA			1 (1%)
*ANUS	(119)	(127)	(173)
FIBROSARCOMA		1 (1%)	

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

**TABLE D5. MALE HAMSTERS: NEOPLASMS (CONTINUED)**

	CONTROL	DMH	IR CHRYSOTILE PLUS DMH
URINARY SYSTEM			
#KIDNEY TUBULAR-CELL ADENOMA	(119) 1 (1%)	(127)	(173)
-----			
ENDOCRINE SYSTEM			
#PITUITARY CARCINOMA, NOS ADENOMA, NOS	(80)	(87) 1 (1%)	(123) 1 (1%) 1 (1%)
#ADRENAL CORTICAL ADENOMA CORTICAL CARCINOMA PHEOCHROMOCYTOMA PHEOCHROMOCYTOMA, MALIGNANT NEUROBLASTOMA NEURILEMOMA	(117) 3 (3%) 4 (3%) 3 (3%)  1 (1%)	(127) 3 (2%) 2 (2%) 4 (3%)   1 (1%)	(171) 8 (5%) 7 (4%) 3 (2%) 3 (2%) 1 (1%)
#ADRENAL MEDULLA NEUROBLASTOMA	(117) 1 (1%)	(127)	(171)
#THYROID ADENOMA, NOS C-CELL ADENOMA C-CELL CARCINOMA	(107) 1 (1%)	(118) 2 (2%)	(163) 3 (2%) 1 (1%)
#PARATHYROID ADENOMA, NOS	(64) 1 (2%)	(81)	(118) 2 (2%)
#PANCREATIC ISLETS ISLET-CELL ADENOMA ISLET-CELL CARCINOMA	(110) 8 (7%)	(114) 6 (5%)	(167) 10 (6%) 1 (1%)
-----			
REPRODUCTIVE SYSTEM			
*EPIDIDYMIS ADENOMA, NOS	(119)	(127)	(173) 1 (1%)
-----			
NERVOUS SYSTEM			
#BRAIN SARCOMA, NOS ASTROCYTOMA	(113) 1 (1%)	(124)	(169) 1 (1%)
-----			
SPECIAL SENSE ORGANS			
NONE			
-----			
MUSCULOSKELETAL SYSTEM			
*STERNUM OSTEOMA	(119) 1 (1%)	(127)	(173)
*MUSCLE HIP/THIGH RHABDOMYOSARCOMA	(119)	(127)	(173) 1 (1%)
-----			
BODY CAVITIES			
*ABDOMINAL CAVITY FIBROSARCOMA	(119)	(127)	(173) 1 (1%)
*PERITONEUM FIBROSARCOMA MESOTHELIOMA, MALIGNANT	(119) 1 (1%)	(127) 1 (1%)	(173)
-----			
ALL OTHER SYSTEMS			
NONE			

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

**TABLE D5. MALE HAMSTERS: NEOPLASMS (CONTINUED)**

	CONTROL	DMH	IR CHRYSOTILE PLUS DMH
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	125	127	176
NATURAL DEATH <sup>a</sup>	98	101	141
MORIBUND SACRIFICE	27	25	35
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED		1	
TERMINAL SACRIFICE			
ANIMAL MISSING			
<sup>a</sup> INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	27	29	51
TOTAL PRIMARY TUMORS	36	33	61
TOTAL ANIMALS WITH BENIGN TUMORS	19	20	31
TOTAL BENIGN TUMORS	23	21	33
TOTAL ANIMALS WITH MALIGNANT TUMORS	12	12	26
TOTAL MALIGNANT TUMORS	13	12	28
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	3	5
TOTAL SECONDARY TUMORS	2	3	6
TOTAL ANIMALS WITH TUMORS UNCERTAIN- BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN- PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

\* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS

# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE D6.

**SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE HAMSTERS ADMINISTERED  
1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH) BY GAVAGE OR DMH PLUS  
INTERMEDIATE RANGE (I.R.) CHRYSOTILE ASBESTOS IN THE DIET**

	CONTROL	DMH	IR CHRYSOTILE PLUS DMH
ANIMALS INITIALLY IN STUDY	128	126	174
ANIMALS MISSING	1		2
ANIMALS NECROPSIED	120	122	161
ANIMALS EXAMINED HISTOPATHOLOGICALLY	120	122	161
-----			
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE FIBROSARCOMA	(120)	(122) 1 (1%)	(161)
-----			
RESPIRATORY SYSTEM			
#LUNG	(119)	(122)	(160)
UNDIFFERENTIATED CARCINOMA METAS			1 (1%)
ALVEOLAR/BRONCHIOLAR CARCINOMA			1 (1%)
SARCOMA, NOS, METASTATIC		1 (1%)	3 (2%)
FIBROSARCOMA, METASTATIC		1 (1%)	
OLIGODENDROGLIOMA, METASTAT.		1 (1%)	
-----			
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(120)	(122)	(161)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	2 (2%)	1 (1%)	3 (2%)
LEUKEMIA, NOS	1 (1%)		
#SPLEEN	(119)	(121)	(159)
FIBROSARCOMA, METASTATIC		1 (1%)	
#LYMPH NODE	(119)	(121)	(161)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (1%)	
#CERVICAL LYMPH NODE	(119)	(121)	(161)
UNDIFFERENTIATED CARCINOMA METAS			1 (1%)
SARCOMA, NOS			1 (1%)
-----			
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(120)	(122)	(161)
HEMANGIOSARCOMA	1 (1%)		
-----			
#UTERUS	(120)	(116)	(156)
ADENOCARCINOMA, NOS		1 (1%)	
CYSTADENOMA, NOS	1 (1%)		
FIBROMA			1 (1%)
LEIOMYOMA			1 (1%)
ENDOMETRIAL STROMAL POLYP		1 (1%)	
#CERVIX UTERI	(120)	(116)	(156)
PAPILLARY ADENOMA	1 (1%)		
-----			
NERVOUS SYSTEM			
#BRAIN	(118)	(119)	(156)
OLIGODENDROGLIOMA		1 (1%)	
-----			
SPECIAL SENSE ORGANS			
*EYE APPENDAGE	(120)	(122)	(161)
SARCOMA, NOS		1 (1%)	
-----			
MUSCULOSKELETAL SYSTEM			
NONE			

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

TABLE D6. FEMALE HAMSTERS: NEOPLASMS (CONTINUED)

	CONTROL	DMH	IR CHRYSOTILE PLUS DMH
BODY CAVITIES			
NONE			
-----			
ALL OTHER SYSTEMS			
NONE			
-----			
#SPLEEN HEMANGIOMA	(119)	(121)	(159) 1 (1%)
-----			
DIGESTIVE SYSTEM			
*GALLBLADDER PAPILLOMA, NOS	(120) 1 (1%)	(122)	(161)
#COLON ADENOMATOUS POLYP, NOS	(120)	(118) 1 (1%)	(159)
#CECUM LIPOMA	(120) 1 (1%)	(118)	(159)
*RECTUM SQUAMOUS CELL CARCINOMA	(120)	(122) 1 (1%)	(161)
-----			
URINARY SYSTEM			
#KIDNEY UNDIFFERENTIATED CARCINOMA METAS	(120)	(122)	(161) 1 (1%)
-----			
ENDOCRINE SYSTEM			
#PITUITARY OLIGODENDROGLIOMA, METASTAT.	(62)	(59) 1 (2%)	(109)
#ADRENAL CORTICAL ADENOMA CORTICAL CARCINOMA	(120) 3 (3%)	(120) 2 (2%)	(158) 6 (4%) 2 (1%)
#THYROID C-CELL CARCINOMA	(112) 1 (1%)	(108)	(141)
#PARATHYROID ADENOMA, NOS	(74) 1 (1%)	(57) 2 (4%)	(91)
#PANCREATIC ISLETS ISLET-CELL ADENOMA	(116) 5 (4%)	(119) 2 (2%)	(149) 4 (3%)
-----			
REPRODUCTIVE SYSTEM			
*VAGINA PAPILLOMA, NOS	(120)	(122)	(161) 1 (1%)

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

**TABLE D6. FEMALE HAMSTERS: NEOPLASMS (CONTINUED)**

	CONTROL	DMH	IR CHRYSOTILE PLUS DMH
<b>ANIMAL DISPOSITION SUMMARY</b>			
ANIMALS INITIALLY IN STUDY	128	126	174
NATURAL DEATH <sup>a</sup>	115	108	163
MORIBUND SACRIFICE	12	18	8
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE			
ANIMAL MISSING	1		2
<sup>a</sup> INCLUDES AUTOLYZED ANIMALS			
<b>TUMOR SUMMARY</b>			
TOTAL ANIMALS WITH PRIMARY TUMORS*	15	15	19
TOTAL PRIMARY TUMORS	18	15	21
TOTAL ANIMALS WITH BENIGN TUMORS	12	8	14
TOTAL BENIGN TUMORS	13	8	14
TOTAL ANIMALS WITH MALIGNANT TUMORS	5	7	7
TOTAL MALIGNANT TUMORS	5	7	7
TOTAL ANIMALS WITH SECONDARY TUMORS#		3	4
TOTAL SECONDARY TUMORS		5	6
TOTAL ANIMALS WITH TUMORS UNCERTAIN- BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN- PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

\* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS

# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

## **APPENDIX E**

### **INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF HAMSTERS ADMINISTERED CHRYSOTILE ASBESTOS IN THE DIET**







**TABLE E1. MALE HAMSTERS: TUMOR PATHOLOGY (CONTINUED) CONTROL**

ANIMAL NUMBER	272	278	288	289	292	293	300	303	304	311	312	322	331	334	344	345	355	356	366	368	371
WEEKS ON STUDY	041	127	068	088	005	097	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000
<b>RESPIRATORY SYSTEM</b>																					
LUNGS AND BRONCHI	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
<b>HEMATOPOIETIC SYSTEM</b>																					
BONE MARROW	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	-	+	+	+	+	+	A	-	+	+	+	+	+	+	+	+	+	+	-	+
<b>CIRCULATORY SYSTEM</b>																					
HEART	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
<b>DIGESTIVE SYSTEM</b>																					
SALIVARY GLAND	+	+	+	+	+	-	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	+	+	N	N	A	N	N	+	N	+	N	N	N	N	N	N	+
PANCREAS	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+
STOMACH SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE ADENOMA, NOS	+	+	+	+	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+
<b>URINARY SYSTEM</b>																					
KIDNEY	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
<b>ENDOCRINE SYSTEM</b>																					
PITUITARY	+	-	+	-	+	+	-	A	+	+	-	+	-	+	+	-	+	-	+	+	+
ADRENAL CORTICAL ADENOMA CORTICAL CARCINOMA PHEOCHROMOCYTOMA	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID C-CELL ADENOMA C-CELL CARCINOMA	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	X
PARATHYROID	-	-	-	+	+	+	-	A	-	+	+	+	+	+	+	-	-	+	-	+	+
PANCREATIC ISLETS ISLET-CELL ADENOMA ISLET-CELL CARCINOMA	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
<b>REPRODUCTIVE SYSTEM</b>																					
MAMMARY GLAND	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	-	+	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+
<b>NERVOUS SYSTEM</b>																					
BRAIN ASTROCYTOMA	+	+	+	+	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+
<b>ALL OTHER SYSTEMS</b>																					
MULTIPLE ORGANS NOS MALIG. LYMPHOMA, LYMPHOCYTIC TYPE MALIG. LYMPHOMA, HISTIOCYTIC TYPE	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N

+: TISSUE EXAMINED MICROSCOPICALLY  
 -: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY  
 X: TUMOR INCIDENCE  
 N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION  
 : NO TISSUE INFORMATION SUBMITTED  
 C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL  
 A: AUTOLYSIS  
 M: ANIMAL MISSING  
 B: NO NECROPSY PERFORMED















































**TABLE E2. FEMALE HAMSTERS: TUMOR PATHOLOGY (CONTINUED) SHORT RANGE**

ANIMAL NUMBER	653	661	662	663	664	665	666	667	668	669	670	671	672	673	674	675	676	677	678	679	680	681	682	683	684	685	686	687	688	689	690	
WEEKS ON STUDY	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
INTEGUMENTARY SYSTEM																																
SUBCUTANEOUS TISSUE SARCOMA, NOS FIBROSARCOMA LIPOMA	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
RESPIRATORY SYSTEM																																
LUNGS AND BRONCHI SARCOMA, NOS, METASTATIC	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
TRACHEA	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMATOPOIETIC SYSTEM																																
BONE MARROW	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SPLEEN HEMANGIOMA	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LYMPH NODES	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
THYMUS	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
CIRCULATORY SYSTEM																																
HEART	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
DIGESTIVE SYSTEM																																
SALIVARY GLAND	-	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LIVER	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
BILE DUCT	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
GALLBLADDER & COMMON BILE DUCT	+	A	N	+	N	A	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
PANCREAS	-	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ESOPHAGUS	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
STOMACH	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SMALL INTESTINE	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LARGE INTESTINE ADENOCARCINOMA, NOS	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
URINARY SYSTEM																																
KIDNEY	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
URINARY BLADDER	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ENDOCRINE SYSTEM																																
PITUITARY CHROMOPHOBE ADENOMA	-	A	-	+	-	A	A	+	+	+	-	+	-	+	+	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	
ADRENAL CORTICAL ADENOMA PHEOCHROMOCYTOMA NEURILEMOMA	+	A	+	+	+	A	A	+	+	+	X	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
THYROID	+	A	-	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
PARATHYROID ADENOMA, NOS	+	A	-	+	+	A	A	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
PANCREATIC ISLETS ISLET-CELL ADENOMA	-	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
REPRODUCTIVE SYSTEM																																
MAMMARY GLAND	N	A	N	N	N	A	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
UTERUS PAPILLOMA, NOS PAPILLARY CARCINOMA ADENOMA, NOS PAPILLARY ADENOMA LEIOMYOMA	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
OVARY FIBROMA	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ALL OTHER SYSTEMS																																
MULTIPLE ORGANS NOS MALIG. LYMPHOMA, LYMPHOCYTIC TYPE	N	A	N	N	N	A	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
SITE UNKNOWN SARCOMA, NOS OSTEOSARCOMA	A					A	A																									

+: TISSUE EXAMINED MICROSCOPICALLY  
 -: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY  
 X: TUMOR INCIDENCE  
 N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION  
 : NO TISSUE INFORMATION SUBMITTED  
 C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL  
 A: AUTOLYSIS  
 M: ANIMAL MISSING  
 B: NO NECROPSY PERFORMED

**TABLE E2. FEMALE HAMSTERS: TUMOR PATHOLOGY (CONTINUED) SHORT RANGE**

ANIMAL NUMBER	7 6 1	7 6 2	7 6 3	7 6 1	7 6 2	7 6 3	7 6 1	7 6 2	7 6 3	8 0 1	8 0 2	8 0 3																				
WEEKS ON STUDY	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
<b>INTEGUMENTARY SYSTEM</b>																																
SUBCUTANEOUS TISSUE SARCOMA, NOS FIBROSARCOMA LIPOMA	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	
<b>RESPIRATORY SYSTEM</b>																																
LUNGS AND BRONCHI SARCOMA, NOS, METASTATIC TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	
<b>HEMATOPOIETIC SYSTEM</b>																																
BONE MARROW SPLEEN HEMANGIOMA LYMPH NODES THYMUS	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	
<b>CIRCULATORY SYSTEM</b>																																
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	
<b>DIGESTIVE SYSTEM</b>																																
SALIVARY GLAND LIVER BILE DUCT GALLBLADDER & COMMON BILE DUCT PANCREAS ESOPHAGUS STOMACH SMALL INTESTINE LARGE INTESTINE ADENOCARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+
<b>URINARY SYSTEM</b>																																
KIDNEY URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	
<b>ENDOCRINE SYSTEM</b>																																
PITUITARY CHROMOPHOBE ADENOMA ADRENAL CORTICAL ADENOMA PHEOCHROMOCYTOMA NEURILEIOMA THYROID PARATHYROID ADENOMA, NOS PANCREATIC ISLETS ISLET-CELL ADENOMA	+	-	+	+	-	+	+	+	+	-	+	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	A	+	+	-	
<b>REPRODUCTIVE SYSTEM</b>																																
MAMMARY GLAND UTERUS PAPILLOMA, NOS PAPILLARY CARCINOMA ADENOMA, NOS PAPILLARY ADENOMA LEIOMYOMA OVARY FIBROMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N
<b>ALL OTHER SYSTEMS</b>																																
MULTIPLE ORGANS NOS MALIG. LYMPHOMA, LYMPHOCYTIC TYPE SITE UNKNOW SARCOMA, NOS OSTEOSARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N

+: TISSUE EXAMINED MICROSCOPICALLY  
 -: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY  
 X: TUMOR INCIDENCE  
 N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION  
 I: NO TISSUE INFORMATION SUBMITTED  
 C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL  
 A: AUTOLYSIS  
 M: ANIMAL MISSING  
 B: NO NECROPSY PERFORMED









































































TABLE E5.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE HAMSTERS ADMINISTERED 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH) BY GAVAGE WITH AND WITHOUT INTERMEDIATE RANGE CHRYSOTILE ASBESTOS IN THE DIET

DMH

ANIMAL NUMBER	0	1	1	1	2	2	3	3	3	4	4	4	5	5	5	6	6	6	7	7	7	8	8	8	9	9
WEEKS ON STUDY	0	1	0	0	0	0	0	0	0	0	0	0	1	2	0	1	0	0	0	0	0	1	0	0	0	0
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
UNDIFFERENTIATED CARCINOMA METAST																										
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
THYMUS	-	+	+	+	+	-	+	-	-	+	-	-	+	-	+	-	+	-	+	-	+	-	-	+	-	
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEPATOCELLULAR ADENOMA																										
HEMANGIOMA																										
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
GALLBLADDER & COMMON BILE DUCT	N	+	+	N	N	+	N	N	N	N	N	+	+	N	N	+	+	N	+	+	+	N	+	N		
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOMA, NOS																										
PAPILLARY ADENOMA																										
RECTUM	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
FIBROSARCOMA																										
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ENDOCRINE SYSTEM																										
PITUITARY	+	+	-	+	+	+	+	+	+	-	-	+	-	-	+	+	+	-	+	+	-	+	-	+	-	
CARCINOMA, NOS																										
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
CORTICAL ADENOMA																										
CORTICAL CARCINOMA																										
PHEOCHROMOCYTOMA																										
THYROID	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
C-CELL ADENOMA	X																									
PARATHYROID	+	+	-	-	-	+	+	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ISLET-CELL ADENOMA																										
REPRODUCTIVE SYSTEM																										
MAMMARY 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	
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
PROSTATE	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
BODY CAVITIES																										
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
FIBROSARCOMA																										
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	
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE																										
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																										

+: TISSUE EXAMINED MICROSCOPICALLY  
 -: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY  
 X: TUMOR INCIDENCE  
 N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION  
 : NO TISSUE INFORMATION SUBMITTED  
 C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL  
 A: AUTOLYSIS  
 M: ANIMAL MISSING  
 B: NO NECROPSY PERFORMED





















**TABLE E5. MALE HAMSTERS: TUMOR PATHOLOGY (CONTINUED) IR CHRYSOTILE PLUS DMH**

ANIMAL NUMBER	27	27	27	28	28	28	29	29	30	30	30	31	31	31	32	32	32	33	33	33	34	34	34	35	35	35	
WEEKS ON STUDY	1	0	0	1	1	0	1	1	0	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
<b>INTEGUMENTARY SYSTEM</b>																											
SUBCUTANEOUS TISSUE FIBROSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>RESPIRATORY SYSTEM</b>																											
LUNGS AND BRONCHI UNDIFFERENTIATED CARCINOMA METAST	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>HEMATOPOIETIC SYSTEM</b>																											
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SPLEEN	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LYMPH NODES C-CELL CARCINOMA, METASTATIC FIBROSARCOMA, METASTATIC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
THYMUS	+	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<b>CIRCULATORY SYSTEM</b>																											
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>DIGESTIVE SYSTEM</b>																											
SALIVARY GLAND	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LIVER SARCOMA, NOS HEMANGIOMA HEMANGIOSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
PANCREAS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
STOMACH SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LARGE INTESTINE PAPILLOMA, NOS FIBROSARCOMA, METASTATIC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
RECTUM PAPILLARY ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>URINARY SYSTEM</b>																											
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>ENDOCRINE SYSTEM</b>																											
PITUITARY CARCINOMA, NOS ADENOMA, NOS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADRENAL CORTICAL ADENOMA CORTICAL CARCINOMA PHEOCHROMOCYTOMA PHEOCHROMOCYTOMA, MALIGNANT NEUROBLASTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
THYROID C-CELL ADENOMA C-CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
PARATHYROID ADENOMA, NOS	+	+	-	+	+	-	+	+	+	-	-	+	-	-	+	-	-	+	-	-	+	+	+	+	+	+	
PANCREATIC ISLETS ISLET-CELL ADENOMA ISLET-CELL CARCINOMA	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>REPRODUCTIVE SYSTEM</b>																											
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
EPIDIDYMIS ADENOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	

+: TISSUE EXAMINED MICROSCOPICALLY  
 -: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY  
 X: TUMOR INCIDENCE  
 N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION  
 : NO TISSUE INFORMATION SUBMITTED  
 C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL  
 A: AUTOLYSIS  
 M: ANIMAL MISSING  
 B: NO NECROPSY PERFORMED







**TABLE E5. MALE HAMSTERS: TUMOR PATHOLOGY (CONTINUED) IR CHRYSOTILE PLUS DMH**

ANIMAL NUMBER	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	5	5	5	5	5	5	5	5		
WEEKS ON STUDY	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	1	1	1	2	
<b>INTEGUMENTARY SYSTEM</b>																												
SUBCUTANEOUS TISSUE FIBROSARCOMA	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	N	+	+	+	+	N	+	+	
<b>RESPIRATORY SYSTEM</b>																												
LUNGS AND BRONCHI UNDIFFERENTIATED CARCINOMA METAST	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>HEMATOPOIETIC SYSTEM</b>																												
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LYMPH NODES C-CELL CARCINOMA, METASTATIC FIBROSARCOMA, METASTATIC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
THYMUS	+	+	+	-	-	+	+	-	-	+	+	+	+	+	+	-	+	+	-	+	-	-	-	-	-	-	+	
<b>CIRCULATORY SYSTEM</b>																												
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>DIGESTIVE SYSTEM</b>																												
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LIVER SARCOMA, NOS HEMANGIOMA HEMANGIOSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
STOMACH SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LARGE INTESTINE PAPILLOMA, NOS FIBROSARCOMA, METASTATIC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
RECTUM PAPILLARY ADENOMA	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	
<b>URINARY SYSTEM</b>																												
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>ENDOCRINE SYSTEM</b>																												
PITUITARY CARCINOMA, NOS ADENOMA, NOS	-	-	+	+	-	+	+	+	+	+	+	+	+	-	-	+	+	+	-	-	-	-	+	-	+	+	+	
ADRENAL CORTICAL ADENOMA CORTICAL CARCINOMA PHEOCHROMOCYTOMA PHEOCHROMOCYTOMA, MALIGNANT NEUROBLASTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
THYROID C-CELL ADENOMA C-CELL CARCINOMA	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	
PARATHYROID ADENOMA, NOS	+	+	+	-	-	+	+	-	-	+	+	-	-	+	+	+	+	+	-	+	+	-	+	+	-	+	+	
PANCREATIC ISLETS ISLET-CELL ADENOMA ISLET-CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>REPRODUCTIVE SYSTEM</b>																												
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
EPIDIDYMS ADENOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	

+: TISSUE EXAMINED MICROSCOPICALLY  
 -: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY  
 X: TUMOR INCIDENCE  
 N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION  
 I: NO TISSUE INFORMATION SUBMITTED  
 C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL  
 A: AUTOLYSIS  
 M: ANIMAL MISSING  
 B: NO NECROPSY PERFORMED

**TABLE E5. MALE HAMSTERS: TUMOR PATHOLOGY (CONTINUED) IR CHRYSOTILE PLUS DMH**

ANIMAL NUMBER	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	5	5	5	5	5	5	5	5	5
WEEKS ON STUDY	0	0	0	0	0	1	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1	1	1	0	0
NERVOUS SYSTEM																											
BRAIN SARCOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUSCULOSKELETAL SYSTEM																											
MUSCLE RHABDOMYOSARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
BODY CAVITIES																											
PERITONEUM FIBROSARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ALL OTHER SYSTEMS																											
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE																											
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																											

+: TISSUE EXAMINED MICROSCOPICALLY  
 -: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY  
 X: TUMOR INCIDENCE  
 N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION  
 : NO TISSUE INFORMATION SUBMITTED  
 C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL  
 A: AUTOLYSIS  
 M: ANIMAL MISSING  
 B: NO NECROPSY PERFORMED



**TABLE E5. MALE HAMSTERS: TUMOR PATHOLOGY (CONTINUED) IR CHRYSOTILE PLUS DMH**

ANIMAL NUMBER	522	523	524	525	526	527	528	529	530	531	532	533	534	535	536	537	538	539	540	541	542	543	544	545	546	547	548	549	550	551	552	553	554	555	556	557	558	559	560	561	562	563	564	565	566	567	568	569	570	571	572	573	574	575	576	577	578	579	580	581	582	583	584	585	586	587	588	589	590	591	592	593	594	595	596	597	598	599	600	601	602	603	604	605	606	607	608	609	610	611	612	613	614	615	616	617	618	619	620	621	622	623	624	625	626	627	628	629	630	631	632	633	634	635	636	637	638	639	640	641	642	643	644	645	646	647	648	649	650	651	652	653	654	655	656	657	658	659	660	661	662	663	664	665	666	667	668	669	670	671	672	673	674	675	676	677	678	679	680	681	682	683	684	685	686	687	688	689	690	691	692	693	694	695	696	697	698	699	700	701	702	703	704	705	706	707	708	709	710	711	712	713	714	715	716	717	718	719	720	721	722	723	724	725	726	727	728	729	730	731	732	733	734	735	736	737	738	739	740	741	742	743	744	745	746	747	748	749	750	751	752	753	754	755	756	757	758	759	760	761	762	763	764	765	766	767	768	769	770	771	772	773	774	775	776	777	778	779	780	781	782	783	784	785	786	787	788	789	790	791	792	793	794	795	796	797	798	799	800	801	802	803	804	805	806	807	808	809	810	811	812	813	814	815	816	817	818	819	820	821	822	823	824	825	826	827	828	829	830	831	832	833	834	835	836	837	838	839	840	841	842	843	844	845	846	847	848	849	850	851	852	853	854	855	856	857	858	859	860	861	862	863	864	865	866	867	868	869	870	871	872	873	874	875	876	877	878	879	880	881	882	883	884	885	886	887	888	889	890	891	892	893	894	895	896	897	898	899	900	901	902	903	904	905	906	907	908	909	910	911	912	913	914	915	916	917	918	919	920	921	922	923	924	925	926	927	928	929	930	931	932	933	934	935	936	937	938	939	940	941	942	943	944	945	946	947	948	949	950	951	952	953	954	955	956	957	958	959	960	961	962	963	964	965	966	967	968	969	970	971	972	973	974	975	976	977	978	979	980	981	982	983	984	985	986	987	988	989	990	991	992	993	994	995	996	997	998	999	1000	1001	1002	1003	1004	1005	1006	1007	1008	1009	1010	1011	1012	1013	1014	1015	1016	1017	1018	1019	1020	1021	1022	1023	1024	1025	1026	1027	1028	1029	1030	1031	1032	1033	1034	1035	1036	1037	1038	1039	1040	1041	1042	1043	1044	1045	1046	1047	1048	1049	1050	1051	1052	1053	1054	1055	1056	1057	1058	1059	1060	1061	1062	1063	1064	1065	1066	1067	1068	1069	1070	1071	1072	1073	1074	1075	1076	1077	1078	1079	1080	1081	1082	1083	1084	1085	1086	1087	1088	1089	1090	1091	1092	1093	1094	1095	1096	1097	1098	1099	1100	1101	1102	1103	1104	1105	1106	1107	1108	1109	1110	1111	1112	1113	1114	1115	1116	1117	1118	1119	1120	1121	1122	1123	1124	1125	1126	1127	1128	1129	1130	1131	1132	1133	1134	1135	1136	1137	1138	1139	1140	1141	1142	1143	1144	1145	1146	1147	1148	1149	1150	1151	1152	1153	1154	1155	1156	1157	1158	1159	1160	1161	1162	1163	1164	1165	1166	1167	1168	1169	1170	1171	1172	1173	1174	1175	1176	1177	1178	1179	1180	1181	1182	1183	1184	1185	1186	1187	1188	1189	1190	1191	1192	1193	1194	1195	1196	1197	1198	1199	1200	1201	1202	1203	1204	1205	1206	1207	1208	1209	1210	1211	1212	1213	1214	1215	1216	1217	1218	1219	1220	1221	1222	1223	1224	1225	1226	1227	1228	1229	1230	1231	1232	1233	1234	1235	1236	1237	1238	1239	1240	1241	1242	1243	1244	1245	1246	1247	1248	1249	1250	1251	1252	1253	1254	1255	1256	1257	1258	1259	1260	1261	1262	1263	1264	1265	1266	1267	1268	1269	1270	1271	1272	1273	1274	1275	1276	1277	1278	1279	1280	1281	1282	1283	1284	1285	1286	1287	1288	1289	1290	1291	1292	1293	1294	1295	1296	1297	1298	1299	1300	1301	1302	1303	1304	1305	1306	1307	1308	1309	1310	1311	1312	1313	1314	1315	1316	1317	1318	1319	1320	1321	1322	1323	1324	1325	1326	1327	1328	1329	1330	1331	1332	1333	1334	1335	1336	1337	1338	1339	1340	1341	1342	1343	1344	1345	1346	1347	1348	1349	1350	1351	1352	1353	1354	1355	1356	1357	1358	1359	1360	1361	1362	1363	1364	1365	1366	1367	1368	1369	1370	1371	1372	1373	1374	1375	1376	1377	1378	1379	1380	1381	1382	1383	1384	1385	1386	1387	1388	1389	1390	1391	1392	1393	1394	1395	1396	1397	1398	1399	1400	1401	1402	1403	1404	1405	1406	1407	1408	1409	1410	1411	1412	1413	1414	1415	1416	1417	1418	1419	1420	1421	1422	1423	1424	1425	1426	1427	1428	1429	1430	1431	1432	1433	1434	1435	1436	1437	1438	1439	1440	1441	1442	1443	1444	1445	1446	1447	1448	1449	1450	1451	1452	1453	1454	1455	1456	1457	1458	1459	1460	1461	1462	1463	1464	1465	1466	1467	1468	1469	1470	1471	1472	1473	1474	1475	1476	1477	1478	1479	1480	1481	1482	1483	1484	1485	1486	1487	1488	1489	1490	1491	1492	1493	1494	1495	1496	1497	1498	1499	1500	1501	1502	1503	1504	1505	1506	1507	1508	1509	1510	1511	1512	1513	1514	1515	1516	1517	1518	1519	1520	1521	1522	1523	1524	1525	1526	1527	1528	1529	1530	1531	1532	1533	1534	1535	1536	1537	1538	1539	1540	1541	1542	1543	1544	1545	1546	1547	1548	1549	1550	1551	1552	1553	1554	1555	1556	1557	1558	1559	1560	1561	1562	1563	1564	1565	1566	1567	1568	1569	1570	1571	1572	1573	1574	1575	1576	1577	1578	1579	1580	1581	1582	1583	1584	1585	1586	1587	1588	1589	1590	1591	1592	1593	1594	1595	1596	1597	1598	1599	1600	1601	1602	1603	1604	1605	1606	1607	1608	1609	1610	1611	1612	1613	1614	1615	1616	1617	1618	1619	1620	1621	1622	1623	1624	1625	1626	1627	1628	1629	1630	1631	1632	1633	1634	1635	1636	1637	1638	1639	1640	1641	1642	1643	1644	1645	1646	1647	1648	1649	1650	1651	1652	1653	1654	1655	1656	1657	1658	1659	1660	1661	1662	1663	1664	1665	1666	1667	1668	1669	1670	1671	1672	1673	1674	1675	1676	1677	1678	1679	1680	1681	1682	1683	1684	1685	1686	1687	1688	1689	1690	1691	1692	1693	1694	1695	1696	1697	1698	1699	1700	1701	1702	1703	1704	1705	1706	1707	1708	1709	1710	1711	1712	1713	1714	1715	1716	1717	1718	1719	1720	1721	1722	1723	1724	1725	1726	1727	1728	1729	1730	1731	1732	1733	1734	1735	1736	1737	1738	1739	1740	1741	1742	1743	1744	1745	1746	1747	1748	1749	1750	1751	1752	1753	1754	1755	1756	1757	1758	1759	1760	1761	1762	1763	1764	1765	1766	1767	1768	1769	1770	1771	1772	1773	1774	1775	1776	1777	1778	1779	1780	1781	1782	1783	1784	1785	1786	1787	1788	1789	1790	1791	1792	1793	1794	1795	1796	1797	1798	1799	1800	1801	1802	1803	1804	1805	1806	1807	1808	1809	1810	1811	1812	1813	1814	1815	1816	1817	1818	1819	1820	1821	1822	1823	1824	1825	1826	1827	1828	1829	1830	1831	1832	1833	1834	1835	1836	1837	1838	1839	1840	1841	1842	1843	1844	1845	1846	1847	1848	1849	1850	1851	1852	1853	1854	1855	1856	1857	1858	1859	1860	1861	1862	1863	1864	1865	1866	1867	1868	1869	1870	1871	1872	1873	1874	1875	1876	1877	1878	1879	1880	1881	1882	1883	1884	1885	1886	1887	1888	1889	1890	1891	1892	1893	1894	1895	1896	1897	1898	1899	1900	1901	1902	1903	1904	1905	1906	1907	1908	1909	1910	1911	1912	1913	1914	1915	1916	1917	1918	1919	1920	1921	1922	1923	1924	1925	1926	1927	1928	1929	1930	1931	1932	1933	1934	1935	1936	193
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**TABLE E6. FEMALE HAMSTERS: TUMOR PATHOLOGY (CONTINUED) CONTROL**

ANIMAL NUMBER	322	323	331	332	333	351	352	353	354	355	361	362	363	371	372	373	391	392	393	411	412	413	421	422	423	431	432	433	
WEEKS ON STUDY	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
RESPIRATORY SYSTEM																													
LUNGS AND BRONCHI	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
TRACHEA	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMATOPOIETIC SYSTEM																													
BONE MARROW	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	A	
SPLEEN	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LYMPH NODES	A	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
THYMUS	A	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	+	A	
CIRCULATORY SYSTEM																													
HEART	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	
DIGESTIVE SYSTEM																													
SALIVARY GLAND	A	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	A	
LIVER	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	
BILE DUCT PAPILLOMA, NOS	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	A	
GALLBLADDER & COMMON BILE DUCT	A	N	N	N	N	N	N	N	N	N	N	N	N	+	+	N	N	N	N	N	N	N	N	N	N	N	N	A	
PANCREAS	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	
ESOPHAGUS	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	
STOMACH	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	
SMALL INTESTINE	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	
LARGE INTESTINE LIPOMA	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	A	
URINARY SYSTEM																													
KIDNEY	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	
URINARY BLADDER	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	
ENDOCRINE SYSTEM																													
PITUITARY	A	-	-	+	+	-	+	+	-	+	-	+	+	+	+	+	+	+	+	+	-	+	+	-	-	-	-	A	
ADRENAL CORTICAL ADENOMA	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	
THYROID C-CELL CARCINOMA	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+	+	A	
PARATHYROID ADENOMA, NOS	A	-	+	+	-	-	+	-	-	+	-	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	A	
PANCREATIC ISLETS ISLET-CELL ADENOMA	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+	+	A	
REPRODUCTIVE SYSTEM																													
MAMMARY GLAND	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	
UTERUS PAPILLARY ADENOMA CYSTADENOMA, NOS	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	A	
OVARY	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	
ALL OTHER SYSTEMS																													
MULTIPLE ORGANS NOS HEMANGIOSARCOMA MALIG. LYMPHOMA, LYMPHOCYTIC TYPE LEUKEMIA, NOS	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	

+: TISSUE EXAMINED MICROSCOPICALLY  
 -: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY  
 X: TUMOR INCIDENCE  
 N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION  
 I: NO TISSUE INFORMATION SUBMITTED  
 C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL  
 A: AUTOLYSIS  
 M: ANIMAL MISSING  
 B: NO NECROPSY PERFORMED



TABLE E6.

**INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE HAMSTERS ADMINISTERED 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (DMH) BY GAVAGE WITH AND WITHOUT INTERMEDIATE RANGE CHRYSOTILE ASBESTOS IN THE DIET**

**DMH**

ANIMAL NUMBER	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	
WEEKS ON STUDY	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25		
<b>INTEGUMENTARY SYSTEM</b>																											
SUBCUTANEOUS TISSUE FIBROSARCOMA	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	N	+	
<b>RESPIRATORY SYSTEM</b>																											
LUNGS AND BRONCHI SARCOMA, NOS, METASTATIC FIBROSARCOMA, METASTATIC OLIGODENDROGLIOMA, METASTAT.	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>HEMATOPOIETIC SYSTEM</b>																											
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	
SPLEEN FIBROSARCOMA, METASTATIC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LYMPH NODES MALIG. LYMPHOMA, HISTIOCYTIC TYPE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	
<b>CIRCULATORY SYSTEM</b>																											
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>DIGESTIVE SYSTEM</b>																											
SALIVARY GLAND	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
GALLBLADDER & COMMON BILE DUCT	+	N	N	N	+	N	N	+	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LARGE INTESTINE ADENOMATOUS POLYP, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
RECTUM SQUAMOUS CELL CARCINOMA	N	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>URINARY SYSTEM</b>																											
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
URINARY BLADDER	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	
<b>ENDOCRINE SYSTEM</b>																											
PITUITARY OLIGODENDROGLIOMA, METASTAT.	-	-	-	-	+	-	+	+	-	+	-	-	+	-	-	+	-	-	+	-	-	+	-	-	+	+	
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	
PARATHYROID ADENOMA, NOS	+	-	+	+	+	+	+	-	-	-	-	-	+	+	-	+	-	-	+	-	-	+	-	-	+	-	
PANCREATIC ISLETS ISLET-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>REPRODUCTIVE SYSTEM</b>																											
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
UTERUS ADENOCARCINOMA, NOS ENDOMETRIAL STROMAL POLYP	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
OVARY	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	
<b>NERVOUS SYSTEM</b>																											
BRAIN OLIGODENDROGLIOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<b>SPECIAL SENSE ORGANS</b>																											
EYE APPENDAGES SARCOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
<b>ALL OTHER SYSTEMS</b>																											
MULTIPLE ORGANS NOS MALIG. LYMPHOMA, LYMPHOCYTIC TYPE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	

+: TISSUE EXAMINED MICROSCOPICALLY  
 -: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY  
 X: TUMOR INCIDENCE  
 N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION  
 : NO TISSUE INFORMATION SUBMITTED  
 C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL  
 A: AUTOLYSIS  
 M: ANIMAL MISSING  
 B: NO NECROPSY PERFORMED



















**TABLE E6. FEMALE HAMSTERS: TUMOR PATHOLOGY (CONTINUED) IR CHRYSOTILE PLUS DMH**

ANIMAL NUMBER	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	5	5	5	5	5	5	5	5	5	5	
WEEKS ON STUDY	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9	9	9	2	3	9	6	0	0	1	7	0	0	2	4	0	7	6	9	4	4	6	2	2	4	1	
<b>RESPIRATORY SYSTEM</b>																											
LUNGS AND BRONCHI UNDIFFERENTIATED CARCINOMA METAST ALVEOLAR/BRONCHIOLAR CARCINOMA SARCOMA, NOS, METASTATIC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A -	
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A -	
<b>HEMATOPOIETIC SYSTEM</b>																											
BONE MARROW	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A +	
SPLEEN HEMANGIOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A +	
LYMPH NODES UNDIFFERENTIATED CARCINOMA METAST SARCOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A +	
THYMUS	-	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	-	-	+	+	+	-	+	+	+	A -	
<b>CIRCULATORY SYSTEM</b>																											
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A -	
<b>DIGESTIVE SYSTEM</b>																											
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A -	
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A +	
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A +	
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A N	
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A -	
<b>ESOPHAGUS</b>																											
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A +	
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A +	
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A +	
<b>URINARY SYSTEM</b>																											
KIDNEY UNDIFFERENTIATED CARCINOMA METAST	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A +	
URINARY BLADDER	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	A -	
<b>ENDOCRINE SYSTEM</b>																											
PITUITARY	-	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	A -	
ADRENAL CORTICAL ADENOMA CORTICAL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A -	
THYROID	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A -	
PARATHYROID	-	+	+	+	+	-	-	+	-	+	+	+	+	-	-	-	-	-	-	-	-	-	-	-	-	A -	
PANCREATIC ISLETS ISLET-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A -	
<b>REPRODUCTIVE SYSTEM</b>																											
MAMMARY 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	A N	
VAGINA PAPILLOMA, 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	A N	
UTERUS FIBROMA LEIOMYOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	A -	
OVARY	+	+	+	+	+	+	-	-	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	A -	
<b>ALL OTHER SYSTEMS</b>																											
MULTIPLE ORGANS NOS MALIG. LYMPHOMA, LYMPHOCYTIC TYPE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A N	

+: TISSUE EXAMINED MICROSCOPICALLY  
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 B: NO NECROPSY PERFORMED

