

NATIONAL TOXICOLOGY PROGRAM
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No. 295



TOXICOLOGY AND CARCINOGENESIS

STUDIES OF

CHRYBOTILE ASBESTOS

(CAS NO. 12001-29-5)

IN F344/N RATS

(FEED STUDIES)

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

NATIONAL TOXICOLOGY PROGRAM

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

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

NTP TECHNICAL REPORT
ON THE
TOXICOLOGY AND CARCINOGENESIS
STUDIES OF
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NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 27709

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NOTE TO THE READER

These studies are designed and conducted to characterize and evaluate the toxicologic potential, including carcinogenic activity, of selected chemicals in laboratory animals (usually two species, rats and mice). 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.

Five categories of interpretative conclusions were adopted for use in June 1983 in the Technical Reports series to specifically emphasize consistency and the concept of actual evidence of carcinogenicity. For each definitive study result (male rats, female rats, male mice, female mice), one of the following quintet will be selected to describe the findings. These categories refer to the strength of the experimental evidence and not to either potency or mechanism.

- **Clear Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing a chemically related increased incidence of malignant neoplasms, studies that exhibit a substantially increased incidence of benign neoplasms, or studies that exhibit an increased incidence of a combination of malignant and benign neoplasms where each increases with dose.
- **Some Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing a chemically related increased incidence of benign neoplasms, studies that exhibit marginal increases in neoplasms of several organs/tissues, or studies that exhibit a slight increase in uncommon malignant or benign neoplasms.
- **Equivocal Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing a chemically related marginal increase of neoplasms.
- **No Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing no chemically related increases in malignant or benign neoplasms.
- **Inadequate Study of Carcinogenicity** demonstrates that because of major qualitative or quantitative limitations, the studies cannot be interpreted as valid for showing either the presence or absence of a carcinogenic effect.

Additionally, the following concepts (as patterned from the International Agency for Research on Cancer Monographs) have been adopted by the NTP to give further clarification of these issues:

The term *chemical carcinogenesis* generally means the induction by chemicals of neoplasms not usually observed, the earlier induction by chemicals of neoplasms that are commonly observed, or the induction by chemicals of more neoplasms than are generally found. Different mechanisms may be involved in these situations. Etymologically, the term *carcinogenesis* means induction of cancer, that is, of malignant neoplasms; however, the commonly accepted meaning is the induction of various types of neoplasms or of a combination of malignant and benign neoplasms. In the Technical Reports, the words *tumor* and *neoplasm* are used interchangeably.

This study was conducted under contract to the National Institute of Environmental Health Sciences, National Toxicology Program. The studies described in this Technical Report have been conducted in compliance with NTP chemical health and safety requirements and must meet or exceed all applicable Federal, state, and local health and safety regulations. All NTP toxicology and carcinogenesis studies are subjected to a data audit before being presented for peer review.

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

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CONTENTS

	PAGE
ABSTRACT	12
CONTRIBUTORS	14
PEER REVIEW PANEL	16
SUMMARY OF PEER REVIEW COMMENTS	17
I. INTRODUCTION	19
II. MATERIALS AND METHODS	23
PROCUREMENT AND CHARACTERIZATION OF TEST MATERIALS	24
PREPARATION OF FORMULATED DIETS AND DOSE MIXTURES	24
FORMULATED DIETS	24
DOSE MIXTURES OF ASBESTOS FOR GAVAGE ADMINISTRATION	26
DOSE MIXTURES OF 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE FOR GAVAGE ADMINISTRATION	26
LIFETIME STUDIES OF SHORT-RANGE OR INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	26
STUDY DESIGN	26
SOURCE AND SPECIFICATIONS OF TEST ANIMALS	26
ANIMAL MAINTENANCE	27
SAFETY PRECAUTIONS	27
CLINICAL EXAMINATIONS AND PATHOLOGY	27
STATISTICAL METHODS	31
III. RESULTS	33
LIFETIME STUDIES OF SHORT-RANGE OR INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	34
ESTABLISHMENT OF TEST GROUPS	34
BODY WEIGHTS AND FEED CONSUMPTION	34
PATHOGEN BURDEN	34
CLINICAL SIGNS	39
SURVIVAL	40
PATHOLOGY AND STATISTICAL ANALYSES OF RESULTS	44
IV. DISCUSSION AND CONCLUSIONS	55
V. REFERENCES	61

TABLES

		PAGE
TABLE 1	FIBER CHARACTERISTICS AND CHEMICAL-INSTRUMENTAL ANALYSES OF CHRYSOTILE ASBESTOS	25
TABLE 2	SUMMARY OF DISTRIBUTION OF RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	26
TABLE 3	EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE AND INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	29
TABLE 4	MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS	35
TABLE 5	MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	37
TABLE 6	SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS	40
TABLE 7	SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS AT VARIOUS TIME POINTS	40
TABLE 8	SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	42
TABLE 9	SURVIVAL OF RATS IN THE LIFETIME STUDIES OF 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE WITH AND WITHOUT INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS IN THE FEED	42
TABLE 10	SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS AT VARIOUS TIME POINTS	44
TABLE 11	ALIMENTARY TRACT TUMORS IN RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS	46
TABLE 12	INCIDENCE OF NONNEOPLASTIC LESIONS IN THE ALIMENTARY TRACT OF RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS	47
TABLE 13	ALIMENTARY TRACT TUMORS IN RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	48

TABLES (Continued)

	PAGE
TABLE 14 INCIDENCE OF NONNEOPLASTIC LESIONS IN THE ALIMENTARY TRACT OF RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	49
TABLE 15 ANALYSIS OF INTEGUMENTARY SYSTEM TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	50
TABLE 16 ANALYSIS OF CLITORAL GLAND TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	50
TABLE 17 SUMMARY OF GASTROINTESTINAL TUMORS IN RATS ADMINISTERED 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE WITH AND WITHOUT INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	52
TABLE 18 SUMMARY OF NONGASTROINTESTINAL TUMORS IN RATS ADMINISTERED 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE WITH AND WITHOUT INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	53
TABLE 19 ANALYSIS OF KIDNEY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS WITH 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE	53
TABLE 20 ANALYSIS OF THYROID GLAND TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS WITH 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE	54

FIGURES

	PAGE
FIGURE 1 SCHEDULE OF MAJOR EVENTS IN RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	28
FIGURE 2 GROWTH CURVES FOR RATS FED DIETS CONTAINING SHORT-RANGE CHRYSOTILE ASBESTOS IN LIFETIME STUDIES	36
FIGURE 3 GROWTH CURVES FOR RATS FED DIETS CONTAINING INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS WITH AND WITHOUT 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE IN LIFETIME STUDIES	38
FIGURE 4 KAPLAN-MEIER SURVIVAL CURVES FOR RATS FED DIETS CONTAINING SHORT-RANGE CHRYSOTILE ASBESTOS IN LIFETIME STUDIES	41
FIGURE 5 KAPLAN-MEIER SURVIVAL CURVES FOR RATS FED DIETS CONTAINING INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS WITH AND WITHOUT 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE IN LIFETIME STUDIES	43

APPENDIXES

	PAGE
APPENDIX A	SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS 67
TABLE A1	SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS 68
TABLE A2	SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS 73
TABLE A3	INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS 78
TABLE A4	INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS 106
APPENDIX B	SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS 135
TABLE B1	SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS ... 136
TABLE B2	SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS ... 145
TABLE B3	INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFE- TIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS 152
TABLE B4	INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFE- TIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS 212
APPENDIX C	SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS ... 273
TABLE C1	SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS ... 274
TABLE C2	SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS 282

APPENDIXES (Continued)

		PAGE
APPENDIX D	SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	289
TABLE D1	SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	290
TABLE D2	SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	303
APPENDIX E	ANALYSES OF PRIMARY TUMORS IN RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE AND INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS AND INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE	313
TABLE E1	ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS	314
TABLE E2	ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS	318
TABLE E3	ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	321
TABLE E4	ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	326
TABLE E5	ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE	329
TABLE E6	ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE	334
APPENDIX F	INCIDENCES OF TUMORS IN F344/N RATS RECEIVING NO TREATMENT IN CONTEMPORARY LIFETIME ASBESTOS STUDIES	339
TABLE F1	INCIDENCE OF EPITHELIAL TUMORS OF THE LARGE INTESTINE IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES	340

APPENDIXES (Continued)

	PAGE
TABLE F2 INCIDENCE OF INTEGUMENTARY SYSTEM KERATOACANTHOMAS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES	340
TABLE F3 INCIDENCE OF CLITORAL GLAND TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES	341
TABLE F4 INCIDENCE OF ADRENAL GLAND TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES	341
TABLE F5 INCIDENCE OF MESOTHELIOMAS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES	341
APPENDIX G ANALYSIS OF FORMULATED DIETS AND DOSE MIXTURES	343
TABLE G1 ANALYSIS OF FORMULATED DIETS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS	345
TABLE G2 ANALYSIS OF FORMULATED DIETS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	346
TABLE G3 ANALYSIS OF DOSE MIXTURES OF 1,2-DIMETHYLHYDRAZINE DIHYDRO-CHLORIDE IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	348
APPENDIX H FEED AND COMPOUND CONSUMPTION BY RATS IN THE LIFETIME FEED STUDIES OF CHRYSOTILE ASBESTOS	349
TABLE H1 FEED AND COMPOUND CONSUMPTION BY MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS	350
TABLE H2 FEED AND COMPOUND CONSUMPTION BY FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS	351
TABLE H3 FEED AND COMPOUND CONSUMPTION BY MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	352
TABLE H4 FEED AND COMPOUND CONSUMPTION BY FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	353
TABLE H5 FEED AND COMPOUND CONSUMPTION BY MALE RATS RECEIVING DMH WITH AND WITHOUT INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS ...	354

APPENDIXES (Continued)

	PAGE
TABLE H6	FEED AND COMPOUND CONSUMPTION BY FEMALE RATS RECEIVING DMH WITH AND WITHOUT INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS .. 355
APPENDIX I	PATHOGEN BURDEN IN RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS 357
TABLE I1	INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F₀ RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS 359
TABLE I2	MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F₀ RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS 360
TABLE I3	MURINE VIRUS ANTIBODY DETERMINATION IN F₀ RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS 361
TABLE I4	INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F₁ RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS 363
TABLE I5	MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F₁ RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS 364
APPENDIX J	PATHOGEN BURDEN IN RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS 365
TABLE J1	INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F₀ RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS 368
TABLE J2	MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F₀ RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS 369
TABLE J3	MURINE VIRUS ANTIBODY DETERMINATION IN F₁ RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS 371
TABLE J4	INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F₁ RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS 372
TABLE J5	MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F₁ RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS 373

APPENDIXES (Continued)

		PAGE
APPENDIX K	CLINICAL SIGNS IN RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS	375
TABLE K1	SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS: UNTREATED CONTROL	376
TABLE K2	SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE	377
APPENDIX L	CLINICAL SIGNS IN RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS	379
TABLE L1	SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: UNTREATED CONTROL	380
TABLE L2	SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: DMH	381
TABLE L3	SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE	383
TABLE L4	SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: IR + DMH	385
TABLE L5	SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: IR/PW	387
APPENDIX M	DATA AUDIT SUMMARY	389

ABSTRACT

Lifetime toxicology and carcinogenesis studies of short-range (SR) and intermediate-range (IR) fiber length chrysotile asbestos were conducted in groups of 88-250 male and female F344/N rats. Both forms of asbestos were administered at a concentration of 1% in pelleted diet for the lifetime of the rats, starting with the dams of the test animals. Subgroups of 100 male and 100 female IR chrysotile-exposed rats also received 0.47 mg/g IR chrysotile asbestos in water by gavage during lactation (preweaning [PW]). At 9 weeks of age, additional subgroups (125-175) of control and IR chrysotile-exposed rats received 7.5 mg/kg (male) or 15 mg/kg (female) 1,2-dimethylhydrazine dihydrochloride (DMH) by gavage every other week for a total of five doses. When the survival of either the control or test group reached 10%, both groups were killed.

Neither type of fiber affected fertility or litter size. The offspring from mothers exposed to SR chrysotile were similar in body weight to the controls at birth and remained so throughout their lives. The offspring of IR chrysotile-exposed mothers were similar in weight at birth but were slightly smaller (13%) at weaning and remained so throughout their lives, with the exception of those in the IR/PW chrysotile group, which weighed slightly more during their lifetimes. Feed consumption and survival were comparable among the SR and IR chrysotile asbestos groups and controls. The DMH-exposed groups showed decreased survival due primarily to the development of lethal neoplasms.

The administration of SR chrysotile for the lifetime of exposed male and female rats did not cause any overt toxicity. In addition, no neoplastic or nonneoplastic disease was associated with SR chrysotile exposure.

Male and female rats exposed to IR chrysotile asbestos did not show any adverse clinical signs. Benign epithelial neoplasms (adenomatous polyps) were observed in the large intestine of IR chrysotile asbestos male rats (9/250, 3.6%). Although not statistically significant ($P=0.08$) compared with concurrent controls (0/85), the incidence of these neoplasms was highly significant ($P=0.003$) when compared with the incidence of epithelial neoplasms (benign and malignant combined) of the large intestine in the pooled male control groups of all the NTP oral asbestos lifetime studies (3/524, 0.6%). The biologic importance of this finding was supported by the observation of lesions of similar morphology in the small intestine or glandular stomach of four additional IR chrysotile male rats and by a low incidence (2/100, 2.0%) of adenomatous polyps in the large intestine of male rats in the IR/PW group.

A significant ($P<0.05$) increase in keratoacanthomas of the skin was observed in male IR (19/250, 7.6%) and IR/PW (8/100, 8.0%) chrysotile-exposed rats compared with the concurrent controls (1/88, 1.1%). The biologic importance of this observation was discounted because the incidence in these groups did not greatly exceed the rate observed in the combined male control groups from all the other NTP oral asbestos studies (19/441, 4.3%). An apparent increase in the incidence of clitoral gland neoplasms in female IR (18/250, 7.2%) and IR/PW (4/100, 4.0%) chrysotile-exposed rats compared with that in the concurrent controls (1/88, 1.1%) was also discounted because of a lack of statistical significance when compared with the pooled female control groups from the other NTP oral asbestos studies (21/441, 4.8%).

Rats exposed to DMH and DMH plus IR chrysotile asbestos exhibited neoplasia in those organs known to be targets for DMH (gastrointestinal tract, Zymbal gland, liver, and kidney). There was a significant difference ($P<0.05$) in the incidence of DMH-induced mixed-cell tumors of the kidney between the DMH alone (13/125, 10%) and DMH plus IR chrysotile asbestos (34/175, 19%) female groups. An increased incidence of thyroid follicular cell tumors was observed in DMH plus IR chrysotile male rats (28/175, 16.0%) compared with the DMH alone group (9/124, 7.3%). The biologic importance of both observations is questionable, since neither organ represents a primary target organ for

asbestos and no difference between DMH and DMH plus IR chrysotile was observed for the primary target organs (intestine and mesothelium).

An audit of the experimental data was conducted for these lifetime carcinogenesis studies of chrysotile asbestos. No data discrepancies were found that influenced the final interpretations.

Under the conditions of these lifetime studies, short-range and intermediate-range chrysotile asbestos did not induce overt toxicity and did not affect survival when ingested at a level of 1% in the diet by male and female F344/N rats. There was *no evidence of carcinogenicity** in male or female rats exposed to SR chrysotile asbestos or in female rats exposed to IR chrysotile asbestos. There was *some evidence of carcinogenicity* in male rats exposed to IR chrysotile asbestos as indicated by an increased incidence of adenomatous polyps in the large intestine. The cocarcinogenesis studies of 1,2-dimethylhydrazine dihydrochloride and IR chrysotile asbestos were considered inconclusive for determining whether IR chrysotile asbestos had either a tumor-enhancing or protective effect, although an increased incidence of neoplasms was observed in the kidneys of female rats exposed to DMH plus IR chrysotile as compared with those exposed to DMH alone.

*Categories of evidence of carcinogenicity are defined in the Note to the Reader on page 2.

CONTRIBUTORS

The NTP Technical Report on the Toxicology and Carcinogenesis Studies of Chrysotile Asbestos is based on the lifetime studies that began in October 1977 and ended in May 1980 at Hazleton Laboratories America, Inc.

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PEER REVIEW PANEL

The members of the Peer Review Panel who evaluated the draft Technical Report on chrysotile asbestos on July 27, 1984, are listed below. Panel members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, Panel members have five major responsibilities: (a) to ascertain that all relevant literature data have been adequately cited and interpreted, (b) to determine if the design and conditions of the NTP studies were appropriate, (c) to ensure that the Technical Report presents the experimental results and conclusions fully and clearly, (d) to judge the significance of the experimental results by scientific criteria, and (e) to assess the evaluation of the evidence of carcinogenicity and other observed toxic responses.

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

On July 27, 1984, the draft Technical Report on the toxicology and carcinogenesis studies of chrysotile asbestos received peer review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The review meeting began at 9:00 a.m. in the Conference Center, Building 101, South Campus, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.

Dr. Jones, a principal reviewer, agreed with the conclusions as written. Dr. Jones agreed also with the decision to discount the biologic significance of the increased incidences of keratoacanthomas in males and neoplasms of the clitoral gland in females but asked that the reasons for this decision be discussed in greater depth. He noted that prior to the meeting he had examined the slides of large intestine sections from male rats exposed to the IR form and agreed that the adenomatous polyps were clearly neoplastic.

Dr. Turnbull, a second principal reviewer, also agreed with the conclusions. He suggested, however, that more details be given regarding the choice of a 1% dose and the relation of this dose to the maximum tolerated dose, if any. Dr. R. Shapiro, NIEHS, said the 1% level represented an appropriate dose based on earlier feed studies in rats and was much greater than the estimated dose to which humans are exposed. Dr. Turnbull asked for clarification of the use and temporal relationship of the various control groups. Dr. E. McConnell, NTP, explained that the rats used for concurrent controls in this study and those used for pooled control groups in the three previous NTP dosed feed studies of the other asbestos fiber types came from the same animal source, were used in studies conducted at the same laboratory, and were on test at approximately the same times. Dr. J. Haseman, NIEHS, said the concurrent controls were used in the primary statistical analysis. When a possible carcinogenic effect was observed, the additional control groups were employed to help evaluate further the biologic significance of the effect.

A third principal reviewer, Dr. Davis, questioned the use of the pooled control data to support the biologic importance and statistical significance of the intestinal tumors and, on the other hand, to discount the importance of the keratoacanthomas in male rats and clitoral gland neoplasms in female rats. Dr. McConnell stated that no increases in incidences of skin neoplasms have been observed in asbestos inhalation studies sponsored by the NTP or by others in which the whole animal was exposed. Dr. Friess said the reason for discounting needed to be highlighted nonetheless. Dr. Davis asked if the standard paper feed bags were impermeable to the pelleted asbestos and if the pelleting process may have altered the fiber size of the asbestos. Mr. Beliczky wondered whether there may have been incidental inhalation exposure of the test animals. Dr. McConnell replied that a pelleted dose form was used to minimize exposure of laboratory personnel and the amount of exposure by inhalation. Dr. Shapiro noted that fiber size distribution for all the fiber types was examined before and after pelleting, and few or no differences were found.

Dr. Kotelchuck observed that the apparent kidney-tumor-enhancing effect of IR asbestos in female rats dosed with dimethylhydrazine dihydrochloride should be noted in the conclusions. Dr. McConnell agreed. Dr. A. Berlin, Commission of the European Communities, asked if there had been any attempt to measure asbestos at the tumor sites. Dr. McConnell replied that since this was a lifetime exposure, the presence of fibers throughout the intestine would be expected, and further, translocation artifacts would likely confound such an analysis.

Dr. Jones moved that the Technical Report on the toxicology and carcinogenesis studies of chrysotile asbestos be accepted with the modifications as discussed. Dr. Turnbull seconded the motion and the report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION

I. INTRODUCTION

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 (Bureau of Mines, 1980).

Studies conducted during the past 25 years have established a clear association between occupational exposure to asbestos and increased risk of cancer. Human studies have shown that increased tumor risk is associated with crocidolite, chrysotile, amosite, and anthophyllite exposure. Crocidolite asbestos is considered the most "dangerous" form of asbestos in humans because of its strong association with mesothelioma (Craighead, 1982). Excellent reviews of the carcinogenic and public health effects associated with inhaled asbestos are those by Selikoff (1980) and Selikoff and Hammond (1979) and those published by the U.S. Environmental Protection Agency (USEPA, 1980), the International Agency for Research on Cancer (IARC, 1977), and Environmental Health Perspectives (EHP, 1983). Lung cancer and mesothelioma are the neoplasms most frequently observed in humans exposed to asbestos. A modest increase in the incidence of gastrointestinal tumors has been observed in asbestos insulation workers, miners, and factory workers. The increased incidence of gastrointestinal cancer and possible peritoneal mesothelioma in occupationally exposed populations may be the consequence of direct fiber ingestion or ingestion of inhaled fibers that were cleared from the nasal or tracheobronchial portions of the respiratory system by mucociliary processes.

Large portions of the population ingest chrysotile asbestos through consumption of food and water (Rowe, 1983). Analysis of water samples from 359 cities found that 65% of the samples had detectable levels of various types of asbestos, including chrysotile (Millette et al., 1983). The water supplies of 41 cities have had asbestos concentrations in water which exceeded

10 million fibers per liter, but the length of the vast majority of fibers is under 5 μm . Asbestos or asbestos-like fibers may enter water supplies as a result of mining (e.g., operations at Lake Superior). Natural serpentine or amphibole deposits have been detected in watersheds (Seattle, Washington, and San Francisco, California); under certain conditions, the presence of asbestos may have resulted from the use of chrysotile asbestos-cement pipe for municipal water supplies (USEPA, 1980). In the latter instance, erosion of the pipe (and release of fibers) is associated with the "aggressiveness" of the water, a term representing a mathematical expression of alkalinity and calcium content. Approximately 69% of the water systems in the United States have aggressive water that has the potential to erode asbestos-cement pipe (USEPA, 1980).

The health effects of ingested asbestos have been reviewed recently (EHP, 1983). 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. Statistically significant trends for the incidence of several cancer types, including stomach, gallbladder, esophageal, and peritoneal cancer, were found when census tracts were analyzed on a gradient of low to high asbestos content in municipal water in the San Francisco Bay area (Cooper et al., 1979). The association between asbestos concentration in San Francisco Bay area drinking water and cancer was confirmed in subsequent studies (Kanarek, 1983; Conforti, 1983). The presence of chrysotile asbestos in the drinking water (200×10^6 fibers/liter) was not clearly associated with an increased cancer risk in the Everett, Washington area (Polissar et al., 1983).

Beer and wine have in the past contained asbestos, possibly from asbestos filters used in the preparation of these products (Cunningham and Pontefract, 1971). According to one hypothesis, the ingestion of rice treated with talc that contains chrysotile asbestos is associated with an increased incidence of stomach cancer in Japan (Merliss, 1971a,b).

Studies of the migration of asbestos fibers through the gastrointestinal mucosa have been

confounded by asbestos contamination from water during tissue section preparation; contamination from the gut lumen, blood plasma, or lymph fluid; or contamination from filters used for sample preparation (Meek, 1983). Several studies have provided evidence that ingestion of asbestos in either food or water can result in the migration of asbestos through the gastrointestinal mucosa. Chrysotile asbestos has been reported in the urine of humans and in the lymph fluid and kidney cortex of rats (Patel-Mandlik and Millette, 1983) and baboons (Patel-Mandlik and Millette, 1980) exposed by ingestion or gavage. The amounts of chrysotile detected accounted for only 10^{-4} to 10^{-7} of the amount ingested (Cook, 1983; Sebastien et al., 1980).

Inhalation of asbestos by laboratory animals produces 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. These studies have been reviewed by Levine (1978).

Stanton et al. (1981) in their classic intrapleural inoculation studies have clearly shown that the carcinogenic potential of various types of natural and manmade fibers are related to their length and width and the ratio thereof (aspect ratio). They determined that the more carcinogenic fibers were greater than 8 μm in length and less than 1.5 μm in diameter.

Asbestos (chrysotile, amosite, and crocidolite) has been shown to be cytotoxic in vitro to human embryonic intestinal cells, mouse epithelial-like colon-derived cells, and rat liver epithelial cells (Reiss et al., 1979). Chrysotile asbestos was far more toxic than the amphibole fibers, and the effects were more pronounced in the intestine-derived cells than in those from the liver. Asbestos also was found to be cytotoxic to Syrian hamster (Bey and Harrington, 1971) and mouse (Wright et al., 1983) peritoneal macrophages and to rabbit alveolar macrophages (Desai and Richards, 1983).

Chrysotile asbestos was not mutagenic in *Salmonella typhimurium* or *Escherichia coli* (Chamberlain and Tarmy, 1977) or at the

HGPRT locus in mammalian cells (Reiss et al., 1982; Oshimura et al., 1984). However, Huang et al. (1978) reported a weak but statistically significant increase in mutation frequency at the HGPRT locus in V79 cells if the results of several experiments were combined. Although chrysotile asbestos does not appear to cause gene mutations, it has been shown to cause chromosomal aberrations and alterations in the number of chromosomes. Chrysotile asbestos induced chromosomal aberrations in Chinese hamster ovary (CHO) cells (Sincock and Seabright, 1975; Sincock, 1977), human lymphocytes in vitro (Valerio et al., 1983), and Syrian hamster embryo (SHE) cells (Oshimura et al., 1984). However, it did not induce chromosomal aberrations in the bone marrow of Rhesus monkeys or Swiss mice (Lavappa et al., 1975) or in primary human fibroblasts or human lymphoblastoid lines (Sincock et al., 1983). Chrysotile asbestos did not induce sister-chromatid exchanges (SCE's) in rat mesothelial cells (Kaplan et al., 1980) or human fibroblasts, human lymphoblastoid, or CHO cells (Casey, 1983); however, in another study, chrysotile did induce SCE's in CHO cells (Babu et al., 1981).

Ploidy, which is the gain of one or more entire sets of chromosomes, was associated with chrysotile asbestos treatment of CHO cells (Sincock and Seabright, 1975; Sincock, 1977) and SHE cells (Oshimura et al., 1984). However, chrysotile asbestos did not induce ploidy in human lymphocytes (Valerio et al., 1983) or human fibroblasts (Sincock et al., 1983). Chrysotile asbestos also has been shown to induce aneuploidy, which is the gain or loss of one or more individual chromosomes, in human lymphocytes in vitro (Valerio et al., 1983) and in SHE cells (Oshimura et al., 1984). In addition, chrysotile asbestos has been shown to induce binucleated cells (Brown et al., 1979; Jaurand et al., 1983; Oshimura et al., 1984). Recently, Hesterberg and Barrett (1984) and Oshimura et al. (1984) have shown that chrysotile asbestos caused morphologic transformation of SHE cells. In summary, chrysotile asbestos does not appear to be a gene mutagen, but it does induce cytogenetic alterations, including chromosomal aberrations, ploidy, and aneuploidy. It also causes morphologic transformation of mammalian cells in vitro.

I. INTRODUCTION

In 1973, the National Institute of Environmental Health Sciences and the Environmental Protection Agency cosponsored a symposium on the possible biologic effects of ingested asbestos (EHP, 1974). The participants at this conference concluded that the data concerning the effects of ingested asbestos were inadequate and that specific research was needed.

A subcommittee of the Department of Health, Education, and Welfare Committee to Coordinate Toxicology and Related Programs subsequently reviewed existing data and prepared a draft research protocol that the Committee felt was responsive to the major public health consensus. On the basis of comments received, a revised protocol was developed for long-term animal toxicology and carcinogenesis studies. The forms of asbestos included chrysotile tested in Syrian golden hamsters (NTP TR 246, in press) and in F344/N rats (this report), amosite in Syrian golden hamsters (NTP, 1983) and in F344/N rats (NTP TR 279, in press), crocidolite in F344/N rats (NTP TR 280, in press), and a nonfibrous tremolite, which contained low levels of asbestiform fibers, in F344/N rats (NTP TR 277, in press). Certain studies (IR chrysotile in

hamsters and amosite and IR chrysotile in rats) also incorporated the intestinal carcinogen 1,2-dimethylhydrazine dihydrochloride (DMH) as part of the protocol to test the cocarcinogenic effects of asbestos. DMH is a well-known intestinal carcinogen in animals and produces epithelial neoplasms at sites of intimate exposure to asbestos. All studies encompassed the lifetime of the animal, including exposure of the dam from which the test animals were derived. A single dose level of 1% of the diet was chosen because it represented the highest dose thought to be reasonable from a biologic standpoint and could be tolerated in a lifetime study.

This Technical Report presents the results of those studies undertaken to determine the effects of short-range (SR) or intermediate-range (IR) chrysotile asbestos fed to male and female F344/N rats in the diet. These studies were conducted because of the widespread human exposure via the oral route and the known carcinogenic potential of inhaled asbestos in animals and humans. In addition, the study was designed to determine if the ingestion of IR chrysotile asbestos modified the response to DMH.

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF TEST MATERIALS

PREPARATION OF FORMULATED DIETS AND DOSE MIXTURES

Formulated Diets

Dose Mixtures of Asbestos for Gavage Administration

Dose Mixtures of 1,2-Dimethylhydrazine Dihydrochloride for Gavage Administration

LIFETIME STUDIES OF SHORT-RANGE OR INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Study Design

Source and Specifications of Test Animals

Animal Maintenance

Safety Precautions

Clinical Examinations and Pathology

Statistical Methods

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF TEST MATERIALS

Asbestos is a general term applied to certain natural silicates when they are present in a fibrous form. Chrysotile is a fibrous member of the serpentine mineral group; its chemical formula is $Mg_3Si_2O_5(OH)_4$. Two types of chrysotile were selected for testing; they are referred to as short-range (SR) and intermediate-range (IR) chrysotile based on relative fiber length (Table 1).

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

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

Each of the two chrysotile asbestos test materials was purchased in quantities of about 1,000 pounds. Each material was packaged in new fiberboard drums of 25 (short-range) or 50 (intermediate-range) pounds 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 (Bureau of Mines, 1980) and by the Fine Particle Laboratories, Illinois Institute of Technology Research Institute, Chicago, Illinois (IITRI, 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 that define differences between the two chrysotile test materials are given in Table 1.

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

Crystalline 1,2-dimethylhydrazine dihydrochloride (DMH) (greater than 97% pure) was obtained from Aldrich Chemical, Metuchen, New Jersey, (lot no. 072967JA). Thin-layer chromatographic analysis of a 200- μ g sample did not detect any hydrazine or 1,1-dimethylhydrazine. Faint traces of methylazoxymethane and azoxymethane were detected by high-performance liquid chromatography (Fiala et al., 1976). Three percent of the impurities in DMH were not accounted for. 1,2-Dimethylhydrazine dihydrochloride was stored at 4° C.

PREPARATION OF FORMULATED DIETS AND DOSE MIXTURES

Formulated Diets

NIH 31 open formula rodent diet, prepared by Zeigler Brothers Inc. (Gardners, Pennsylvania), was used. The appropriate chrysotile asbestos at a concentration of 1% was mixed with feed. Pilot studies were conducted in which transmission electron microscopy was used to assess fiber distribution and alteration; and atomic absorption analysis for magnesium was used to assess chrysotile concentration. From these studies, it was determined that a homogeneous mixture of asbestos and feed could be obtained by mixing alternate layers of feed and asbestos in a Patterson-Kelly® V-blender equipped with an intensifier bar. All feed was pelleted with a California pellet mill; the pellets were oval, three-eighths of an inch by three-fourths of an inch. Pelleted feed was packaged in 25-lb, color-coded, standard paper feed bags. Each lot of blended feed was analyzed for asbestos concentration by atomic absorption analysis for magnesium; the results of these analyses are given in Appendix G. The concentration of IR chrysotile asbestos in feed was within 10% of the target concentration 79% (31/39) of the time. The concentration of SR chrysotile asbestos in feed was within 10% of the target concentration 59% (13/22) of the time.

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

	Short Range	Intermediate Range
Fiber Characteristics		
Surface area (m ² /g)	(b) 54.3 ± 3.9 (c) 54.2 ± 0.9	(b) 20.2 ± 0.1 (c) 24.9 ± 2.2
Density (g/cm ³)	2.577 ± 0.022 (8)	2.807 ± 0.016 (8)
Measurement, transmission electron microscopy		
Fiber count/gram	0.6081 × 10 ¹⁸	0.1291 × 10 ¹²
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 (length divided by diameter)	11.1698	8.435
Frequency distribution by length (μm); optical microscopy		
10 percentile	1.3	1.4
20 percentile	1.7	1.9
30 percentile	2.2	3.0
40 percentile	2.6	5.4
50 percentile	3.1	14.0
60 percentile	3.8	29.0
70 percentile	4.5	48.0
80 percentile	5.8	76.0
90 percentile	7.8	130.0
Chemical Instrument Analyses (expressed as weight percent)		
Al ₂ O ₃	0.66	1.47
CaO	0.32	0.05
FeO	Not detected	Not detected
Fe ₂ O ₃	2.02	2.93
MgO	40.62	40.26
K ₂ O	Not detected	0.08
SiO ₂	39.77	39.90
Na ₂ O	0.01	0.04
TiO ₂	0.03	0.04
MnO	0.07	0.06
Cr ₂ O ₃	0.17	0.06
NiO	0.17	0.06
Co ₂ O ₃	0.01	Not detected
CO ₂	0.78	0.51
H ₂ O ⁻	1.54	1.17
H ₂ O ⁺	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 (RI 8452, 1980).

(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) Short range comprises short fibers, with 98% < 10 μm. Intermediate range consists of 65% > 10 μm, with a significant number of fibers (~14%) longer than 100 μm.

II. MATERIALS AND METHODS

Dose Mixtures of Asbestos for Gavage Administration

The appropriate weighed amount of IR chrysotile asbestos was mixed with sterile water in a beaker with a magnetic stirrer to prepare the dosing suspension.

Dose Mixtures of 1,2-Dimethylhydrazine Dihydrochloride for Gavage Administration

Immediately before use, DMH was mixed with ice-cooled 0.2 M acetate buffer (pH 5.0) in 15-ml screw-cap, Teflon®-lined centrifuge tubes in an ice bath. Results of colorimetric analysis of the dose mixtures indicated that the concentration of DMH was usually less than 80% of the target concentration of 3.9 and 7.8 mg/ml (Appendix G, Table G3).

LIFETIME STUDIES OF SHORT-RANGE OR INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Study Design

Groups of 88-250 rats of each sex were fed pelleted diets containing 0% or 1% chrysotile asbestos (either SR or IR) in lifetime studies. The mothers of those in the groups that were administered asbestos started receiving asbestos

7-12 days before mating. Subgroups of 100 male and 100 female rats also received 0.47 mg/g IR chrysotile asbestos in water by gavage, 7 days per week for 3 weeks, starting at 1 day of age. These two groups were referred to as the preweaning (PW) gavage groups. At 9 weeks of age, subgroups of 125-175 rats (one control and one IR group) received 7.5 mg/kg (male) or 15 mg/kg (female) DMH in acetate buffer (pH 5.0) by gavage, every other week for a total of five doses. These doses were based on a pilot study (McConnell et al., 1980) which showed that DMH at these doses produced an incidence of approximately 15% intestinal neoplasia. When the survival of either of the paired groups reached 10%, both groups were killed (Table 2).

Source and Specifications of Test Animals

Parental Generation: The male and female F344/N rats used in this study were produced under strict barrier conditions at Charles River Breeding Laboratories under a contract to the Carcinogenesis Program. Breeding starts for the foundation colony at the production facility originated at the National Institutes of Health Repository. Animals shipped for testing were progeny of defined microflora-associated parents that were transferred from isolators to barrier-maintained rooms. The rats were shipped to the testing laboratory and were quarantined for 4 weeks (intermediate-range studies) or 5 weeks

TABLE 2. SUMMARY OF DISTRIBUTION OF RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Generation	Test Group	No. of Animals		Chrysotile		DMH (mg/kg) (a)	
		Male	Female	Percent	mg/g	Male	Female
F ₀	control	60	120	0	--	--	--
	IR chrysotile (b)	200	400	1.0	--	--	--
F ₁	control	88	88	0	--	--	--
	DMH	125	125	0	--	7.5	15.0
	IR chrysotile	250	250	1.0	--	--	--
	IR chrysotile and DMH	175	175	1.0	--	7.5	15.0
	IR chrysotile and preweaning gavage	100	100	1.0	(c) 0.47	--	--

(a) 1,2-dimethylhydrazine dihydrochloride (DMH) administered by gavage

(b) Intermediate-range chrysotile asbestos

(c) Preweaning gavage with IR chrysotile

II. MATERIALS AND METHODS

(short-range studies) (Figure 1). Thereafter, a complete pathologic examination was performed on eight animals of each sex to assess their health. Males and females then were assigned to test or control diets, according to a table of random numbers. After 11-13 days (intermediate range) or 7 days (short range), the parents of the test rats were placed in breeding cages (one male to two females). After approximately 20 days, females were housed individually and males were rehoused two per cage.

Filial Generation: Litters were culled to no more than eight pups. Litters of the control and dosed groups were assigned to the corresponding control or dosed groups such that birth dates were equally distributed. Litters in which only one sex was present were excluded. After weaning at 21 days, pups from exposed or control dams were randomly assigned to various exposed (except the IR/PW gavage group) or control groups according to a table of random numbers (Table 2). Pups assigned to the IR/PW chrysotile gavage group were administered 0.47 mg/g IR chrysotile asbestos in sterile water by gavage during lactation as described previously.

Animal Maintenance

F₁ rats were housed three per cage in polycarbonate cages. Control or formulated diets and water were available ad libitum (Table 3).

Safety Precautions

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

Other measures used for personnel protection included the wearing of fully protective disposable suits, gloves, boots, and bouffant caps and the use of a dust/mist respirator mask approved by the Occupational Safety and Health Administration (OSHA). Personnel leaving the animal rooms were required to dispose of their protective clothing and to take showers. In

addition, physical examinations including pulmonary function tests and chest radiographs were conducted at the initiation of the study, yearly thereafter, and at the end of the study.

Clinical Examinations and Pathology

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

1. Palpable masses within the abdominal cavity (excluding retained testes)
2. Masses protruding from the rectum.
3. Rectal discharge of bright red fluid (an indication of the presence of a bleeding colonic or rectal neoplasm)
4. Large ulcerated masses in the area of the ears or on the side of the face (Zymbal gland tumors)
5. Large subcutaneous masses that were ulcerated or infected.
6. Masses that interfered with breathing and eating or that severely hampered locomotion
7. Huge tissue masses
8. Central nervous system signs accompanied by weight loss (head tilt, circling, incoordination, ataxia, paralysis)
9. Severe weight loss or emaciation
10. Coma or extreme weakness.

When the remaining number of animals of either sex in the DMH group or the corresponding IR + DMH group was reduced to 10% of those starting the study, both groups of that sex were killed. When survival of the control, IR chrysotile, or IR/PW groups of either sex reached 10%, all remaining animals of that sex in those groups were killed.

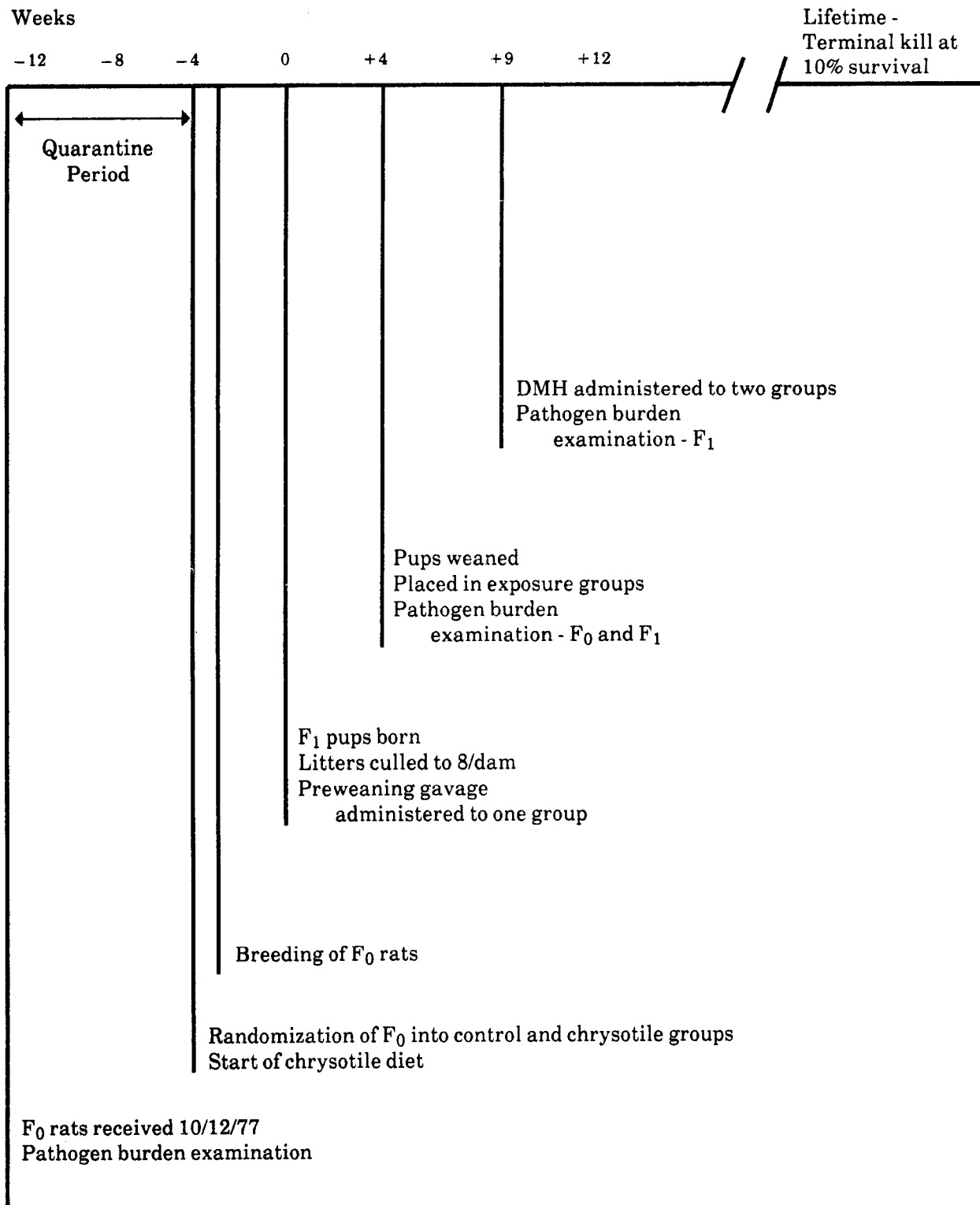


FIGURE 1. SCHEDULE OF MAJOR EVENTS IN RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

TABLE 3. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE AND INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

	Short-Range (SR) Studies	Intermediate-Range (IR) Studies
EXPERIMENTAL DESIGN		
Size of Test Groups	Untreated--88; SR--250 rats of each sex	Untreated--88; IR--250; IR + PW (a)--100; DMH (b)--125; IR + DMH--175 rats of each sex
Doses	0% or 1%	IR--0% or 1%; PW--0.47 mg/g; DMH--7.5 mg/kg (male), 15 mg/kg (female)
Date of First Dose	F ₀ --11/1/77, bred starting 11/8/77; F ₁ --1/15/78 (date of weaning)	F ₀ --11/9-11/11/77, bred starting 11/22/77; F ₁ --1/12/78 (date of weaning)
Duration of Dosing	131 wk (male); 139 wk (female)	IR--136 wk (male), 139 wk (female) DMH--125 wk (male), 112 wk (female)
Type and Frequency of Observation	Observed 2 × d; examined clinically 1 × wk; weighed 1 × wk	Same as SR studies
Necropsy and Histologic Examination	A necropsy was performed on all animals. Tissues examined histologically: blood smear; mandibular lymph node; mammary gland; salivary glands; sternbrae, femur, or vertebrae including marrow; thyroid gland; parathyroids; duodenum; ileum; jejunum; cecum; rectum; colon (carpet rolled); liver; prostate/testes/epididymis or ovaries/uterus; heart; stomach; esophagus; brain; thymus; trachea; pancreas; spleen; kidneys; adrenal glands; urinary bladder; pituitary gland; spinal cord (if neurologic signs were present); eyes (if grossly abnormal); Zymbal gland; lungs and mainstem bronchi; gross lesions; regional lymph nodes	Same as SR studies
ANIMALS AND ANIMAL MAINTENANCE		
Strain and Species	F344/N	F344/N
Animal Source	Charles River Breeding Laboratories (Wilmington, MA)	Same as SR studies
Testing Laboratory	Hazleton Laboratories of America	Same as SR studies
Time Held Before Test	F ₀ --5 wk	F ₀ --4 wk
Age When Placed on Study	F ₀ --9-10 wk	F ₀ --8-9 wk
Age When Killed	F ₁ --131 wk (male); 139 wk (female)	F ₁ --IR and IR + PW--136 wk (male), 139 wk (female); DMH--125 wk (male), 112 wk (female)

TABLE 3. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE AND INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS (Continued)

	Short-Range Studies	Intermediate-Range Studies
ANIMALS AND ANIMAL MAINTENANCE (Continued)		
Necropsy Dates	Lifetime study	Lifetime study
Method of Animal Distribution	Computer-generated random number tables	Same as SR studies
Feed	NIH 31 autoclavable pellets (Zeigler Bros., Inc., Gardners, PA); available ad libitum	Same as SR studies
Bedding	Sani Chips® (J. P. Murphy, Rochelle Park, NJ, and Shurfire, Baltimore, MD)	Same as SR studies
Water	Tap water ad libitum	Same as SR studies
Cages	Polycarbonate (Hazleton Systems, Aberdeen, MD)	Same as SR studies
Cage Filters	Remay nonwoven polyester sheets (Nationwide Papers, Washington, DC)	Same as SR studies
Animals per Cage	F ₀ --1 male, 2 females during breeding, 2 males, 1 female after breeding; F ₁ --3	Same as SR studies
Other Chemicals on Test in the Same Room	None	None (control and dosed animals housed in separate rooms)
Animal Room Environment	Temp--23° C ± 2° C; hum--50% ± 10%; fluorescent light 12 h/d 10-15 room air changes/h	Same as SR studies
CHEMISTRY		
Lot Numbers Used	N/A	IR--N/A; DMH--072967JA
Supplier	Union Carbide (Niagara Falls, NY); obtained from serpentine mass in the southern Diablo range, CA	Johns Manville; obtained from Jeffrey Mine, Asbestos, Quebec, Canada
CHEMICAL/VEHICLE		
Preparation	20 lb asbestos/ton of feed mixed in a Patterson-Kelly® V-blender with intensifier bar; pellets prepared with a California model CL-3 pellet mill	IR--same as SR studies DMH--mixed with ice-cooled 0.2 M acetate buffer, pH 5.0; PW--gavage solution mixed with sterile water on a magnetic stirrer
Maximum Storage Time	N/A	IR--N/A; DMH--used on the day of preparation
Storage Conditions	N/A	IR--N/A; DMH--kept on ice during use

(a) PW--preweaning gavage

(b) DMH--1,2-dimethylhydrazine dihydrochloride

II. MATERIALS AND METHODS

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

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Tissues examined microscopically are listed in Table 3.

When the pathology examination was completed, the slides, individual animal data records, and summary tables were sent to an independent quality assurance laboratory. Individual animal records and tables were compared for accuracy, slides and tissue counts were verified, and histotechnique was evaluated. All tumor diagnoses, all target tissues, and all tissues from a randomly selected 10% of the animals were evaluated by a quality assurance pathologist. Slides of all target tissues and those about which the original and quality assurance pathologists disagreed were submitted to the Chairperson of the Pathology Working Group (PWG) for evaluation. Representative coded slides selected by the Chairperson were reviewed by PWG pathologists, who reached a consensus and compared their findings with the original and quality assurance diagnoses. When diagnostic differences were

found, the PWG sent the appropriate slides and comments to the original pathologist for review. This procedure has been described, in part, by Maronpot and Boorman (1982) and Boorman et al. (1985). The final diagnoses represent a consensus of contractor pathologists and the NTP Pathology Working Group.

Statistical Methods

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

Survival Analyses: The probability of survival was estimated by the product-limit procedure of Kaplan and Meier (1958) and is presented in the form of graphs. Animals were censored from the survival analyses at the time they were found dead of other than natural causes or were found to be missing; animals dying from natural causes were not censored. Statistical analyses for a possible dose-related effect on survival used the method of Cox (1972). All reported P values for the survival analysis are two-sided.

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

Analysis of Tumor Incidence: Three statistical methods are used to analyze tumor incidence data. The two that adjust for intercurrent mortality employ the classical method for combining contingency tables developed by Mantel and Haenszel (1959). Tests of significance included pairwise comparisons of

II. MATERIALS AND METHODS

dosed groups with untreated controls and with each other.

For studies in which compound administration has little effect on survival, the results of the three alternative analyses will generally be similar. When differing results are obtained by the three methods, the final interpretation of the data will depend on the extent to which the tumor under consideration is regarded as being the cause of death. All reported P values for tumor analyses are one-sided.

Life Table Analyses--The first method of analysis assumed that all tumors of a given type observed in animals dying before the end of the study were "fatal"; i.e., they either directly or indirectly caused the death of the animal. According to this approach, the proportions of tumor-bearing animals in the various groups were compared at each point in time at which an animal died with a tumor of interest. The denominators of these proportions were the total number of animals at risk in each group. These results, including the data from animals killed at the end of the study, were then combined by the Mantel-Haenszel method to obtain an overall P value. This method of adjusting for intercurrent mortality is the life table method of Cox (1972).

Incidental Tumor Analyses--The second method of analysis assumed that all tumors of a given

type observed in animals that died before the end of the study were "incidental"; i.e., they were merely observed at necropsy in animals dying of an unrelated cause. According to this approach, the proportions of tumor-bearing animals in dosed and control groups were compared in each of five time intervals: DMH studies (including controls)--0-52 weeks, 53-78 weeks, 79-104 weeks, week 105 to the week before the terminal kill period, and the terminal kill period; IR chrysotile (including controls) without DMH and SR chrysotile studies--0-60 weeks, 61-86 weeks, 87-112 weeks, 113-126 weeks, and week 127 to the end of the studies. The denominators of these proportions were the number of animals on which a necropsy was actually performed during the time interval. The individual time interval comparisons were then combined by the previously described method to obtain a single overall result. (See Haseman, 1984, for the computational details of both methods.)

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

III. RESULTS

LIFETIME STUDIES OF SHORT-RANGE OR INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Establishment of Test Groups

Body Weights and Feed Consumption

Pathogen Burden

Clinical Signs

Survival

Pathology and Statistical Analyses of Results

III. RESULTS

LIFETIME STUDIES OF SHORT-RANGE OR INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Establishment of Test Groups

The experiment was designed to evaluate the effects of ingested chrysotile asbestos during the entire life of the animal. When the first litters were born, therefore, the mated female rats had been on test diets for approximately 4 weeks. To minimize the chance that the mothers would reject or cannibalize their young, the litters were not handled during lactation except for weighing and culling at birth, and the animals were administered IR chrysotile by preweaning gavage. Litter size and survival of offspring were unaffected by the presence of SR or IR chrysotile asbestos in the mothers' diet. The average number of live fetuses born to SR chrysotile-exposed dams was 7.7 versus 7.6 for the control groups; the average number born to IR chrysotile-exposed dams was 7.5 versus 7.6 for the control group. The average weight at birth of the SR chrysotile-exposed pups was 5.2 g versus 5.1 g for the controls, and average weight of the IR-exposed groups was 5.3 versus 5.0 for the controls. Fetal weights were determined by dividing the weight of each litter by the number of live pups. The SR chrysotile-exposed offspring were slightly larger (8%) at weaning, 29.1 g versus 26.7 g for the controls, whereas the IR chrysotile offspring were slightly smaller (13%) at weaning (23.3 g vs 26.8 g).

A summary of groups, number of animals, diets for the parental (F₀) animals, as well as the distribution of and diets for the filial (F₁) animals is presented in Table 2.

Body Weights and Feed Consumption

Short Range Groups: Mean body weights of dosed and control rats were comparable throughout the studies (Table 4 and Figure 2). The average daily feed consumption per rat by SR rats was 100% that of the controls for males and females (Appendix H, Tables H1 and H2).

Intermediate-Range and Preweaning Groups: The mean body weight of the male IR/PW group was approximately 5% greater than that of the

controls and 14% greater than that of the IR group at week 7; for females the mean body weight of the IR/PW group was approximately 4% lower than that of controls and 5% greater than that of the IR group (Table 5 and Figure 3). The mean body weights of the males and females in the IR/PW groups were greater than those of the IR groups throughout most of the studies; the mean body weights of the IR groups were 8% lower than those of the controls at week 7 and remained lower throughout most of the studies. Average daily feed consumption by IR rats was 100% that of the controls for males and females. Average daily feed consumption by IR/PW rats was 102% that of controls for males and 100% for females (Appendix H, Tables H3 and H4).

1,2-Dimethylhydrazine Dihydrochloride With and Without Intermediate-Range Chrysotile Asbestos: The mean body weights of the controls and of the groups that received DMH without IR chrysotile asbestos were comparable throughout most of the studies (Table 5 and Figure 3). The mean body weights of groups that received DMH and IR chrysotile asbestos, especially female rats, were lower than those of groups that received DMH without IR chrysotile asbestos. Average daily feed consumption by male rats that received DMH with and without IR chrysotile asbestos was 100% that of controls. Average daily feed consumption by female rats was 100% that of the controls for those that received DMH without IR chrysotile asbestos and 92% that of the controls for those that received DMH with IR chrysotile asbestos.

Pathogen Burden

Short-Range: All lung sections of the F₀ animals evaluated for pathogen burden revealed evidence of mild respiratory disease (Appendix I). In some rats, small foci of mononuclear cells were present adjacent to the bronchial tissue and in other rats, small cuffs of lymphoid cells were evident, particularly at the bifurcation of the bronchi. These lesions were very mild.

In the lungs of all F₁ rats examined, evidence of early respiratory disease was again present. In one male rat of Group 1 (basal control) and one male rat of Group 2 (SR chrysotile), only small foci of mononuclear cells were present adjacent

TABLE 4. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS

Weeks on Study (from birth)	Control		One Percent		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors
MALE					
6	129	88	130	101	250
7	152	88	156	103	250
8	175	88	182	104	250
9	200	88	205	103	250
10	222	88	224	101	250
11	236	88	240	102	250
12	250	88	254	102	250
13	262	88	267	102	250
14	271	88	275	101	250
15	280	88	285	102	250
16	283	88	290	102	250
17	295	88	291	99	250
18	301	88	299	99	250
19	310	88	308	99	250
20	314	88	316	101	250
30	366	88	356	97	250
40	394	88	396	101	250
50	423	85	424	100	250
60	430	85	429	100	249
70	452	84	451	100	248
80	467	81	462	99	246
90	470	78	470	100	237
100	461	71	456	99	213
110	444	60	430	97	180
120	430	51	411	96	131
130	376	24	383	102	73
FEMALE					
6	109	88	114	105	250
7	124	88	129	104	250
8	135	88	139	103	250
9	143	88	149	104	250
10	153	88	156	102	250
11	157	88	162	103	250
12	163	88	168	103	250
13	167	88	172	103	250
14	170	88	175	103	250
15	175	88	180	103	250
16	174	88	180	103	250
17	181	88	180	99	250
18	182	88	181	99	250
19	187	88	185	99	250
20	188	88	189	101	250
30	206	88	204	99	250
40	220	88	223	101	249
50	247	88	244	99	248
60	262	88	269	103	246
70	290	88	291	100	246
80	311	87	316	102	240
90	326	84	331	102	233
100	332	73	328	99	209
110	324	63	308	95	182
120	326	44	312	96	132
130	303	26	291	96	85
140	293	15	279	95	33

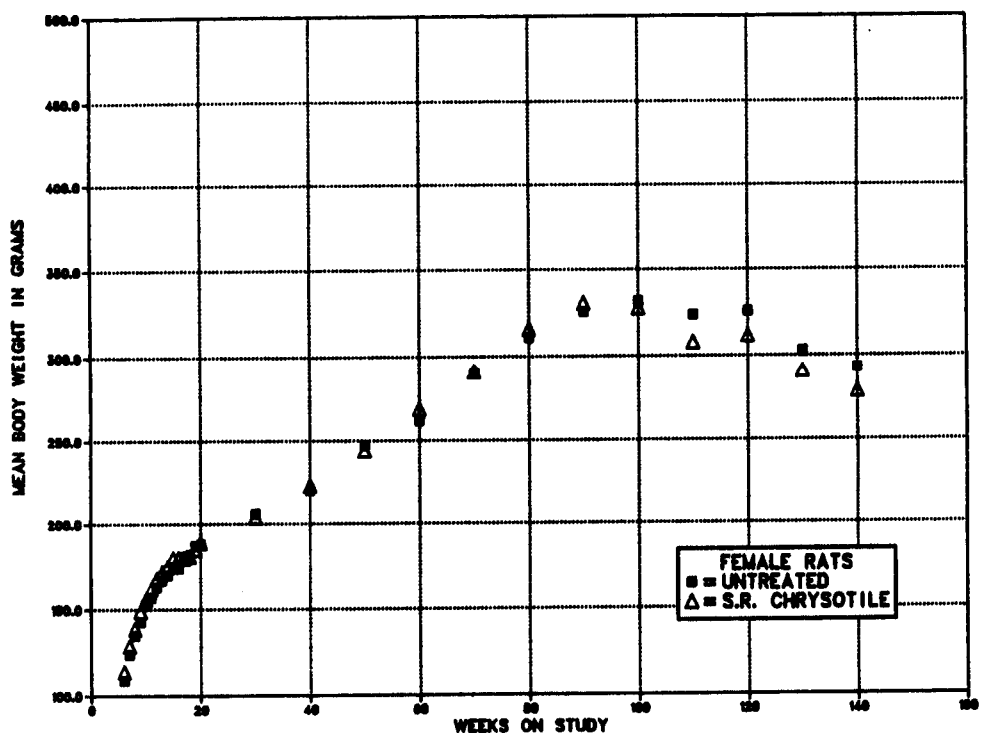
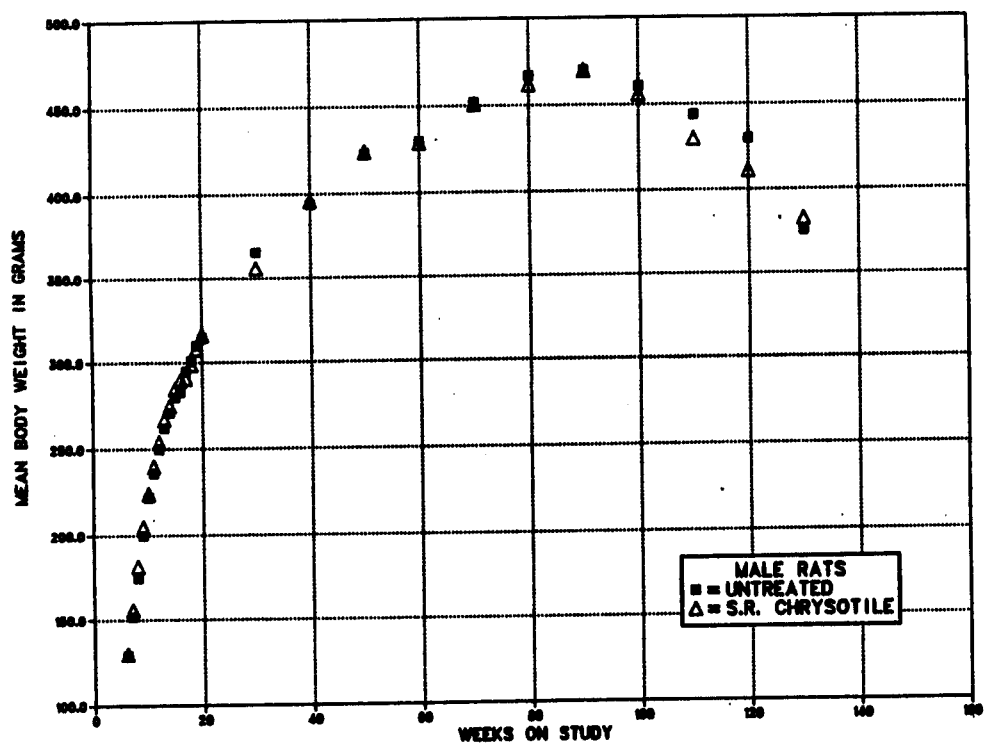


FIGURE 2. GROWTH CURVES FOR RATS FED DIETS CONTAINING SHORT-RANGE CHRYSOTILE ASBESTOS IN LIFETIME STUDIES

TABLE 5. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Weeks on Study (from birth)	Control		DMH			IR			IR + DMH			IR/PW		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (% of controls)	No. of Survivors	Av. Wt. (grams)	Wt. (% of controls)	No. of Survivors	Av. Wt. (grams)	Wt. (% of controls)	No. of Survivors	Av. Wt. (grams)	Wt. (% of controls)	No. of Survivors
MALE														
7	115	88	111	97	125	106	92	250	101	88	175	121	105	100
8	134	88	131	98	125	136	101	250	134	100	175	148	110	100
9	159	88	150	94	125	160	101	250	154	97	175	166	104	100
10	183	88	177	97	125	180	98	250	181	99	175	195	107	100
11	203	88	199	98	125	197	97	250	197	97	175	221	109	100
12	218	88	216	99	125	216	99	250	214	98	175	234	107	100
13	231	88	226	98	125	227	98	250	221	98	175	245	106	100
14	246	88	245	100	125	234	96	250	233	95	175	254	103	100
15	256	88	252	98	125	245	96	250	242	96	175	268	104	100
16	258	88	259	100	125	257	100	250	253	98	175	276	107	100
17	267	88	262	98	125	267	100	250	261	98	175	286	107	100
18	278	88	274	99	125	276	99	250	270	97	175	295	106	99
19	285	88	282	99	125	281	99	250	277	97	175	303	106	99
20	294	88	294	100	125	290	99	250	281	96	175	312	106	99
21	293	88	290	99	125	292	100	250	288	98	175	319	109	99
31	344	88	340	99	124	333	97	248	332	97	175	355	103	99
41	393	88	390	99	124	371	94	248	370	94	175	400	102	97
51	402	88	416	103	122	396	99	248	390	97	173	419	104	95
61	417	88	421	101	121	401	98	248	402	96	169	417	100	94
71	443	87	446	101	117	424	96	244	423	95	164	441	100	94
81	460	86	452	98	112	433	94	238	426	93	159	458	100	91
91	463	82	462	100	96	432	93	227	437	94	125	462	100	87
101	452	77	461	102	72	423	94	208	421	93	96	447	99	84
111	446	67	447	100	56	415	93	183	407	91	74	426	96	78
121	423	43	410	97	37	393	93	128	387	91	48	405	96	55
131	394	28	374	95	19	359	91	85	362	92	20	373	95	28
141	352	9	---	---	---	327	93	35	---	---	---	354	101	18
FEMALE														
7	106	88	102	96	125	97	92	250	93	88	175	102	96	100
8	119	88	115	97	125	114	96	250	110	92	175	116	97	100
9	131	88	126	96	125	126	96	250	120	92	175	130	99	100
10	141	88	137	97	125	134	95	250	133	94	175	140	99	100
11	144	88	145	101	125	143	99	250	137	95	175	151	105	100
12	154	88	152	99	125	149	97	250	144	94	175	155	101	100
13	158	88	152	96	125	151	96	250	144	91	175	159	101	100
14	165	88	161	98	125	154	93	250	151	92	175	164	99	100
15	166	88	160	96	125	157	95	250	153	92	175	168	101	100
16	167	88	162	97	125	162	97	250	160	96	175	173	104	100
17	169	88	164	97	125	166	98	250	162	98	175	175	104	100
18	173	88	168	97	125	169	98	250	166	96	174	180	104	100
19	175	88	173	99	125	171	98	250	170	97	174	182	104	100
20	180	88	179	99	125	175	97	250	170	94	174	184	102	100
21	178	88	174	98	125	175	98	250	173	97	174	189	106	100
31	196	88	196	100	125	190	97	249	190	97	173	201	103	99
41	219	88	217	99	124	207	95	248	204	93	172	223	102	99
51	235	88	239	102	121	224	95	247	224	95	170	241	103	99
61	259	88	261	101	119	251	97	247	247	95	165	257	99	98
71	280	88	285	102	111	272	97	244	267	95	153	277	99	97
81	303	86	303	100	104	291	96	240	280	92	137	303	100	94
91	323	81	316	98	74	302	93	229	293	91	110	313	97	87
101	330	76	325	98	46	303	92	207	294	89	71	320	97	82
111	329	63	314	95	28	303	92	179	284	86	44	315	96	73
121	324	49	---	---	---	300	93	132	---	---	---	315	97	56
131	308	27	---	---	---	268	87	91	---	---	---	301	98	31
141	286	13	---	---	---	255	89	41	---	---	---	287	100	15

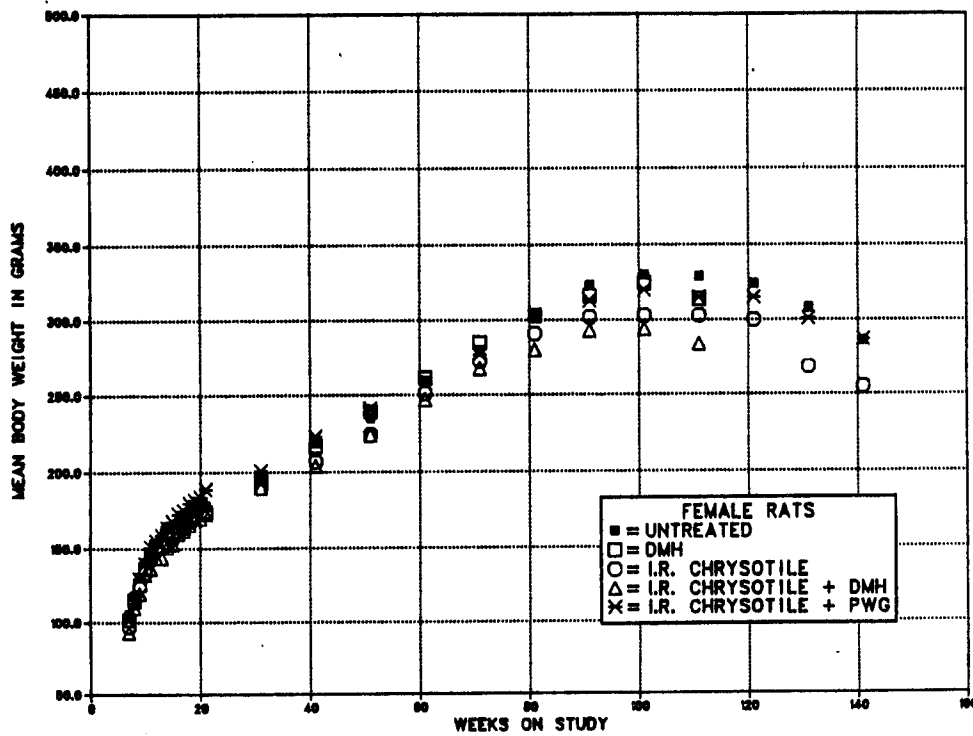
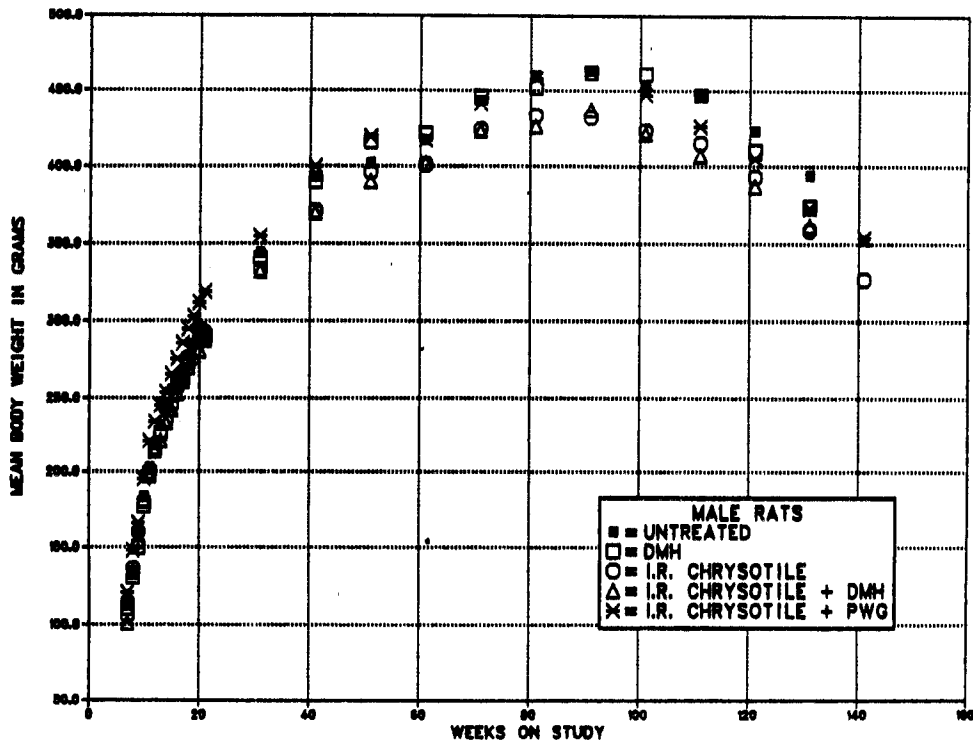


FIGURE 3. GROWTH CURVES FOR RATS FED DIETS CONTAINING INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS WITH AND WITHOUT 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE IN LIFETIME STUDIES

to the bronchioles. In the remaining rats, minimal-to-slight peribronchial lymphoid hyperplasia was present.

Intermediate Range: The tissues of the F₀ animals evaluated for pathogen burden revealed evidence of early respiratory disease present in nearly all animals (Appendix J). This consisted of minimal-to-moderate peribronchial lymphoid hyperplasia in six males and seven females, a few focal accumulations of mononuclear cells in two males, focal accumulations of alveolar macrophages in one female, and minimal perivascular lymphoid hyperplasia in another female. In nearly all the F₁ animals examined, evidence of early respiratory disease, consisting of minimal-to-slight peribronchial lymphoid hyperplasia, was present. No serologic evidence of Sendai virus was present in either F₀ or F₁ animals.

Clinical Signs

Short Range: A summary of clinical signs observed before moribund kill is presented in Appendix K. Specific clinical signs occurred at essentially comparable frequencies in the control group and the dosed group throughout the studies. No distinct compound-related signs were noted in any of the dosed animals during the first 52 weeks on study. The following representative findings were observed at generally comparable frequencies among all groups: soft feces; urine stains; pale, thin and/or hunched appearance; depression; localized alopecia or sores on head or body; rough haircoats; abnormal eyes (pale, cloudy, bloody crust, red, lacrimation, squinting, enlarged, sores, swollen, red discharge, protruding, small and/or necrotic); head tilt; salivation; localized swellings; stains on fur; bloated appearance; necrotic or abscessed tail; discharge from anus or vagina; protruding penis or vagina; small or enlarged testes; wheezing; wasting feed or decreased feed consumption; and labored respiration and/or abnormal central nervous system responses (circling, hyperactivity, loss of equilibrium, tremors, isolated occurrences of paralysis and/or ataxia).

As the study proceeded, the incidence of clinical signs increased among all the groups. At intervals in which a large number of animals were killed in a moribund condition in any one

particular group, the clinical signs most frequently observed were supportive of the conditions for moribund kills previously outlined in the Materials and Methods section.

Intermediate Range: Specific clinical signs occurred at essentially comparable frequencies in the control group and the DMH group throughout the studies. No distinct compound-related signs were noted in any of the dosed animals during the first 52 weeks on study. The following representative findings were observed at generally comparable frequencies among all groups: soft feces; urine stains; pale, thin, and/or hunched appearance; depression; localized alopecia or sores on head or body; rough haircoats; abnormal eyes (pale, cloudy, bloody crust, red, lacrimation, squinting, enlarged, sores, swollen, red discharge, protruding, small and/or necrotic); head tilt; salivation; localized swellings; stains on fur; bloated appearance; necrotic or abscessed tail; discharge from anus or vagina; small or enlarged testes; wheezing; wasting feed or decreased feed consumption; and labored respiration and/or abnormal central nervous system responses (circling, hyperactivity, loss of equilibrium, tremors, isolated occurrences of paralysis and/or ataxia). A summary of clinical signs observed before moribund kills is presented in Appendix L.

As the study proceeded, the incidences of clinical signs increased among all the groups. At intervals in which a large number of animals were killed in a moribund condition in any one particular group, the clinical signs most frequently observed were supportive of the conditions for moribund kills previously outlined in the Materials and Methods section. A comparison of clinical signs observed during the same selected intervals between all the groups revealed a larger number of palpable abdominal masses, tissue masses, and red discharge and protruding masses from the rectum in the DMH group and the IR plus DMH group. In addition, the incidence of tissue masses, nodules, and wart-like lesions of the head and ear region was greater in the DMH group and the IR plus DMH group throughout the studies. These findings were not clinically observed with any frequency in any group administered only IR chrysotile and thus are presumed to be due to administration of 1,2-dimethylhydrazine dihydrochloride.

III. RESULTS

Survival

Estimates of the probabilities of the survival of male and female rats fed diets containing chrysotile asbestos at the concentrations used in these studies and those of the controls are shown in the Kaplan and Meier curves in Figures 4 and 5.

Additional survival data are summarized in Tables 6 through 10.

Short Range: Survival of rats exposed to SR was similar to that of the controls throughout the studies (Tables 6 and 7).

TABLE 6. SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS

	Untreated Control	SR (a)
MALE (b)		
Animals initially in study	88	250
Nonaccidental deaths before termination (c)	76	224
Accidentally killed	3	0
Killed at termination	9	26
Survival P values (d)		0.676
FEMALE (b)		
Animals initially in study	88	250
Nonaccidental deaths before termination (c)	79	225
Killed at termination	9	25
Survival P values (d)		0.978

- (a) Administered 1% short-range (SR) chrysotile asbestos in the diet
- (b) Terminal kill period: male--week 137; female--week 145
- (c) Includes animals killed in a moribund condition
- (d) The result of the life table pairwise comparison with the controls

TABLE 7. SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS AT VARIOUS TIME POINTS

Group	Age in Weeks	Male		Female	
		No. Alive/ Total No.	Percent Survival	No. Alive/ Total No.	Percent Survival
Control	100	71/88	81	73/88	83
	110	60/88	68	63/88	72
	120	51/88	58	44/88	50
	130	24/88	27	26/88	30
SR	100	213/250	85	209/250	84
	110	180/250	72	182/250	73
	120	131/250	52	132/250	53
	130	73/250	29	85/250	34

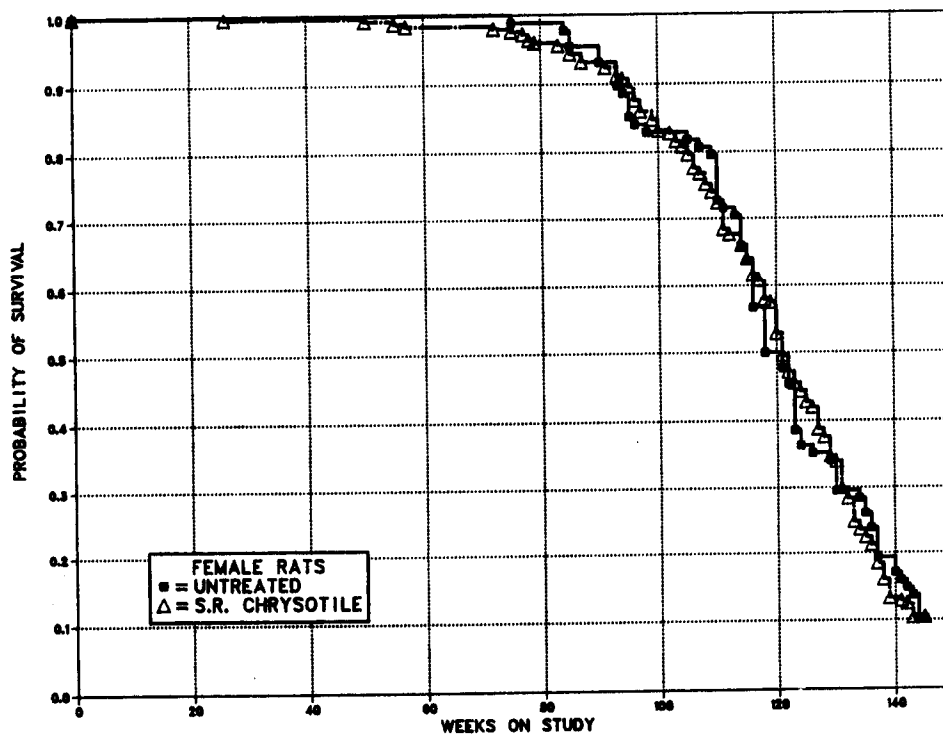
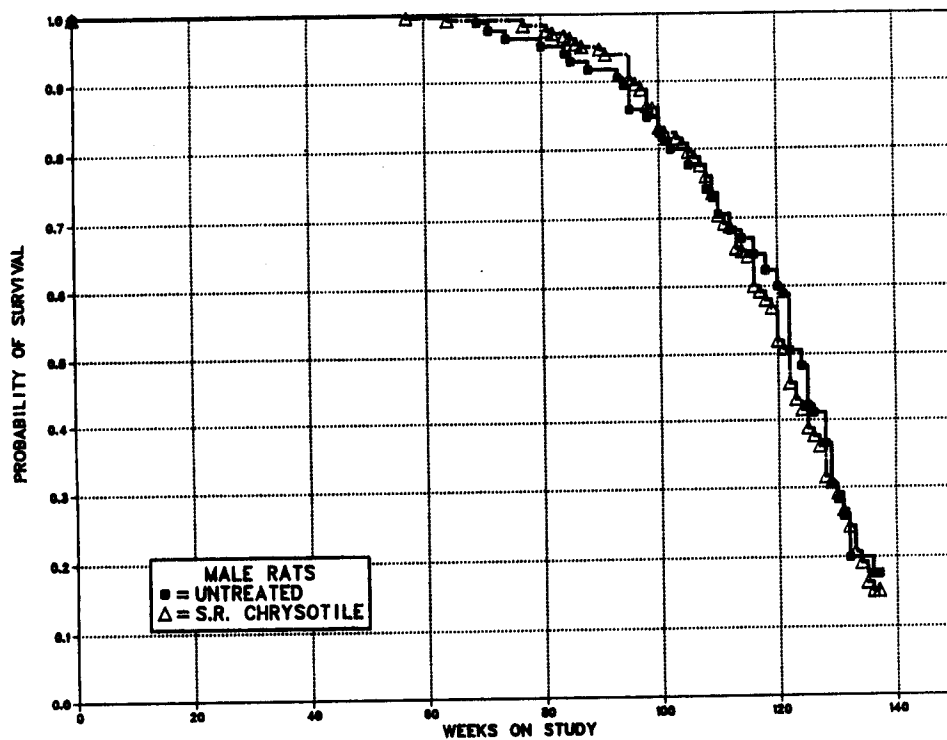


FIGURE 4. KAPLAN-MEIER SURVIVAL CURVES FOR RATS FED DIETS CONTAINING SHORT-RANGE CHRYSOTILE ASBESTOS IN LIFETIME STUDIES

III. RESULTS

Intermediate Range: Survival of untreated controls was similar to that of dosed IR groups throughout the studies (Table 8). The survival of both groups of DMH-exposed rats was

considerably lower than that of the untreated controls. However, survival of the IR plus DMH group was comparable to that of the DMH alone group (Table 9).

TABLE 8. SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

	Untreated Control	IR (a)	IR/PW	IR vs IR/PW
MALE (b)				
Animals initially in study	88	250	100	
Nonaccidental deaths before termination (c)	81	220	89	
Accidentally killed	0	1	0	
Killed at termination	7	29	11	
Survival P values (d)		0.590	0.885	0.750
FEMALE (b)				
Animals initially in study	88	250	100	
Nonaccidental deaths before termination (c)	79	225	91	
Killed at termination	9	25	9	
Survival P values (d)		0.793	0.982	0.713

(a) Administered 1% intermediate-range (IR) chrysotile asbestos in the diet

(b) Terminal kill period: male--week 144; female--week 146

(c) Includes animals killed in a moribund condition

(d) The results of the life table pairwise comparisons with the controls are in the dosed columns. The third value is the pairwise comparison between the dosed groups.

TABLE 9. SURVIVAL OF RATS IN THE LIFETIME STUDIES OF 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE WITH AND WITHOUT INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS IN THE FEED

	Untreated Control	DMH (a)	IR + DMH (b)	DMH vs IR + DMH
MALE (c)				
Animals initially in study	88	125	175	
Nonaccidental deaths before termination (d)	81	107	159	
Killed at termination	7	18	14	
Died during termination period	0	0	2	
Survival P values (e)		< 0.001	< 0.001	0.348
FEMALE (c)				
Animals initially in study	88	125	175	
Nonaccidental deaths before termination (d)	79	109	148	
Killed at termination	9	16	26	
Died during termination period	0	0	1	
Survival P values (e)		< 0.001	< 0.001	0.558

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

(b) Administered 1% intermediate-range (IR) chrysotile asbestos in the diet and DMH by gavage

(c) Terminal kill period: male--control, week 144; DMH, week 129; IR plus DMH, week 132; female--control, week 146; DMH, week 116; IR plus DMH, week 119

(d) Includes animals killed in a moribund condition

(e) The results of the life table pairwise comparisons with the controls are in the dosed columns. The third value is the pairwise comparison between the dosed groups.

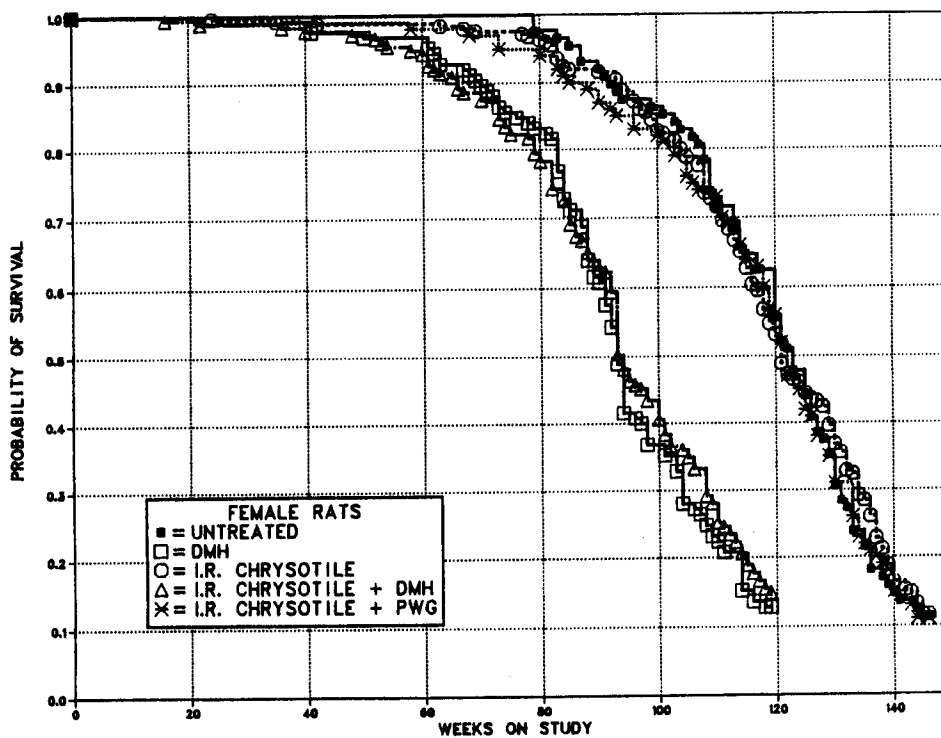
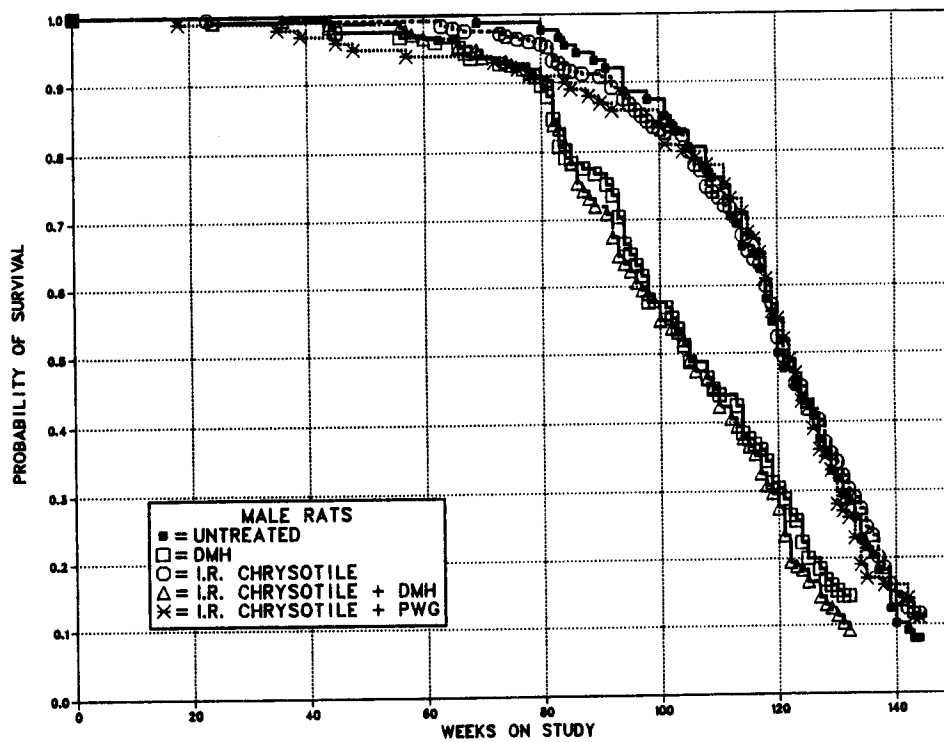


FIGURE 5. KAPLAN-MEIER SURVIVAL CURVES FOR RATS FED DIETS CONTAINING INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS WITH AND WITHOUT 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE IN LIFETIME STUDIES

TABLE 10. SURVIVAL OF RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS AT VARIOUS TIME POINTS

Group	Age in Weeks	Male		Female	
		No. Alive/ Total No.	Percent Survival	No. Alive/ Total No.	Percent Survival
Control	111	67/88	76	63/88	72
	121	43/88	49	49/88	56
	131	28/88	32	27/88	31
	141	9/88	10	13/88	15
DMH	111	55/125	44	28/125	22
	121	37/125	30	--	--
	131	19/125	15	--	--
	141	--	--	--	--
IR	111	183/250	73	179/250	72
	121	128/250	51	132/250	53
	131	85/250	34	91/250	36
	141	35/250	14	41/250	16
IR+DMH	111	74/175	42	44/175	25
	121	48/175	27	--	--
	131	20/175	11	--	--
	141	--	--	--	--
IR/PW	111	78/100	78	73/100	73
	121	55/100	55	56/100	56
	131	28/100	28	31/100	31
	141	16/100	16	15/100	15

Pathology and Statistical Analyses of Results

This section describes the significant or noteworthy changes in the incidences of rats with neoplastic or nonneoplastic lesions. Histopathologic findings on neoplasms in rats are summarized in Appendix A (Tables A1 and A2) (short range) and Appendix B (Tables B1 and B2) (intermediate range); Appendix A (Tables A3 and A4) and Appendix B (Tables B3 and B4) give the survival and tumor status for individual male and female rats. Findings on nonneoplastic lesions are summarized in Appendix C (Tables C1 and C2) (short range) and Appendix D (Tables D1 and D2) (intermediate range). Appendix E (Tables E1-E6) contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups. The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes).

Classification of Observed Gastrointestinal Tract Neoplasms

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

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

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

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

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

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

Short-Range Groups

At no site was the incidence of neoplasms in dosed groups significantly greater than that in the control groups. The incidences of neoplastic and nonneoplastic lesions of the alimentary tract are shown in Tables 11 and 12.

Decreased Incidence of Primary Neoplasms: A decreased incidence of neoplasms in male SR chrysotile groups occurred in the following organs: liver (neoplastic nodules/carcinomas combined)--15/88, 17% (control) versus 19/248, 8% (SR chrysotile) and parathyroid gland (adenomas)--6/83, 7% (control) versus 4/229, 2% (SR chrysotile).

Intermediate-Range and Prewaning Gavage Groups

Alimentary Tract: The incidences of epithelial neoplasms of the alimentary tract are summarized in Table 13 by site and morphologic type. Only the incidence of adenomatous polyp of the large intestine (dosed, 9/250 (4%) versus control, 0/85) in male rats is possibly compound related.

There were also two polyps in the descending colon in the male IR/PW chrysotile group. All of these polyps were grossly visible at necropsy. If epithelial neoplasms of similar morphology from the small intestine and glandular stomach are also counted, the incidence is 14/250, 6% (IR chrysotile) versus 0/88 (control) and 2/100, 2% (IR/PW chrysotile). There were also 3/250 animals with neoplasms of squamous cell origin (squamous cell papilloma, keratoacanthoma, and squamous cell carcinoma) in the oral cavity in the male IR chrysotile group and none in the controls. No increase in epithelial neoplasms was observed in IR chrysotile-exposed female rats.

No nonneoplastic lesions were associated with the administration of IR chrysotile asbestos (Table 14).

TABLE 11. ALIMENTARY TRACT TUMORS IN RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE (SR) CHRYSOTILE ASBESTOS

	Male		Female	
	Control	SR	Control	SR
Hard palate (No. examined)	88	250	88	250
Squamous cell papilloma	0	1 (<1%)	0	0
Oral mucous membrane (No. examined)	88	250	88	250
Squamous cell carcinoma	0	0	0	1 (<1%)
Tongue (No. examined)	88	250	88	250
Squamous cell papilloma	0	0	0	1 (<1%)
Squamous cell carcinoma	0	0	0	1 (<1%)
Stomach (No. examined)	88	248	87	245
Squamous cell papilloma	0	1 (<1%)	0	0
Squamous cell carcinoma	0	1 (<1%)	0	1 (<1%)
Sarcoma	0	1 (<1%)	0	0
Forestomach (No. examined)	88	248	87	245
Squamous cell papilloma	1 (1%)	0	0	0
Gastric fundus (No. examined)	88	248	87	245
Carcinoma-in-situ	0	1 (<1%)	0	0
Duodenum (No. examined)	88	248	87	244
Adenomatous polyp	0	1 (<1%)	0	0
Leiomyosarcoma	0	0	0	2 (1%)
Jejunum (No. examined)	88	248	87	244
Mucinous cystadenocarcinoma	1 (1%)	0	0	1 (<1%)
Adenocarcinoma in adenomatous polyp	0	0	0	1 (<1%)
Leiomyoma	0	0	0	1 (<1%)
Ileum (No. examined)	88	248	87	244
Leiomyosarcoma	0	0	1 (1%)	0
Total small intestine (No. examined)	88	248	87	244
Adenomatous polyp	0	1 (<1%)	0	0
Mucinous cystadenocarcinoma	1 (1%)	0	0	1 (<1%)
Adenocarcinoma in adenomatous polyp	0	0	0	1 (<1%)
Leiomyoma	0	0	0	1 (<1%)
Leiomyosarcoma	0	0	1 (1%)	2 (1%)
Cecum (No. examined)	87	248	87	244
Lipoma	0	1 (<1%)	0	0
Leiomyosarcoma	0	1 (<1%)	0	0
Adenomatous polyp	0	0	1 (1%)	0
Colon (No. examined)	87	248	87	244
Adenomatous polyp	0	1 (<1%)	0	0
Leiomyosarcoma	0	1 (<1%)	0	0
Transverse colon (No. examined)	87	248	87	244
Leiomyosarcoma	1 (1%)	0	0	0
Adenomatous polyp	0	0	0	1 (<1%)
Descending colon (No. examined)	87	248	87	244
Adenomatous polyp	0	0	0	2 (1%)
Leiomyosarcoma	0	0	0	1 (<1%)
Total large intestine (No. examined)	87	248	87	244
Adenomatous polyp	0	1 (<1%)	1 (1%)	3 (1%)
Lipoma	0	1 (<1%)	0	0
Leiomyosarcoma	1 (1%)	2 (1%)	0	1 (<1%)

TABLE 12. INCIDENCE OF NONNEOPLASTIC LESIONS IN THE ALIMENTARY TRACT OF RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE (SR) CHRYSOTILE ASBESTOS

	Male		Female	
	Control	SR	Control	SR
Esophagus (No. examined)	86	247	87	244
Hyperkeratosis	6 (7%)	16 (6%)	4 (5%)	8 (3%)
Stomach (No. examined)	88	248	87	245
Mineralization	3 (3%)	2 (1%)	0	0
Inflammation	12 (14%)	35 (14%)	16 (18%)	46 (19%)
Ulcer	4 (5%)	10 (4%)	7 (8%)	21 (9%)
Adhesion	1 (1%)	1 (<1%)	2 (2%)	1 (<1%)
Necrosis	13 (15%)	40 (16%)	14 (16%)	35 (14%)
Hyperplasia, epithelial	3 (3%)	0	0	0
Hyperkeratosis	8 (9%)	29 (12%)	21 (24%)	59 (24%)
Acanthosis	11 (13%)	36 (15%)	19 (22%)	59 (24%)
Gastric muscularis (No. examined)	88	248	87	245
Degeneration	2 (2%)	0	0	1 (<1%)
Colon (No. examined)	87	248	87	244
Inflammation			2 (2%)	2 (1%)
Parasitism	13 (15%)	22 (9%)	8 (9%)	13 (5%)
Cecum (No. examined)	87	248	87	244
Inflammation	0	6 (2%)	2 (2%)	5 (2%)
Necrosis	0	5 (2%)	2 (2%)	3 (1%)

TABLE 13. ALIMENTARY TRACT TUMORS IN RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS

	Male			Female		
	Control	IR	IR/PW	Control	IR	IR/PW
Mouth/oral cavity (No. examined)	88	250	100	88	250	100
Squamous cell carcinoma	0	1 (<1%)	0	0	1 (<1%)	0
Hard palate (No. examined)	88	250	100	88	250	100
Keratoacanthoma	0	1 (<1%)	0	0	0	0
Squamous cell papilloma	0	0	1 (1%)	0	1 (<1%)	0
Squamous cell carcinoma	0	0	0	0	0	1 (1%)
Tongue (No. examined)	88	250	100	88	250	100
Squamous cell papilloma	0	1 (<1%)	0	1 (1%)	0	1 (1%)
Esophagus (No. examined)	83	250	98	88	250	100
Fibrosarcoma	0	0	1 (1%)	0	0	0
Stomach (No. examined)	85	250	100	87	250	99
Squamous cell papilloma	0	0	0	0	0	1 (1%)
Squamous cell carcinoma	0	0	0	1 (1%)	0	1 (1%)
Adenomatous polyp	0	0	0	0	1 (<1%)	0
Adenocarcinoma	0	1 (<1%)	0	0	0	0
Carcinoid tumor	0	0	0	0	2 (1%)	0
Leiomyosarcoma	0	0	0	0	1 (<1%)	0
Small intestine (No. examined)	85	250	100	87	249	99
Leiomyosarcoma	0	0	1 (1%)	0	0	0
Duodenum (No. examined)	85	250	100	87	249	99
Adenomatous polyp	0	1 (<1%)	0	0	0	0
Mucinous cystadenocarcinoma	0	1 (<1%)	0	0	0	0
Signet ring carcinoma	0	1 (<1%)	0	0	0	0
Leiomyoma	0	1 (<1%)	0	1 (1%)	0	0
Jejunum (No. examined)	85	250	100	87	249	99
Leiomyosarcoma	0	2 (1%)	0	0	0	0
Ileum (No. examined)	85	250	100	87	249	99
Leiomyoma	1 (1%)	0	1 (1%)	0	0	0
Total small intestine (No. examined)	85	250	100	87	249	99
Adenomatous polyp	0	1 (<1%)	0	0	0	0
Mucinous cystadenocarcinoma	0	1 (<1%)	0	0	0	0
Signet ring carcinoma	0	1 (<1%)	0	0	0	0
Leiomyoma	1 (1%)	1 (<1%)	1 (1%)	1 (1%)	0	0
Leiomyosarcoma	0	2 (1%)	1 (1%)	0	0	0
Ascending colon (No. examined)	85	250	100	87	250	99
Adenomatous polyp	0	2 (1%)	0	0	0	0
Leiomyoma	0	0	0	0	0	1 (1%)
Transverse colon (No. examined)	85	250	100	87	250	99
Leiomyosarcoma	0	0	1 (1%)	0	0	0
Descending colon (No. examined)	85	250	100	87	250	99
Adenomatous polyp	0	7 (3%)	2 (2%)	0	1 (<1%)	0
Leiomyoma	0	0	0	0	1 (<1%)	0
Total large intestine (No. examined)	85	250	100	87	250	99
Adenomatous polyp	0	9 (4%)	2 (2%)	0	1 (<1%)	0
Leiomyoma	0	0	0	0	1 (<1%)	1 (1%)
Leiomyosarcoma	0	0	1 (1%)	0	0	0

TABLE 14. INCIDENCE OF NONNEOPLASTIC LESIONS IN THE ALIMENTARY TRACT OF RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS

	Male			Female		
	Control	IR	IR/PW	Control	IR	IR/PW
Esophagus (No. examined)	83	250	98	86	250	99
Hyperkeratosis	1 (1%)	0	2 (2%)	0	0	2 (2%)
Stomach (No. examined)	85	250	100	87	250	99
Mineralization	1 (1%)	5 (2%)	0	0	0	0
Cyst	2 (2%)	1 (<1%)	0	1 (1%)	1 (<1%)	1 (1%)
Edema	5 (6%)	0	0	0	0	0
Ulcer	13 (15%)	27 (11%)	9 (9%)	7 (8%)	26 (10%)	7 (7%)
Inflammation	18 (22%)	29 (12%)	9 (9%)	9 (10%)	33 (13%)	10 (10%)
Necrosis, focal	0	4 (2%)	0	0	2 (1%)	1 (1%)
Hyperplasia, epithelial	0	0	1 (1%)	0	1 (<1%)	0
Hyperplasia, basal cell	1 (1%)	1 (<1%)	0	0	0	0
Hyperkeratosis	7 (8%)	0	0	2 (2%)	4 (2%)	5 (5%)
Acanthosis	10 (12%)	18 (7%)	14 (14%)	7 (8%)	20 (8%)	10 (10%)
Gastric submucosa (No. examined)	85	250	100	87	250	99
Edema	1 (1%)	23 (9%)	10 (10%)	2 (2%)	14 (6%)	2 (2%)
Large intestine (No. examined)	85	250	100	87	250	99
Parasitism	3 (4%)	0	0	0	0	0
Colon (No. examined)	85	250	100	87	250	99
Parasitism	0	11 (4%)	0	0	6 (2%)	1 (1%)
Cecum (No. examined)	85	250	100	87	250	99
Edema	0	5 (2%)	0	0	0	0
Inflammation	2 (2%)	1 (<1%)	0	0	3 (1%)	3 (3%)

III. RESULTS

Integumentary System: The incidences of keratoacanthomas of the integumentary system in male rats in the IR and IR/PW groups were significantly greater than that in the controls (Table 15).

Clitoral Gland: The incidence of carcinomas or squamous cell carcinomas (combined) in the female IR group (but not the IR/PW group) was

significantly greater than that in the controls (Table 16).

Adrenal Gland: The incidence of pheochromocytomas or malignant pheochromocytomas (combined) in the male IR/PW group (32/100, 32%) but not in the IR group (63/250, 25%) was significantly greater than that in the controls (17/85, 20%).

TABLE 15. ANALYSIS OF INTEGUMENTARY SYSTEM TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS (a)

	Untreated Control	IR (b)	IR/PW	IR vs IR/PW
Keratoacanthoma				
Overall Rates	1/88 (1%)	19/250 (8%)	8/100 (8%)	
Adjusted Rates	3.2%	23.9%	32.7%	
Terminal Rates	0/7 (0%)	3/29 (10%)	3/11 (27%)	
Life Table Test		P=0.039	P=0.048	P=0.506
Incidental Tumor Test		P=0.027	P=0.026	P=0.512

(a) The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes).

(b) Administered 1% intermediate-range (IR) chrysotile asbestos in the diet

TABLE 16. ANALYSIS OF CLITORAL GLAND TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

	Untreated Control	IR (a)	IR/PW	IR vs IR/PW
Carcinoma				
Overall Rates	0/88 (0%)	16/250 (6%)	4/100 (4%)	
Carcinoma or Squamous Cell Carcinoma				
Overall Rates	1/88 (1%)	18/250 (7%)	4/100 (4%)	
Adjusted Rates	3.2%	26.1%	12.6%	
Terminal Rates	0/10 (0%)	5/29 (17%)	0/11 (0%)	
Life Table Test		P=0.037	P=0.214	P=0.218N
Incidental Tumor Test		P=0.031	P=0.247	P=0.186N

(a) Administered 1% intermediate-range (IR) chrysotile asbestos in the diet

Decreased Incidence of Primary Neoplasms: The only organ that showed a decreased tumor incidence in the IR-chrysotile groups compared with the controls was the pituitary gland in female rats (controls--53/87, 61%; IR--117/249, 47%; IR/PW--51/100, 51%)

Liver: The incidences of cystic degeneration in the male IR and IR/PW groups were greater than those in the controls (male: control, 4/85, 5%; IR, 44/250, 18%; IR/PW, 21/100, 21%; female: control, 0/87; IR, 0/250; IR/PW, 2/99, 2%).

Prostate: The incidences of inflammation (acute, acute focal, suppurative, acute/chronic, or chronic) or abscess in the IR and IR/PW groups were greater than that in the controls (control, 17/85, 20%; IR, 87/249, 35%; IR/PW, 45/99, 45%). The incidence of hyperplasia (NOS, focal, or epithelial) was increased in the IR group as compared with that in the controls (control, 2/85, 2%; IR, 31/249, 12%; IR/PW, 3/99, 3%).

Lymph nodes: The incidence of hyperplasia (lymphoid, reticulum, and plasma cell) in the mandibular lymph node of the male rats was greater in the IR (57/250, 23%) and IR/PW groups (47/100, 47%) than in the concurrent controls (12/88, 14%). Similar types of hyperplasia were not observed in other lymph nodes (cervical, mediastinal, celiac, pancreatic, mesenteric, ileocolic, iliac, renal, or axillary) in the males or in any lymph node in IR-exposed female rats.

The incidences of pigmentation in the mediastinal lymph node of the male IR group (58/250, 23%) and IR/PW group (41/100, 41%) were increased as compared with the control group (5/85, 6%). A similar observation was noted in the mesenteric lymph nodes (IR: 28/250, 11%; IR/PW: 28/100, 28%; control: 0/85) and possibly the pancreatic lymph node (IR: 14/250, 6%; IR/PW: 6/100, 6%; control: 0/85).

The incidence of pigmentation was increased in certain lymph nodes of female IR-exposed rats:

mediastinal (IR: 91/250, 36%; IR/PW: 39/99, 39%; control: 22/87, 25%); pancreatic (IR: 19/250, 8%; IR/PW: 5/99, 5%; control: 0/87); and mesenteric (IR: 40/250, 16%; IR/PW: 4/99, 4%; control: 10/87, 11%).

DMH With and Without Intermediate-Range Chrysotile Asbestos

DMH was associated with increased incidences of neoplasms in multiple organs: skin, liver, kidney, pancreas, thyroid gland, Zymbal gland, hematopoietic system, and gastrointestinal tract (Tables 17 and 18). The only significant differences in the incidences of neoplasms between the DMH group and the IR/DMH group were observed in the kidneys of female rats and the thyroid gland of male rats (Tables 19 and 20).

Large Intestine: The incidences of adenomatous polyps, mucinous cystadenocarcinomas, and adenomatous polyps, adenocarcinomas, or mucinous cystadenocarcinomas (combined) in DMH and IR plus DMH groups were comparable (Table 17) in male (DMH, 32%; IR plus DMH, 35%) and female (DMH, 37%; IR plus DMH, 35%) rats.

Kidney: The incidence of mixed malignant tumors of the kidney in female rats that received IR chrysotile plus DMH was significantly ($P < 0.05$) greater than that in the group that received DMH alone (Table 19).

Thyroid Gland: The incidence of follicular cell adenomas in male rats that received IR chrysotile asbestos plus DMH was significantly greater than in those that received DMH without IR chrysotile. The incidence of follicular cell carcinomas in male rats receiving DMH was approximately the same as that in male rats that received both DMH and IR chrysotile asbestos. The incidences of follicular cell adenomas, follicular cell carcinomas, and follicular cell adenomas or carcinomas (combined) in males that received IR chrysotile asbestos plus DMH were significantly ($P < 0.05$) greater than those in the controls (Table 20).

**TABLE 17. SUMMARY OF GASTROINTESTINAL TUMORS IN RATS ADMINISTERED
1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE WITH AND WITHOUT INTERMEDIATE-RANGE
CHRYSOTILE ASBESTOS**

	Male		Female	
	DMH (a)	IR + DMH (b)	DMH	IR + DMH
Tongue				
Squamous cell papilloma	0/125 (0%)	1/175 (1%)	1/125 (1%)	0/175 (0%)
Squamous cell carcinoma	0/125 (0%)	0/175 (0%)	1/125 (1%)	0/175 (0%)
Small intestine, Site unknown				
Mucinous cystadenocarcinoma	0/125 (0%)	0/175 (0%)	0/125 (0%)	1/175 (1%)
Duodenum				
Adenocarcinoma	0/125 (0%)	1/175 (1%)	0/125 (0%)	0/175 (0%)
Mucinous cystadenocarcinoma	0/125 (0%)	1/175 (1%)	2/125 (2%)	2/175 (1%)
Signet ring carcinoma	0/125 (0%)	1/175 (1%)	0/125 (0%)	2/175 (1%)
Jejunum				
Adenomatous polyp	0/125 (0%)	0/175 (0%)	0/125 (0%)	1/175 (1%)
Adenocarcinoma	0/125 (0%)	1/175 (1%)	0/125 (0%)	0/175 (0%)
Mucinous cystadenocarcinoma	0/125 (0%)	1/175 (1%)	0/125 (0%)	0/175 (0%)
Ileum				
Adenocarcinoma in adenomatous polyp	0/125 (0%)	0/175 (0%)	0/125 (0%)	1/175 (1%)
Total small intestine				
Adenomatous polyp	0/125 (0%)	0/175 (0%)	0/125 (0%)	1/175 (1%)
Adenocarcinoma	0/125 (0%)	2/175 (1%)	0/125 (0%)	0/175 (0%)
Mucinous cystadenocarcinoma	0/125 (0%)	2/175 (1%)	2/125 (2%)	3/175 (3%)
Adenocarcinoma in adenomatous polyp	0/125 (0%)	0/175 (0%)	0/125 (0%)	1/175 (1%)
Signet ring carcinoma	0/125 (0%)	1/175 (1%)	0/125 (0%)	2/175 (1%)
Colon				
Adenomatous polyp	0/125 (0%)	0/175 (0%)	2/125 (2%)	1/175 (1%)
Mucinous cystadenocarcinoma	0/125 (0%)	0/175 (0%)	0/125 (0%)	1/175 (1%)
Cecum				
Adenocarcinoma	1/125 (1%)	0/175 (0%)	1/125 (1%)	0/175 (0%)
Adenomatous polyp	0/125 (0%)	1/175 (1%)	0/125 (0%)	3/175 (2%)
Mucinous cystadenocarcinoma	4/125 (3%)	4/175 (2%)	(c) 8/125 (6%)	(c) 8/175 (5%)
Signet ring carcinoma	0/125 (0%)	0/175 (0%)	1/125 (1%)	0/175 (0%)
Ascending colon				
Adenocarcinoma,	0/125 (0%)	1/175 (1%)	0/125 (0%)	3/175 (2%)
Adenomatous polyp	3/125 (2%)	3/175 (2%)	2/125 (2%)	6/175 (3%)
Adenocarcinoma in adenomatous polyp	0/125 (0%)	1/175 (1%)	0/125 (0%)	0/175 (0%)
Mucinous cystadenocarcinoma	3/125 (2%)	(c) 11/175 (6%)	5/125 (4%)	6/175 (3%)
Signet ring carcinoma	1/125 (1%)	0/175 (0%)	1/125 (1%)	2/175 (1%)
Leiomyosarcoma	0/125 (0%)	0/175 (0%)	1/125 (1%)	0/175 (0%)
Transverse colon				
Adenocarcinoma	1/125 (1%)	0/175 (0%)	0/125 (0%)	0/175 (0%)
Adenomatous polyp	4/125 (3%)	6/175 (3%)	(c) 9/125 (7%)	(c) 8/175 (5%)
Adenocarcinoma in adenomatous polyp	0/125 (0%)	0/175 (0%)	0/125 (0%)	4/175 (2%)
Mucinous cystadenocarcinoma	0/125 (0%)	0/175 (0%)	0/125 (0%)	1/175 (1%)
Descending colon				
Adenomatous polyp	(c) 24/125 (19%)	(c) 37/175 (21%)	(c) 24/125 (19%)	(c) 30/175 (17%)
Adenocarcinoma in adenomatous polyp	0/125 (0%)	2/175 (1%)	2/125 (2%)	2/175 (1%)
Mucinous cystadenocarcinoma	0/125 (0%)	4/175 (2%)	1/125 (1%)	0/175 (0%)
Signet ring carcinoma	0/125 (0%)	1/175 (1%)	0/125 (0%)	0/175 (0%)
Total large intestine				
Adenomatous polyp	(c) 31/125 (25%)	(c) 45/175 (26%)	(c) 33/125 (26%)	(c) 46/175 (26%)
Adenocarcinoma	2/125 (2%)	1/175 (1%)	1/125 (1%)	3/175 (2%)
Mucinous cystadenocarcinoma	(c) 7/125 (6%)	(c) 19/175 (11%)	(c) 14/125 (11%)	(c) 16/175 (9%)
Adenocarcinoma in adenomatous polyp	0/125 (0%)	3/175 (2%)	2/125 (2%)	6/175 (3%)
Signet ring carcinoma	1/125 (1%)	1/175 (1%)	2/125 (2%)	2/175 (1%)
Leiomyosarcoma	0/125 (0%)	0/175 (0%)	1/125 (1%)	0/175 (0%)
Anus				
Adenomatous polyp	1/125 (1%)	0/175 (0%)	0/125 (0%)	0/175 (0%)

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

(b) Administered 1% intermediate-range (IR) chrysotile asbestos in the diet and DMH by gavage

(c) Incidence significantly greater than that in the controls (P < 0.05)

TABLE 18. SUMMARY OF NONGASTROINTESTINAL TUMORS IN RATS ADMINISTERED 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE WITH AND WITHOUT INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

	Male		Female	
	DMH (a)	IR + DMH (b)	DMH	IR + DMH
Integumentary system				
Keratoacanthoma	(c*) 6/125 (5%)	(c) 11/175 (6%)	0/125 (0%)	2/175 (1%)
Hematopoietic system				
Leukemia	(c*) 42/125 (34%)	(c*) 71/175 (41%)	(c) 70/125 (56%)	(c) 93/175 (53%)
Liver				
Neoplastic nodule	(c*) 12/125 (10%)	10/175 (6%)	(c) 12/125 (10%)	(c) 21/175 (12%)
Hepatocellular carcinoma	(c) 17/125 (14%)	(c) 20/175 (11%)	(c) 12/125 (10%)	(c) 19/175 (11%)
Pancreas				
Acinar cell adenoma	7/124 (6%)	(c) 14/174 (8%)	1/124 (1%)	0/175 (0%)
Kidney				
Mixed tumor, malignant	0/125 (0%)	1/175 (1%)	(c) 13/125 (10%)	(c,d) 34/175 (19%)
Thyroid gland				
Follicular cell adenoma	1/124 (1%)	(c,d) 14/175 (8%)	(c*) 7/124 (6%)	9/174 (5%)
Follicular cell carcinoma	8/124 (6%)	(c*) 14/175 (8%)	(c*) 5/124 (4%)	(c*) 7/174 (4%)
Zymbal gland				
Squamous cell papilloma, adenoma	1/125 (1%)	3/175 (2%)	1/125 (1%)	3/175 (2%)
Squamous cell carcinoma or carcinoma	(c) 18/125 (14%)	(c) 24/175 (14%)	(c) 14/125 (11%)	(c) 26/175 (15%)

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

(b) Administered 1% intermediate-range (IR) chrysotile asbestos in the diet and DMH by gavage

(c) Incidence significantly greater than that in the controls ($P < 0.05$); (c*) differences significant ($P < 0.05$) by life table analysis only

(d) Incidence significantly greater than that in the DMH group ($P < 0.05$)

TABLE 19. ANALYSIS OF KIDNEY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS WITH 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE

	Untreated Control	DMH (a)	IR + DMH (b)	DMH vs IR + DMH
Mixed Tumor, Malignant				
Overall Rates	0/87 (0%)	13/125 (10%)	34/175 (19%)	
Adjusted Rates	0.0%	21.8%	30.0%	
Terminal Rates	0/55 (0%)	1/16 (6%)	0/27 (0%)	
Life Table Test		$P < 0.001$	$P < 0.001$	$P = 0.043$
Incidental Tumor Test		$P = 0.073$	$P = 0.022$	$P = 0.021$

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

(b) Administered 1% intermediate-range (IR) chrysotile asbestos in the diet and DMH by gavage

TABLE 20. ANALYSIS OF THYROID GLAND TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS WITH 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE

	Untreated Control	DMH (a)	IR + DMH (b)	DMH vs IR + DMH
Follicular Cell Adenoma				
Overall Rates	1/84 (1%)	1/124 (1%)	14/175 (8%)	
Adjusted Rates	2.1%	2.8%	28.5%	
Terminal Rates	0/26 (0%)	0/18 (0%)	2/18 (11%)	
Life Table Test		P=0.720	P=0.001	P=0.003
Incidental Tumor Test		P=0.752	P=0.011	P=0.006
Follicular Cell Carcinoma				
Overall Rates	5/84 (6%)	8/124 (6%)	14/175 (8%)	
Adjusted Rates	13.1%	29.9%	19.7%	
Terminal Rates	2/26 (8%)	4/18 (22%)	0/18 (0%)	
Life Table Test		P=0.130	P=0.045	P=0.299
Incidental Tumor Test		P=0.171	P=0.246	P=0.403
Follicular Cell Adenoma or Carcinoma				
Overall Rates	6/84 (7%)	9/124 (7%)	28/175 (16%)	
Adjusted Rates	14.9%	31.8%	42.7%	
Terminal Rates	2/26 (8%)	4/18 (22%)	2/18 (11%)	
Life Table Test		P=0.138	P<0.001	P=0.010
Incidental Tumor Test		P=0.184	P=0.009	P=0.020

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

(b) Administered 1% intermediate-range (IR) chrysotile asbestos in the diet and DMH by gavage

IV. DISCUSSION AND CONCLUSIONS

IV. DISCUSSION AND CONCLUSIONS

Two types (short-range [SR] and intermediate-range [IR] fiber length) of chrysotile asbestos were administered at a level of 1% in the diet to male and female F344/N rats for their lifetime, including exposure of their dams to the test material. A further study included two groups (control and IR chrysotile exposed) of weanling rats exposed to five biweekly doses of 1,2-dimethylhydrazine dihydrochloride (DMH), a known intestinal carcinogen in rodents, to investigate the promotional or cocarcinogenic effects of DMH and IR chrysotile asbestos.

The clinicopathologic results in this study showed that the ingestion of either SR or IR chrysotile asbestos did not adversely affect the fertility of the mothers or the litter size of the F₁ animals. The average weight of the offspring at birth from mothers exposed to either SR or IR chrysotile asbestos before and during gestation was similar to that of the offspring of nonexposed mothers. At weaning, however, the average weight of the offspring of SR chrysotile-exposed mothers was 8% greater, and that of the offspring of IR chrysotile-exposed mothers 13% lower, than that of the offspring of the nonexposed mothers.

The IR chrysotile asbestos-exposed rats remained smaller throughout their lives, although the weight gains paralleled those of the nonexposed rats. Similar findings were reported in previous NTP ingestion studies in rats of amosite (NTP TR 279) and crocidolite (NTP TR 280, in press) asbestos, in which the offspring of exposed mothers were also smaller at weaning and remained so throughout their lives. The cause of the decreased body weight gain is unknown, but the IR chrysotile rats consumed slightly less feed during the study (Appendix H, Tables H3 and H4).

The mean body weight of the rats exposed to the preweaning (PW) gavage and subsequently to IR chrysotile asbestos was slightly greater than that of those exposed to IR chrysotile alone. This may be related to the high rate of mortality (approximately 50%) induced in the neonates by the PW technique, which would allow the remaining pups more milk during lactation. For neonates, the physical stress of gavaging routinely results in a high rate of mortality.

This high mortality resulted in a group of test animals that may not be representative of the group (i.e., biased toward more hardy individuals). Exposure to DMH caused a small reduction in body weight gain in male and female rats.

No clinical signs were observed that could be attributed to the ingestion of either SR or IR chrysotile asbestos. Starting at 9 months of age, the DMH exposed rats showed signs attributable to DMH-related neoplasia, but no difference was noted between the DMH and IR plus DMH groups.

The survival of the rats (control and chrysotile-exposed) in these studies compares favorably with other NTP studies. The survival of males at 111 weeks of age was: untreated control, 67%; IR chrysotile, 73%; and IR/PW, 78%. The percentages of female rats alive at this time were: control, 72%; IR chrysotile, 72%; and IR/PW, 73%. In reviewing 25 recent NTP feed studies, Haseman (1983a) found an average of 66% of control males and 73% of control females alive at 112 weeks of age. In most 2-year carcinogenesis studies involving rats, females survive longer than males.

The survival of rats exposed to DMH was significantly lower than that of the untreated controls and the chrysotile groups. Both males and females that received IR chrysotile and DMH showed similar survival rates throughout the studies compared with those that received DMH alone.

Based on these observations, it appears that the rats could possibly have tolerated a higher level of asbestos exposure, although a level of 1% in the diet for the entire life of the animal is considered substantial. This dose level ranges from 1.6×10^5 to 1.6×10^{10} times the projected level of possible human exposure (DHEW Committee to Coordinate Toxicology and Related Programs, Subcommittee on Asbestos Protocols, unpublished data).

Ingestion of SR chrysotile asbestos over the lifetime of these rats did not cause any biologically significant increase of neoplasms at

IV. DISCUSSION AND CONCLUSIONS

any anatomic site when compared with the concurrent controls. Mesotheliomas (all sites) appeared to be increased (not statistically significant, $P > 0.05$) in male rats receiving SR chrysotile alone compared with the controls (6% vs 2%), but the incidence in the control group was somewhat low compared with the IR chrysotile control group (6%) and pooled male control groups from all the NTP oral asbestos studies (24/529, 4.5% [Appendix F]). Therefore, the biologic importance of this finding is discounted. SR chrysotile also did not produce any apparent increase in nonneoplastic disease. In summary, the ingestion of short-range chrysotile asbestos did not cause any adverse effect in either male or female F344/N rats.

Ingestion of IR chrysotile asbestos was associated with an increased incidence of neoplasia. Since the gastrointestinal tract was designated as a possible target organ based on epidemiologic studies in humans (Cooper et al., 1979) and because the test material was administered via the diet, the incidence of gastrointestinal neoplasms was examined in particular detail. For this reason, the increase in adenomatous polyps, which were grossly visible in the large intestine of IR chrysotile-exposed male rats, deserves special attention. These lesions are uncommon in standard 2-year carcinogenesis studies: 1/1,727 for male and 0/1,777 for female F344/N rats (Haseman et al., 1984). Overall, the incidence in dosed male rats in this study was low (9/250, 4%) and not statistically significant ($P = 0.08$) compared with the concurrent controls (0/85). Despite the apparent marginal significance ($P < 0.10$) of the large intestine tumor incidence in the IR chrysotile groups relative to concurrent controls, the actual level of significance associated with this comparison is greater than the nominal level because of the rarity of adenomatous polyps (Haseman, 1983b). For example, if the background incidence of large intestine tumors in lifetime studies of male F344/N rats is 0.6% (as suggested by the 3/524 rate observed in the pooled asbestos controls), then the probability of observing 9 or more (out of 250) adenomatous polyps of the large intestine by chance alone is less than 1 in 10,000. Further, the overall incidence of adenomatous polyps of the large

intestine (9/250) was significant ($P = 0.003$) relative to the rate in the pooled controls (3/524).

It is noteworthy that the other NTP asbestos studies were carried out at the same laboratory, conducted during an overlapping time frame, and used animals that were received from the same source and exposed to the same environmental conditions. The post mortem examinations were conducted with an identical protocol by the same technicians; the histopathologic examination used the same morphologic classification; and every neoplasm in question was reviewed by the Quality Assurance contractor and the NTP Pathology Working Group. It is particularly appropriate in this study, therefore, to give more credence than usual to the historical data. Further evidence for the relevance of this observation was the occurrence of adenomatous polyps in 2/100 male IR/PW chrysotile asbestos-exposed rats. Also, an additional 4/250 IR chrysotile male rats had neoplasms of similar histogenesis in the small intestine or glandular stomach, whereas none was found in the concurrent control group. These factors support the conclusion that the observed effect in the gastrointestinal tract, particularly the large intestine, of the male IR chrysotile asbestos group is quite unlikely to be due to chance alone.

To place this observation in proper context: First, adenomatous polyps are considered benign neoplasms. Second, no malignant epithelial neoplasms were observed in the large intestine in this study. Third, there was no evidence that any of the polyps had progressed to carcinoma, although this progression occurs with known intestinal carcinogens (e.g., in the DMH portion of this study). Fourth, because this was a lifetime study, more time was available for malignant progression. Fifth, an increase in gastrointestinal epithelial tumors was not observed in female IR chrysotile rats.

The above observations, which show a carcinogenic response to IR chrysotile but not to SR chrysotile asbestos, can probably be explained by the studies of Stanton et al. (1981) in which various types of natural and manmade mineral fibers were implanted into the pleural

IV. DISCUSSION AND CONCLUSIONS

cavity of rats. Using pleural fibrosis and mesothelioma as end points, the investigators observed a correlation between fiber length and width and the fibers' carcinogenic potential. To be carcinogenic, fibers needed to be greater than 8 μm in length and less than 1.5 μm in diameter. Fibers of this type have been referred to as "S" (for Stanton) fibers (Harington, 1975). A far greater number of such "S" fibers were present in the IR than in the SR chrysotile asbestos used in these studies. It is also noteworthy that, when a chrysotile fiber breaks (in vivo or in vitro), it fractures in a longitudinal fashion, theoretically yielding more fibers of the "S" type and thus increasing the carcinogenic potential.

Keratoacanthomas of the skin were significantly increased in male IR chrysotile-exposed rats (19/250, 8%) and in the IR/PW groups (8/100, 8%) as compared with the controls (1/88, 1%). This observation deserves some consideration, since the increase was observed in both IR chrysotile studies; however, the incidence does not greatly exceed the mean control rates observed in all NTP rat oral asbestos studies: 20/529, 4% (Appendix F). Thus, this increase is not clearly related to the administration of IR chrysotile asbestos. The chrysotile asbestos used in these studies was incorporated into solid feed pellets, but the potential for skin exposure remains because asbestos particles are dislodged during eating. Nevertheless, even in inhalation studies in which considerable skin exposure also occurs, no increases in this lesion have been reported. If keratoacanthomas are actually related to chrysotile asbestos, which seems unlikely, direct exposure of the skin rather than a systemic route is the most plausible mechanism for induction of these neoplasms.

The incidence of neoplasms in the clitoral gland of female IR (18/250, 7%) and IR/PW (4/100, 4%) rats was increased compared with the concurrent controls (1/88, 1%). Only in the IR chrysotile alone group was the incidence significantly ($P < 0.05$) increased. The incidence observed in the IR chrysotile groups did not differ significantly from the rate observed in all NTP oral asbestos studies (22/529, 4%). Moreover, no increase in neoplasia was observed in the male preputial gland (histogenetically related to the clitoral gland). Thus, this increase

is not clearly related to the administration of IR chrysotile. Again, if these neoplasms were related to IR chrysotile, a direct route of exposure is the most probable cause.

Pheochromocytomas occurred at a greater incidence in male rats exposed to IR (63/250, 25%) and IR/PW (32/100, 32%) chrysotile than in the controls (17/85, 20%). Only in the IR/PW chrysotile group, however, was the incidence statistically significant (incidental tumor test, $P = 0.02$). These rates are also comparable to those observed in all NTP oral asbestos studies (158/525, 30%). Therefore these neoplasms are not considered to be related to IR chrysotile asbestos exposure.

Nonneoplastic lesions that showed increased incidences in asbestos-exposed groups include cystic degeneration of the liver and inflammation of the prostate in male IR and IR/PW chrysotile groups. An explanation for these findings is not apparent, and their biologic relevance in this study is unknown.

Rats exposed to DMH exhibited neoplasia at those sites known as targets for this chemical: the gastrointestinal tract, Zymbal gland, liver, and kidney. In addition, the appearance of the DMH-induced neoplasms was comparable to those described previously in rats exposed to hydrazine compounds (Pozharisski, 1975). The incidence of intestinal neoplasia was slightly greater (male 32%, female 37%) in the DMH groups than the predicted incidence of $15\% \pm 5\%$ based on a preliminary dose response study (McConnell et al., 1980). In the previous NTP oral amosite asbestos study in rats, in which DMH was administered at the same dose as in this study, the rate of intestinal neoplasia was 60-70%. A similar study of IR chrysotile asbestos and DMH in hamsters failed to elicit any neoplastic response in the intestine (NTP TR 246, in press). Apparently, the neoplastic dose response to DMH is relatively steep and duplication of a given incidence, particularly at the low end of the dose-response curve, is difficult to produce.

In addition to the previously mentioned neoplasms, DMH (with and without IR chrysotile) was also associated with an apparent

IV. DISCUSSION AND CONCLUSIONS

increase in leukemia (decreased latency) in both male and female rats. The difference was statistically significant ($P < 0.05$, life table analysis) compared with the concurrent controls, and the significance was enhanced when compared with the combined incidence of leukemia in the control groups from the other NTP oral asbestos studies. Although leukemia is not usually considered a response to DMH exposure, most DMH studies use a dose that produces a high incidence of lethal neoplasms in other organs. In such studies, the possibility exists that a leukemic effect might not be manifested or recognized due to the lethality of other types of neoplasms. Therefore, the increased incidence in leukemia in female rats in this study is considered to be related to DMH exposure, and IR chrysotile asbestos is not considered to affect its development.

If IR chrysotile has a cocarcinogenic or protective effect on DMH, it should have been manifested in one of the target organs. This relationship is not apparent in the intestine, liver, or Zymbal gland. There was a significant ($P < 0.05$) increase, however, in neoplasms of the kidney in the IR plus DMH rats compared with the female rats that received DMH alone. Although the observation cannot be totally discounted, its biologic significance is questionable in light of the lack of a tumor-enhancing effect in the other three potential target organs.

The only other tumor incidence that was significantly ($P < 0.05$) different in DMH groups as compared with IR plus DMH groups was that of thyroid follicular cell neoplasms (adenomas alone and adenomas or carcinomas combined) in male rats. The incidence in the DMH group was identical to that of the untreated controls, and there was no tumor-enhancing effect in females. For these reasons and because the thyroid gland is not usually affected by administration of either DMH or asbestos, this increase probably lacks biologic significance.

In summary, IR chrysotile asbestos did not appear to influence the rate of neoplasia induced by DMH, especially in the primary target organ (i.e., intestine). In contrast, IR chrysotile alone caused a slight increase in the incidence of adenomatous polyps in the large intestine of male rats. The keratoacanthomas of the skin in

male rats and clitoral gland neoplasms in female rats were probably not related to IR chrysotile exposure.

Studies involving the long-term ingestion of other types of asbestos are few. Donham et al. (1980) reported equivocal tumor results in the intestine of F344 rats that were fed a diet containing 10% chrysotile for their lifetime. Although a significant ($P < 0.05$) increase in the number of tumors in exposed animals was not observed, the authors believed that there was a trend toward increased colon lesions in general. They cited evidence of penetration of asbestos into the colonic mucosa and possible cytotoxicity to colonic tissues and suggested a relationship to peritoneal mesothelioma. Another equivocal study is that reported by Gibel et al. (1976), who described increases in malignant tumors in the lung, kidneys, liver, and reticuloendothelial system but not in intestinal neoplasia in Wistar rats fed asbestos filter material (20 mg/day) for 8-14 months. Cunningham et al. (1977), reported two studies (24 months or 30 months) in which Wistar male rats were administered 1% chrysotile asbestos in the diet. These authors concluded that trace amounts of ingested asbestos can penetrate the walls of the gastrointestinal tract, but evidence of carcinogenicity was inconclusive. No evidence of carcinogenicity was found by Gross et al. (1974), who fed rats a diet containing 5% chrysotile asbestos for 21 months. Bolton et al. (1982) exposed groups of 22-24 male HAN SPF Wistar-derived rats to amosite, crocidolite, or UICC standard reference chrysotile (similar to IR chrysotile) asbestos in the diet at a rate of approximately 250 mg/rat per week for 25 months and monitored the rats for the remainder of their lifespan. They concluded that no significant adverse effects occurred as a result of ingestion of any of these forms of asbestos. Previous NTP oral asbestos studies in rats in which amosite (NTP TR 279, in press) or crocidolite (NTP TR 280, in press) was administered with and without DMH did not show any indication of a carcinogenic response.

An oral asbestos study in hamsters was reported by Smith et al. (1980). Groups of 30 male and 30 female hamsters were exposed via drinking water for their lifetime to amosite asbestos, mine tailings, beach rock, or Lake Superior drinking water. No adverse effects on body

IV. DISCUSSION AND CONCLUSIONS

weight or survival were observed for any of the groups. One peritoneal mesothelioma, one pulmonary carcinoma, and two early squamous cell carcinomas of the nonglandular stomach were found in the hamsters exposed to amosite. The authors concluded that the study was "essentially negative." A subsequent study in rats in which similar materials were used also failed to elicit a carcinogenic response (Hilding et al., 1981)

In companion studies to the rat studies in this report, Syrian golden hamsters were exposed to either short-range or intermediate-range chrysotile asbestos at a rate of 1% in the diet for their natural lifespan (NTP TR 246, in press). In both studies, no adverse effects were observed for body weight gain or survival, and no asbestos-related neoplasms were diagnosed. An ingestion study of amosite asbestos in hamsters using a similar design to this study did not demonstrate a carcinogenic response (NTP, 1983).

Except for the studies of Donham et al. (1980), Smith et al. (1980), Bolton et al. (1982), and the NTP studies, the other studies were conducted with relatively small numbers of animals. Also, some were conducted for an insufficient period of time to adequately test the carcinogenic potential of ingested asbestos.

The inhalation of asbestos fibers is clearly associated with lung cancer in humans (Selikoff, 1980) and in rats (Wagner et al., 1974). In the present studies chrysotile asbestos administered in the feed was associated with adenomatous polyps of the large intestine in male F344/N rats. The carcinogenic potential of chrysotile asbestos may be related to its cytogenetic effects. In support of this view, Oshimura et al. (1984) found an association between chrysotile asbestos and the induction of chromosomal alterations (chromosomal aberrations, polyploidy, and aneuploidy) in Syrian hamster embryo (SHE)

cells. By electron microscopy, Hesterberg et al. (1982) demonstrated that asbestos fibers accumulated in the perinuclear region of SHE cells within 24-48 hours after exposure in vitro. Chromosomal aberrations and changes in the number of chromosomes are associated with a wide variety of rodent and human tumors (Sasaki, 1982; Yunis, 1983), and several mechanisms have been described to explain how certain chromosomal alterations may induce neoplasia (Ohno, 1977; Levan, 1981; Cavenne et al., 1983; Klein, 1983; Sandberg, 1983; Tsutsui et al., 1983). The occurrence of chromosomal aberrations at or near the site of cellular proto-oncogenes provides additional support for the concept that certain chromosomal changes may lead to cancer (Rowley, 1983). In summary, the current evidence suggests that the ability of chrysotile asbestos to induce chromosomal alterations may be a possible mechanism by which chrysotile asbestos induces neoplasia.

Conclusions: Under the conditions of these lifetime studies, short-range and intermediate-range chrysotile asbestos did not induce overt toxicity and did not affect survival when ingested at a level of 1% in the diet by male and female F344/N rats. There was *no evidence of carcinogenicity** in male or female rats exposed to SR chrysotile asbestos or in female rats exposed to IR chrysotile asbestos. There was *some evidence of carcinogenicity* in male rats exposed to IR chrysotile asbestos as indicated by an increased incidence of adenomatous polyps in the large intestine. The cocarcinogenesis studies of 1,2-dimethylhydrazine dihydrochloride and IR chrysotile asbestos were considered inconclusive for determining whether IR chrysotile asbestos had either a tumor-enhancing or protective effect, although an increased incidence of neoplasms was observed in the kidneys of female rats exposed to DMH plus IR chrysotile as compared with those exposed to DMH alone

*Categories of evidence of carcinogenicity are defined in the Note to the Reader on page 2.

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V. REFERENCES

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APPENDIX A

**SUMMARY OF THE INCIDENCE OF NEOPLASMS
IN RATS IN THE LIFETIME FEED STUDIES
OF SHORT-RANGE CHRYSOTILE ASBESTOS**

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS

	CONTROL (UNTR)	SHORT RANGE
ANIMALS INITIALLY IN STUDY	88	250
ANIMALS NECROPSIED	88	250
ANIMALS EXAMINED HISTOPATHOLOGICALLY	88	248
INTEGUMENTARY SYSTEM		
*HARDERIAN GLAND	(88)	(250)
FIBROUS HISTIOCYTOMA, MALIGNANT	1 (1%)	
*MULTIPLE ORGANS	(88)	(250)
FIBROUS HISTIOCYTOMA, MALIGNANT	1 (1%)	1 (0%)
*SKIN	(88)	(250)
SQUAMOUS CELL PAPILLOMA	1 (1%)	7 (3%)
SQUAMOUS CELL CARCINOMA		3 (1%)
BASAL-CELL TUMOR		5 (2%)
BASAL-CELL CARCINOMA	3 (3%)	12 (5%)
TRICHOEPITHELIOMA		1 (0%)
SEBACEOUS ADENOMA		1 (0%)
KERATOACANTHOMA	5 (6%)	14 (6%)
FIBROUS HISTIOCYTOMA		1 (0%)
FIBROUS HISTIOCYTOMA, MALIGNANT	1 (1%)	1 (0%)
*SUBCUT TISSUE	(88)	(250)
SQUAMOUS CELL CARCINOMA, INVASIVE	1 (1%)	
SARCOMA, NOS		3 (1%)
FIBROMA	13 (15%)	25 (10%)
FIBROSARCOMA	4 (5%)	6 (2%)
FIBROUS HISTIOCYTOMA, MALIGNANT		1 (0%)
MYXOSARCOMA		1 (0%)
LIPOMA		1 (0%)
LIPOSARCOMA	1 (1%)	2 (1%)
LEIOMYOSARCOMA, INVASIVE		1 (0%)
NEUROFIBROMA	1 (1%)	9 (4%)
NEUROFIBROSARCOMA	3 (3%)	2 (1%)
RESPIRATORY SYSTEM		
*NASAL TURBINATE	(88)	(250)
CARCINOMA, NOS		1 (0%)
SQUAMOUS CELL CARCINOMA		1 (0%)
#TRACHEA	(87)	(248)
FOLLICULAR-CELL CARCINOMA, INVASIVE		1 (0%)
C-CELL CARCINOMA, METASTATIC		1 (0%)
#LUNG	(88)	(247)
CARCINOMA, NOS, METASTATIC	1 (1%)	
SQUAMOUS CELL CARCINOMA, METASTATIC		3 (1%)
ALVEOLAR/BRONCHIOLAR ADENOMA		1 (0%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	2 (2%)	6 (2%)
C-CELL CARCINOMA, METASTATIC		2 (1%)
FIBROSARCOMA, METASTATIC		1 (0%)
LIPOSARCOMA, METASTATIC		4 (2%)
MESOTHELIOMA, METASTATIC		1 (0%)
OSTEOSARCOMA, METASTATIC		1 (0%)
HEMATOPOIETIC SYSTEM		
*MULTIPLE ORGANS	(88)	(250)
MALIGNANT LYMPHOMA, NOS		2 (1%)
MALIG. LYMPHOMA, UNDIFFER-TYPE		1 (0%)
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE	1 (1%)	1 (0%)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE	1 (1%)	1 (0%)
MYELOMONOCYTIC LEUKEMIA	1 (1%)	
MONOCYTIC LEUKEMIA	34 (39%)	105 (42%)
LEUKEMIA, MONONUCLEAR CELL	1 (1%)	1 (0%)

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
#BONE MARROW	(88)	(247)
LIPOSARCOMA, INVASIVE		1 (0%)
#SPLEEN	(88)	(247)
MESOTHELIOMA, METASTATIC		1 (0%)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE		1 (0%)
#MANDIBULAR L. NODE	(88)	(248)
CARCINOMA, NOS, METASTATIC		1 (0%)
C-CELL CARCINOMA, METASTATIC		1 (0%)
SARCOMA, NOS, INVASIVE		1 (0%)
FIBROSARCOMA, INVASIVE		1 (0%)
#CERVICAL LYMPH NODE	(88)	(248)
C-CELL CARCINOMA, METASTATIC		1 (0%)
#MEDIASTINAL LYMPH NODE	(88)	(248)
MESOTHELIOMA, METASTATIC	1 (1%)	1 (0%)
#ILEOCOLIC LYMPH NODE	(88)	(248)
SQUAMOUS CELL CARCINOMA, METASTATIC		1 (0%)
#RENAL LYMPH NODE	(88)	(248)
INTERSTITIAL-CELL TUMOR, METASTATIC		1 (0%)
#LIVER	(88)	(248)
MONOCYTIC LEUKEMIA	1 (1%)	3 (1%)
#THYMUS	(76)	(197)
CARCINOMA, NOS		1 (1%)
ADENOCARCINOMA, NOS	1 (1%)	
<hr/>		
CIRCULATORY SYSTEM		
*MULTIPLE ORGANS	(88)	(250)
HEMANGIOSARCOMA, METASTATIC		1 (0%)
*MEDIASTINUM	(88)	(250)
HEMANGIOSARCOMA		1 (0%)
*SKIN	(88)	(250)
HEMANGIOMA		1 (0%)
*SUBCUT TISSUE	(88)	(250)
HEMANGIOSARCOMA		2 (1%)
HEMANGIOPERICYTOMA, MALIGNANT	1 (1%)	
#SPLEEN	(88)	(247)
HEMANGIOMA		1 (0%)
HEMANGIOSARCOMA	2 (2%)	5 (2%)
#HEART	(88)	(247)
CARCINOMA, NOS, INVASIVE		1 (0%)
FIBROSARCOMA, METASTATIC		1 (0%)
#LIVER	(88)	(248)
HEMANGIOSARCOMA, METASTATIC		1 (0%)
<hr/>		
DIGESTIVE SYSTEM		
*HARD PALATE	(88)	(250)
SQUAMOUS CELL PAPILLOMA		1 (0%)
#SALIVARY GLAND	(87)	(243)
SARCOMA, NOS		1 (0%)
FIBROSARCOMA		3 (1%)
#LIVER	(88)	(248)
NEOPLASTIC NODULE	12 (14%)	17 (7%)
HEPATOCELLULAR CARCINOMA	3 (3%)	2 (1%)
C-CELL CARCINOMA, METASTATIC		1 (0%)
FIBROSARCOMA, METASTATIC		1 (0%)
#PANCREAS	(86)	(247)
ACINAR-CELL ADENOMA	7 (8%)	14 (6%)
MIXED TUMOR, BENIGN		3 (1%)
#STOMACH	(88)	(248)
SQUAMOUS CELL PAPILLOMA		1 (0%)
SQUAMOUS CELL CARCINOMA		1 (0%)
SARCOMA, NOS		1 (0%)

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
DIGESTIVE SYSTEM (Continued)		
#FORESTOMACH	(88)	(248)
SQUAMOUS CELL PAPILLOMA	1 (1%)	
#GASTRIC FUNDUS	(88)	(248)
CARCINOMA-IN-SITU, NOS		1 (0%)
#DUODENUM	(88)	(248)
ADENOMATOUS POLYP, NOS		1 (0%)
#JEJUNUM	(88)	(248)
MUCINOUS CYSTADENOCARCINOMA	1 (1%)	
#COLON	(87)	(248)
ADENOMATOUS POLYP, NOS		1 (0%)
LEIOMYOSARCOMA		1 (0%)
#CECUM	(87)	(248)
LIPOMA		1 (0%)
LEIOMYOSARCOMA		1 (0%)
#TRANSVERSE COLON	(87)	(248)
LEIOMYOSARCOMA	1 (1%)	
*ANUS	(88)	(250)
LEIOMYOSARCOMA, INVASIVE		1 (0%)
URINARY SYSTEM		
#KIDNEY	(88)	(248)
TUBULAR-CELL ADENOMA	1 (1%)	2 (1%)
TUBULAR-CELL ADENOCARCINOMA	1 (1%)	
MIXED TUMOR, MALIGNANT	1 (1%)	1 (0%)
#URINARY BLADDER	(85)	(247)
SQUAMOUS CELL PAPILLOMA		1 (0%)
TRANSITIONAL-CELL PAPILLOMA	1 (1%)	1 (0%)
ENDOCRINE SYSTEM		
#PITUITARY	(87)	(247)
CARCINOMA, NOS	1 (1%)	3 (1%)
ADENOMA, NOS	20 (23%)	42 (17%)
#ADRENAL	(88)	(248)
CORTICAL ADENOMA		5 (2%)
PHEOCHROMOCYTOMA	25 (28%)	73 (29%)
PHEOCHROMOCYTOMA, MALIGNANT	1 (1%)	7 (3%)
GANGLIONEUROMA		1 (0%)
#THYROID	(86)	(246)
FOLLICULAR-CELL ADENOMA	4 (5%)	13 (5%)
FOLLICULAR-CELL CARCINOMA	2 (2%)	12 (5%)
C-CELL ADENOMA	13 (15%)	28 (11%)
C-CELL CARCINOMA	11 (13%)	24 (10%)
FIBROSARCOMA, INVASIVE		1 (0%)
#PARATHYROID	(83)	(229)
ADENOMA, NOS	6 (7%)	4 (2%)
C-CELL CARCINOMA, INVASIVE	1 (1%)	
#PANCREATIC ISLETS	(86)	(247)
ISLET-CELL ADENOMA	6 (7%)	18 (7%)
ISLET-CELL CARCINOMA	3 (3%)	14 (6%)
REPRODUCTIVE SYSTEM		
*MAMMARY GLAND	(88)	(250)
ADENOMA, NOS		3 (1%)
ADENOCARCINOMA, NOS	3 (3%)	
PAPILLARY ADENOMA		1 (0%)
PAPILLARY CYSTADENOMA, NOS		1 (0%)
FIBROADENOMA	11 (13%)	27 (11%)

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME
FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
REPRODUCTIVE SYSTEM (Continued)		
*PREPUTIAL GLAND	(88)	(250)
CARCINOMA, NOS	4 (5%)	8 (3%)
SQUAMOUS CELL CARCINOMA	2 (2%)	5 (2%)
ADENOMA, NOS		1 (0%)
KERATOACANTHOMA		1 (0%)
#PROSTATE	(87)	(247)
ADENOMA, NOS		2 (1%)
#TESTIS	(87)	(246)
INTERSTITIAL-CELL TUMOR	81 (93%)	238 (97%)
INTERSTITIAL-CELL TUMOR, MALIGNANT		1 (0%)
*EPIDIDYMIS	(88)	(250)
MESOTHELIOMA, INVASIVE	1 (1%)	2 (1%)
*SCROTUM	(88)	(250)
MESOTHELIOMA, INVASIVE	1 (1%)	2 (1%)
NERVOUS SYSTEM		
#CEREBRUM	(88)	(248)
ASTROCYTOMA	2 (2%)	3 (1%)
#BRAIN	(88)	(248)
CARCINOMA, NOS, INVASIVE		1 (0%)
#CEREBELLUM	(88)	(248)
ASTROCYTOMA	2 (2%)	2 (1%)
SPECIAL SENSE ORGANS		
*HARDERIAN GLAND	(88)	(250)
CARCINOMA, NOS	1 (1%)	
*ZYMAL GLAND	(88)	(250)
SQUAMOUS CELL PAPILLOMA	1 (1%)	1 (0%)
SQUAMOUS CELL CARCINOMA	4 (5%)	4 (2%)
MUSCULOSKELETAL SYSTEM		
*SKULL	(88)	(250)
OSTEOSARCOMA		1 (0%)
*MANDIBLE	(88)	(250)
SQUAMOUS CELL CARCINOMA, INVASIVE	1 (1%)	
*LUMBAR VERTEBRA	(88)	(250)
LIPOSARCOMA		1 (0%)
LIPOSARCOMA, INVASIVE		1 (0%)
*SACRUM	(88)	(250)
LIPOSARCOMA, INVASIVE		1 (0%)
*STERNUM	(88)	(250)
OSTEOSARCOMA	1 (1%)	
*RIB	(88)	(250)
OSTEOSARCOMA	1 (1%)	
*FEMUR	(88)	(250)
OSTEOSARCOMA		1 (0%)
BODY CAVITIES		
*MEDIASTINUM	(88)	(250)
ALVEOLAR/BRONCHIOLAR CARCINOMA, INVASIVE		1 (0%)
FIBROSARCOMA, INVASIVE		1 (0%)
*ABDOMINAL CAVITY	(88)	(250)
PHEOCHROMOCYTOMA, METASTATIC		1 (0%)
*MESENTERY	(88)	(250)
FIBROSARCOMA		1 (0%)
MESOTHELIOMA, MALIGNANT		1

**TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME
FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)**

	CONTROL (UNTR)	SHORT RANGE
BODY CAVITIES (Continued)		
*TUNICA VAGINALIS	(88)	(250)
MESOTHELIOMA, MALIGNANT	2 (2%)	14 (6%)
ALL OTHER SYSTEMS		
*MULTIPLE ORGANS	(88)	(250)
CARCINOMA, NOS, INVASIVE	1 (1%)	
SQUAMOUS CELL CARCINOMA, INVASIVE		1 (0%)
C-CELL CARCINOMA, METASTATIC		1 (0%)
PHEOCHROMOCYTOMA, METASTATIC	1 (1%)	
FIBROSARCOMA, INVASIVE		1 (0%)
FIBROUS HISTIOCYTOMA, METASTATIC	1 (1%)	
MESOTHELIOMA, INVASIVE	1 (1%)	13 (5%)
OSTEOSARCOMA, METASTATIC	1 (1%)	
ANIMAL DISPOSITION SUMMARY		
ANIMALS INITIALLY IN STUDY	88	250
NATURAL DEATH@	13	43
MORIBUND SACRIFICE	63	181
SCHEDULED SACRIFICE		
TERMINAL SACRIFICE	9	26
DOSING ACCIDENT		
ACCIDENTALLY KILLED, NDA	3	
ACCIDENTALLY KILLED, NOS		
ANIMAL MISSING		
ANIMAL MISSEXED		
OTHER CASES		
TUMOR SUMMARY		
TOTAL ANIMALS WITH PRIMARY TUMORS**	85	248
TOTAL PRIMARY TUMORS	315	847
TOTAL ANIMALS WITH BENIGN TUMORS	82	244
TOTAL BENIGN TUMORS	197	552
TOTAL ANIMALS WITH MALIGNANT TUMORS	71	199
TOTAL MALIGNANT TUMORS	106	278
TOTAL ANIMALS WITH SECONDARY TUMORS##	7	40
TOTAL SECONDARY TUMORS	12	59
TOTAL ANIMALS WITH TUMORS UNCERTAIN- BENIGN OR MALIGNANT	12	17
TOTAL UNCERTAIN TUMORS	12	17
TOTAL ANIMALS WITH TUMORS UNCERTAIN- PRIMARY OR METASTATIC		
TOTAL UNCERTAIN TUMORS		

* NUMBER OF ANIMALS NECROPSIED

** PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

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

@ INCLUDES AUTOLYZED ANIMALS

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS

	CONTROL (UNTR)	SHORT RANGE
ANIMALS INITIALLY IN STUDY	88	250
ANIMALS NECROPSIED	88	250
ANIMALS EXAMINED HISTOPATHOLOGICALLY	87	245
INTEGUMENTARY SYSTEM		
*SKIN	(88)	(250)
SQUAMOUS CELL PAPILLOMA	1 (1%)	4 (2%)
SQUAMOUS CELL CARCINOMA	1 (1%)	5 (2%)
BASAL-CELL TUMOR		1 (0%)
BASAL-CELL CARCINOMA	1 (1%)	
TRICHOEPITHELIOMA		1 (0%)
KERATOACANTHOMA	2 (2%)	2 (1%)
FIBROSARCOMA		1 (0%)
*SUBCUT TISSUE	(88)	(250)
SQUAMOUS CELL CARCINOMA, INVASIVE	2 (2%)	
FIBROMA	1 (1%)	3 (1%)
FIBROSARCOMA	2 (2%)	3 (1%)
LIPOMA	1 (1%)	1 (0%)
LIPOSARCOMA	1 (1%)	
OSTEOSARCOMA		1 (0%)
NEUROFIBROMA		1 (0%)
RESPIRATORY SYSTEM		
*NASAL TURBINATE	(88)	(250)
SQUAMOUS CELL CARCINOMA	1 (1%)	
SQUAMOUS CELL CARCINOMA, INVASIVE		1 (0%)
#TRACHEA	(87)	(245)
C-CELL CARCINOMA, INVASIVE		1 (0%)
#LUNG	(87)	(245)
SQUAMOUS CELL CARCINOMA, METASTATIC	1 (1%)	
ADENOCARCINOMA, NOS, METASTATIC		2 (1%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (1%)	1 (0%)
FOLLICULAR-CELL CARCINOMA, METASTATIC	1 (1%)	
C-CELL CARCINOMA, METASTATIC		3 (1%)
GRANULOSA-CELL CARCINOMA, METASTATIC		1 (0%)
PHEOCHROMOCYTOMA, METASTATIC		1 (0%)
CARCINOSARCOMA, METASTATIC		1 (0%)
OSTEOSARCOMA, METASTATIC		1 (0%)
HEMATOPOIETIC SYSTEM		
*MULTIPLE SITES	(88)	(250)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE		1 (0%)
*MULTIPLE ORGANS	(88)	(250)
MALIG. LYMPHOMA, UNDIFFER-TYPE		1 (0%)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE	1 (1%)	
MYELOMONOCYTIC LEUKEMIA		1 (0%)
MONOCYTIC LEUKEMIA	26 (30%)	99 (40%)
LEUKEMIA, MONONUCLEAR CELL	1 (1%)	1 (0%)
#CERVICAL LYMPH NODE	(87)	(245)
C-CELL CARCINOMA, METASTATIC		2 (1%)
#MEDIASTINAL L. NODE	(87)	(245)
ADENOCARCINOMA, NOS, METASTATIC		1 (0%)
#RENAL LYMPH NODE	(87)	(245)
ADENOCARCINOMA, NOS, METASTATIC		1 (0%)
#LIVER	(87)	(244)
MONOCYTIC LEUKEMIA	1 (1%)	

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
HEMATOPOIETIC SYSTEM (Continued)		
#THYMUS	(67)	(190)
ADENOCARCINOMA, NOS		2 (1%)
TERATOMA, BENIGN		1 (1%)
MALIG. LYMPHOMA, UNDIFFER-TYPE		1 (1%)
CIRCULATORY SYSTEM		
#SPLEEN	(87)	(245)
ANGIOMA	1 (1%)	
#HEART	(87)	(245)
C-CELL CARCINOMA, METASTATIC		1 (0%)
#ENDOCARDIUM	(87)	(245)
SARCOMA, NOS	1 (1%)	
DIGESTIVE SYSTEM		
*ORAL MUCOUS MEMBRANE	(88)	(250)
SQUAMOUS CELL CARCINOMA		1 (0%)
*TONGUE	(88)	(250)
SQUAMOUS CELL PAPILLOMA		1 (0%)
SQUAMOUS CELL CARCINOMA		1 (0%)
#SALIVARY GLAND	(87)	(243)
SQUAMOUS CELL CARCINOMA, INVASIVE		1 (0%)
#LIVER	(87)	(244)
ISLET-CELL CARCINOMA, METASTATIC		1 (0%)
NEOPLASTIC NODULE	3 (3%)	5 (2%)
C-CELL CARCINOMA, METASTATIC		1 (0%)
OSTEOSARCOMA, METASTATIC		1 (0%)
#PANCREAS	(86)	(245)
ADENOCARCINOMA, NOS	1 (1%)	
ACINAR-CELL ADENOMA	1 (1%)	1 (0%)
ACINAR-CELL CARCINOMA	1 (1%)	
GRANULOSA-CELL CARCINOMA, METASTATIC		1 (0%)
*PHARYNX	(88)	(250)
SQUAMOUS CELL CARCINOMA, INVASIVE	1 (1%)	
#STOMACH	(87)	(245)
CARCINOMA, NOS, METASTATIC		1 (0%)
SQUAMOUS CELL CARCINOMA		1 (0%)
#DUODENUM	(87)	(244)
LEIOMYOSARCOMA		2 (1%)
#JEJUNUM	(87)	(244)
ADENOCA IN ADENOMATOUS POLYP		1 (0%)
MUCINOUS CYSTADENOCARCINOMA		1 (0%)
LEIOMYOMA		1 (0%)
#ILEUM	(87)	(244)
LEIOMYOSARCOMA	1 (1%)	
#CECUM	(87)	(244)
ADENOMATOUS POLYP, NOS	1 (1%)	
#TRANSVERSE COLON	(87)	(244)
ADENOMATOUS POLYP, NOS		1 (0%)
#DESCENDING COLON	(87)	(244)
ADENOMATOUS POLYP, NOS		2 (1%)
LEIOMYOSARCOMA		1 (0%)
URINARY SYSTEM		
#KIDNEY	(87)	(245)
TRANSITIONAL-CELL CARCINOMA		1 (0%)
PHEOCHROMOCYTOMA, METASTATIC		1 (0%)
#URINARY BLADDER	(87)	(242)
ENDOMETRIAL STROMAL SARCOMA, INVASIVE		1 (0%)

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
ENDOCRINE SYSTEM		
#PITUITARY	(87)	(244)
CARCINOMA, NOS	6 (7%)	13 (5%)
ADENOMA, NOS	39 (45%)	101 (41%)
GANGLIONEUROMA		1 (0%)
NEUROFIBROSARCOMA		1 (0%)
#ADRENAL	(87)	(245)
CORTICAL ADENOMA	2 (2%)	8 (3%)
PHEOCHROMOCYTOMA	9 (10%)	38 (16%)
PHEOCHROMOCYTOMA, MALIGNANT		1 (0%)
#THYROID	(87)	(244)
FOLLICULAR-CELL ADENOMA	1 (1%)	4 (2%)
FOLLICULAR-CELL CARCINOMA	4 (5%)	8 (3%)
C-CELL ADENOMA	11 (13%)	20 (8%)
C-CELL CARCINOMA	7 (8%)	21 (9%)
CARCINOSARCOMA, INVASIVE		1 (0%)
#PARATHYROID	(85)	(222)
ADENOMA, NOS		1 (0%)
#PANCREATIC ISLETS	(86)	(245)
ISLET-CELL ADENOMA	2 (2%)	5 (2%)
ISLET-CELL CARCINOMA	2 (2%)	3 (1%)
REPRODUCTIVE SYSTEM		
*MAMMARY GLAND	(88)	(250)
CARCINOMA, NOS	1 (1%)	
ADENOMA, NOS	2 (2%)	14 (6%)
ADENOCARCINOMA, NOS	6 (7%)	19 (8%)
PAPILLARY ADENOCARCINOMA		1 (0%)
PAPILLARY CYSTADENOMA, NOS	1 (1%)	5 (2%)
PAPILLARY CYSTADENOCARCINOMA, NOS	1 (1%)	
FIBROSARCOMA	1 (1%)	1 (0%)
FIBROADENOMA	49 (56%)	146 (58%)
*CLITORAL GLAND	(88)	(250)
CARCINOMA, NOS	1 (1%)	8 (3%)
SQUAMOUS CELL PAPILLOMA		1 (0%)
SQUAMOUS CELL CARCINOMA	1 (1%)	9 (4%)
ADENOMA, NOS	1 (1%)	1 (0%)
KERATOACANTHOMA		4 (2%)
*VAGINA	(88)	(250)
SQUAMOUS CELL PAPILLOMA		1 (0%)
#UTERUS	(87)	(245)
CARCINOMA, NOS	2 (2%)	
ADENOCARCINOMA, NOS		1 (0%)
ENDOMETRIAL STROMAL POLYP	15 (17%)	34 (14%)
ENDOMETRIAL STROMAL SARCOMA		4 (2%)
#CERVIX UTERI	(87)	(245)
CARCINOMA-IN-SITU, NOS	1 (1%)	1 (0%)
ENDOMETRIAL STROMAL SARCOMA, INVASIVE		2 (1%)
#UTERUS/ENDOMETRIUM	(87)	(245)
CARCINOSARCOMA	1 (1%)	
#OVARY	(87)	(245)
THECOMA	2 (2%)	
GRANULOSA-CELL TUMOR	1 (1%)	3 (1%)
GRANULOSA-CELL CARCINOMA		2 (1%)
MESOTHELIOMA, NOS		1 (0%)

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
NERVOUS SYSTEM		
#CEREBRUM	(87)	(245)
CARCINOMA, NOS, INVASIVE	3 (3%)	8 (3%)
CARCINOMA, NOS, METASTATIC	1 (1%)	
ASTROCYTOMA		4 (2%)
MENINGIOMA		1 (0%)
#CEREBELLUM	(87)	(245)
CARCINOMA, NOS, INVASIVE	2 (2%)	3 (1%)
MENINGIOMA		1 (0%)
SPECIAL SENSE ORGANS		
*ZYMBAL GLAND	(88)	(250)
SQUAMOUS CELL PAPILLOMA		1 (0%)
SQUAMOUS CELL CARCINOMA	3 (3%)	1 (0%)
CARCINOSARCOMA		1 (0%)
MUSCULOSKELETAL SYSTEM		
*MAXILLA	(88)	(250)
SQUAMOUS CELL CARCINOMA, INVASIVE		1 (0%)
*SACRUM	(88)	(250)
OSTEOSARCOMA	1 (1%)	
*RIB	(88)	(250)
OSTEOSARCOMA		1 (0%)
*FEMUR	(88)	(250)
OSTEOSARCOMA		1 (0%)
BODY CAVITIES		
*ABDOMINAL CAVITY	(88)	(250)
PHEOCHROMOCYTOMA, INVASIVE		1 (0%)
ALL OTHER SYSTEMS		
*MULTIPLE ORGANS	(88)	(250)
CARCINOMA, NOS, INVASIVE	1 (1%)	
SQUAMOUS CELL CARCINOMA, INVASIVE	2 (2%)	1 (0%)
SARCOMA, NOS, INVASIVE	1 (1%)	
SARCOMA, NOS, METASTATIC	1 (1%)	
CHEEK		
SQUAMOUS CELL CARCINOMA, INVASIVE	1	
LEG		
OSTEOSARCOMA		1
ANIMAL DISPOSITION SUMMARY		
ANIMALS INITIALLY IN STUDY	88	250
NATURAL DEATH@	10	31
MORIBUND SACRIFICE	69	194
SCHEDULED SACRIFICE		
TERMINAL SACRIFICE	9	25
DOSING ACCIDENT		
ACCIDENTALLY KILLED, NDA		
ACCIDENTALLY KILLED, NOS		
ANIMAL MISSING		
ANIMAL MISSEXED		
OTHER CASES		

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
TUMOR SUMMARY		
TOTAL ANIMALS WITH PRIMARY TUMORS**	86	239
TOTAL PRIMARY TUMORS	224	644
TOTAL ANIMALS WITH BENIGN TUMORS	75	212
TOTAL BENIGN TUMORS	142	405
TOTAL ANIMALS WITH MALIGNANT TUMORS	52	177
TOTAL MALIGNANT TUMORS	78	230
TOTAL ANIMALS WITH SECONDARY TUMORS##	11	30
TOTAL SECONDARY TUMORS	17	41
TOTAL ANIMALS WITH TUMORS UNCERTAIN- BENIGN OR MALIGNANT	4	9
TOTAL UNCERTAIN TUMORS	4	9
TOTAL ANIMALS WITH TUMORS UNCERTAIN- PRIMARY OR METASTATIC		
TOTAL UNCERTAIN TUMORS		

* NUMBER OF ANIMALS NECROPSIED

** PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

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

@ INCLUDES AUTOLYZED ANIMALS

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	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
WEEKS ON STUDY	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
ENDOCRINE SYSTEM																											
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS				X						X				X	X		X							X		X	
ADRENAL PHEOCHROMOCYTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA, MALIGNANT			X	X		X		X	X		X			X		X		X		X		X		X		X	
THYROID FOLLICULAR-CELL ADENOMA	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA																											
C-CELL ADENOMA							X		X		X			X											X		
C-CELL CARCINOMA	X								X		X																
PARATHYROID ADENOMA, NOS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA, INVASIVE			X																								
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																											
ISLET-CELL CARCINOMA									X																		
REPRODUCTIVE SYSTEM																											
MAMMARY GLAND ADENOCARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROADENOMA																										X	X
TESTIS INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																											
EPIDIDYMS MESOTHELIOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
NERVOUS SYSTEM																											
BRAIN ASTROCYTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																											
HARDERIAN GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
FIBROUS HISTIOCYTOMA, MALIGNANT																											
ZYMBAL'S GLAND SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA	X																X		X								X
MUSCULOSKELETAL SYSTEM																											
BONE SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
OSTEOSARCOMA																											X
BODY CAVITIES																											
TUNICA VAGINALIS MESOTHELIOMA, MALIGNANT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																											
MULTIPLE ORGANS NOS CARCINOMA, NOS, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PHEOCHROMOCYTOMA, METASTATIC																											
FIBROUS HISTIOCYTOMA, MALIGNANT																											
FIBROUS HISTIOCYTOMA, METASTATIC																											
MESOTHELIOMA, INVASIVE																											
OSTEOSARCOMA, METASTATIC																											
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE																											
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																											
MYELOMONOCYTIC LEUKEMIA																											
MONOCYTIC LEUKEMIA	X	X	X	X		X		X		X		X		X		X		X		X		X		X		X	
LEUKEMIA, MONONUCLEAR CELL																											
SCROTUM NOS MESOTHELIOMA, INVASIVE																											

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	399	500	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			
WEEKS ON STUDY	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1			
	2	1	3	7	2	2	3	3	3	2	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4			
ENDOCRINE SYSTEM																																			
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
ADENOMA, NOS									X																										
ADRENAL PHEOCHROMOCYTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
PHEOCHROMOCYTOMA, MALIGNANT			X				X	X																											
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
FOLLICULAR-CELL CARCINOMA																																			
C-CELL ADENOMA																																			
C-CELL CARCINOMA							X			X	X																								
PARATHYROID ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
C-CELL CARCINOMA, INVASIVE																																			
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
ISLET-CELL ADENOMA																																			
ISLET-CELL CARCINOMA	X						X																												
REPRODUCTIVE SYSTEM																																			
MAMMARY GLAND ADENOCARCINOMA, NOS	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
FIBROADENOMA																																			
TESTIS INTERSTITIAL-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
PROSTATE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
SQUAMOUS CELL CARCINOMA																																			
EPIDIDYMIS MESOTHELIOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
NERVOUS SYSTEM																																			
BRAIN ASTROCYTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SPECIAL SENSE ORGANS																																			
HARDERIAN GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
FIBROUS HISTIOCYTOMA, MALIGNANT																																			
ZYMBAL'S GLAND SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL CARCINOMA																																			
MUSCULOSKELETAL SYSTEM																																			
BONE SQUAMOUS CELL CARCINOMA, INVASIVE	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
OSTEOSARCOMA																																			
BODY CAVITIES																																			
TUNICA VAGINALIS MESOTHELIOMA, MALIGNANT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ALL OTHER SYSTEMS																																			
MULTIPLE ORGANS NOS CARCINOMA, NOS, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
PHEOCHROMOCYTOMA, METASTATIC																																			
FIBROUS HISTIOCYTOMA, MALIGNANT																																			
FIBROUS HISTIOCYTOMA, METASTATIC																																			
MESOTHELIOMA, INVASIVE																																			
OSTEOSARCOMA, METASTATIC																																			
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE																																			
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																																			
MYELOMONOCYTIC LEUKEMIA																																			
MONOCYTIC LEUKEMIA																																			
LEUKEMIA, MONONUCLEAR CELL																																			
SCROTUM NOS HELIOMA, INVASIVE																																			

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	624	625	626	627	628	629	630	631	632	633	634	635	636	637	638	639	640	TOTAL TISSUES TUMORS
WEEKS ON STUDY	137	085	137	118	118	119	119	120	121	122	123	124	125	126	127	128	129	
ENDOCRINE SYSTEM																		
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	87
ADENOMA, NOS	X				X			X		X			X					20
ADRENAL PHEOCHROMOCYTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	88
PHEOCHROMOCYTOMA, MALIGNANT	X				X	X				X								25
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	86
FOLLICULAR-CELL CARCINOMA							X											4
C-CELL ADENOMA			X	X		X	X	X										2
C-CELL CARCINOMA																		13
PARATHYROID ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	83
C-CELL CARCINOMA, INVASIVE													X					6
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	86
ISLET-CELL ADENOMA			X										X		-	+		6
ISLET-CELL CARCINOMA										X								5
REPRODUCTIVE SYSTEM																		
MAMMARY GLAND ADENOCARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	88*
FIBROADENOMA	X		X							X		X						3
TESTIS INTERSTITIAL-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	87
	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	81
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	87
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	88*
SQUAMOUS CELL CARCINOMA		X																4
EPIDIDYMIS MESOTHELIOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	88*
																		1
NERVOUS SYSTEM																		
BRAIN ASTROCYTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	88
																		4
SPECIAL SENSE ORGANS																		
HARDERIAN GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	88*
FIBROUS HISTIOCYTOMA, MALIGNANT																		1
ZYMBAL'S GLAND SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	88*
SQUAMOUS CELL CARCINOMA																		1
																		4
MUSCULOSKELETAL SYSTEM																		
BOLE SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	88*
OSTEOSARCOMA																		1
																		2
BODY CAVITIES																		
TUNICA VAGINALIS MESOTHELIOMA, MALIGNANT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	88*
																		2
ALL OTHER SYSTEMS																		
MULTIPLE ORGANS NOS CARCINOMA, NOS, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	88*
PHEOCHROMOCYTOMA, METASTATIC																		1
FIBROUS HISTIOCYTOMA, MALIGNANT										X								1
FIBROUS HISTIOCYTOMA, METASTATIC																		1
MESOTHELIOMA, INVASIVE																		1
OSTEOSARCOMA, METASTATIC																		1
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE																		1
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																		1
MYELOMONOCYTIC LEUKEMIA																		1
MONOCYTIC LEUKEMIA	X	X		X			X		X									34
LEUKEMIA, MONONUCLEAR CELL							X											1
SCROTUM NOS MESOTHELIOMA, INVASIVE																		1

* ANIMALS NECROPSIED

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE

ANIMAL NUMBER	WEEKS ON STUDY																												
	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	26	27	28
INTEGUMENTARY SYSTEM																													
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL PAPILLOMA																													
SQUAMOUS CELL CARCINOMA																													
BASAL-CELL TUMOR																													
BASAL-CELL CARCINOMA																													
TRICHOEPITHELIOMA																													
SEBACEOUS ADENOMA																													
KERATOCARCINOMA																													
FIBROUS HISTIOCYTOMA																													
FIBROUS HISTIOCYTOMA, MALIGNANT																													
HEMANGIOMA																													
SUBCUTANEOUS TISSUE																													
SARCOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																													
FIBROSARCOMA																													
FIBROUS HISTIOCYTOMA, MALIGNANT																													
MYXOSARCOMA																													
LIPOMA																													
LIPOSARCOMA																													
LEIOMYOSARCOMA, INVASIVE																													
HEMANGIOSARCOMA																													
NEUROFIBROMA																													
NEUROFIBROSARCOMA																													
RESPIRATORY SYSTEM																													
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, METASTAT																													
ALVEOLAR/BRONCHIOLAR ADENOMA																													
ALVEOLAR/BRONCHIOLAR CARCINOMA																													
C-CELL CARCINOMA, METASTATIC																													
FIBROSARCOMA, METASTATIC																													
LIPOSARCOMA, METASTATIC																													
MESOTHELIOMA, METASTATIC																													
OSTEOSARCOMA, METASTATIC																													
TRACHEA																													
POLLICULAR-CELL CARCINOMA, INVASI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA, METASTATIC																													
NASAL CAVITY																													
CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																													
HEPATOGLYCYC SYSTEM																													
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIPOSARCOMA, INVASIVE																													
SPLEEN																													
MESOTHELIOMA, METASTATIC																													
HEMANGIOMA																													
HEMANGIOSARCOMA																													
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																													
LYMPH NODES																													
CARCINOMA, NOS, METASTATIC																													
SQUAMOUS CELL CARCINOMA, METASTAT																													
C-CELL CARCINOMA, METASTATIC																													
INTERSTITIAL-CELL TUMOR, METASTAT																													
SARCOMA, NOS, INVASIVE																													
FIBROSARCOMA, INVASIVE																													
MESOTHELIOMA, METASTATIC																													
THYRUS																													
CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																													
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS, INVASIVE																													
FIBROSARCOMA, METASTATIC																													
DIGESTIVE SYSTEM																													
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL PAPILLOMA																													
SALIVARY GLAND																													
SARCOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA																													
LIVER																													
NEOPLASTIC NODULE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA																													
C-CELL CARCINOMA, METASTATIC																													
FIBROSARCOMA, METASTATIC																													
HEMANGIOSARCOMA, METASTATIC																													
MONOCYTIC LEUKEMIA																													
BILE DUCT																													
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS																													
ACINAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MIXED TUMOR, SERICIN																													
ESOPHAGUS																													
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA-IN-SITU, NOS																													
SQUAMOUS CELL PAPILLOMA																													
SQUAMOUS CELL CARCINOMA																													
SARCOMA, NOS																													
SMALL INTESTINE																													
ADENOMATOUS POLYP, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE																													
ADENOMATOUS POLYP, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIPOMA																													
LEIOMYOSARCOMA																													
RECTUM																													
LEIOMYOSARCOMA, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

+: TISSUE EXAMINED MICROSCOPICALLY
 -: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
 2: TUMOR INDICED
 N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
 3: ANIMAL MIS-SEXED
 1: NO TISSUE INFORMATION SUBMITTED
 0: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
 A: AUTOLYSIS
 M: ANIMAL MISSING
 B: NO NECROPSY PERFORMED

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE (Continued)

ANIMAL NUMBER	WEEKS ON STUDY																												
	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	26	27	28
INTEGUMENTARY SYSTEM																													
SKIN																													
SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																													
BASAL-CELL TUMOR																													
BASAL-CELL CARCINOMA																													
TRICHOEPIITHELIOA																													
SEBACEOUS ADENOMA																													
KERATOACANTHOMA																													
FIBROUS HISTIOCYTOMA																													
FIBROUS HISTIOCYTOMA, MALIGNANT																													
HEMANGIOA																													
SUBCUTANEOUS TISSUE																													
SARCOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																													
FIBROSARCOMA																													
FIBROUS HISTIOCYTOMA, MALIGNANT																													
MYXOSARCOMA																													
LIPOMA																													
LIPOSARCOMA																													
LEIOMYOSARCOMA, INVASIVE																													
HEMANGIOSARCOMA																													
NEUROFIBROMA																													
NEUROFIBROSARCOMA																													
RESPIRATORY SYSTEM																													
LUNGS AND BRONCHI																													
SQUAMOUS CELL CARCINOMA, METASTAT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																													
ALVEOLAR/BRONCHIOLAR CARCINOMA																													
C-CELL CARCINOMA, METASTATIC																													
FIBROSARCOMA, METASTATIC																													
LIPOSARCOMA, METASTATIC																													
MESOTHELIOA, METASTATIC																													
OSTEOSARCOMA, METASTATIC																													
TRACHEA																													
FOLLICULAR-CELL CARCINOMA, INVASI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA, METASTATIC																													
NASAL CAVITY																													
CARCINOMA, NOS	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
SQUAMOUS CELL CARCINOMA																													
HEMATOPOIETIC SYSTEM																													
BONE MARROW																													
LIPOSARCOMA, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SPLEEN																													
MESOTHELIOA, METASTATIC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMANGIOA																													
HEMANGIOSARCOMA																													
HAEMOLYTHOMA, MESTICOTIC TYPE																													
LYPH NODES																													
CARCINOMA, NOS, METASTATIC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL CARCINOMA, METASTAT																													
C-CELL CARCINOMA, METASTATIC																													
INTERSTITIAL-CELL TUMOR, METASTAT																													
SARCOMA, NOS, INVASIVE																													
FIBROSARCOMA, INVASIVE																													
MESOTHELIOA, METASTATIC																													
THYROID																													
CARCINOMA, NOS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
CIRCULATORY SYSTEM																													
HEART																													
CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
FIBROSARCOMA, METASTATIC																													
DIGESTIVE SYSTEM																													
ORAL CAVITY																													
SQUAMOUS CELL PAPILLOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
SALIVARY GLAND																													
SARCOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
FIBROSARCOMA																													
LIVER																													
NEPLASTIC NODULE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEPATOCELLULAR CARCINOMA																													
C-CELL CARCINOMA, METASTATIC																													
FIBROSARCOMA, METASTATIC																													
HEMANGIOSARCOMA, METASTATIC																													
MONOCYTIC LEUKEMIA																													
BILE DUCT																													
GALLBLADDER & COMMON BILE DUCT																													
PANCREAS																													
ACINAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
MIXED TUMOR, BENIGN																													
ESOPHAGUS																													
STOMACH																													
CARCINOMA-IV-SITH, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL PAPILLOMA																													
SQUAMOUS CELL CARCINOMA																													
SARCOMA, NOS																													
SMALL INTESTINE																													
ADENOMATOUS POLYP, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LARGE INTESTINE																													
ADENOMATOUS POLYP, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LIPOMA																													
LEIOMYOSARCOMA																													
RECTUM																													
LEIOMYOSARCOMA, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE (Continued)

ANIMAL NUMBER	RAT NO.																											
	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	26	27	28
INTEGUMENTARY SYSTEM																												
SKIN	+																											
SQUAMOUS CELL PAPILLOMA	+																											
SQUAMOUS CELL CARCINOMA	+																											
BASAL-CELL TUMOR	+																											
BASAL-CELL CARCINOMA	+																											
TRICHOEPITHELIOMA	+																											
SEBACEOUS ADENOMA	+																											
SEBACEOMA	+																											
FIBROUS HISTIOCYTOMA	+																											
FIBROUS HISTIOCYTOMA, MALIGNANT	+																											
HEMANGIOMA	+																											
SUBCUTANEOUS TISSUE																												
SARCOMA, NOS	+																											
FIBROMA	+																											
FIBROSARCOMA	+																											
FIBROUS HISTIOCYTOMA, MALIGNANT	+																											
MYOSARCOMA	+																											
LIPOMA	+																											
LIPOSARCOMA	+																											
LEIOMYOSARCOMA, INVASIVE	+																											
HEMANGIOSARCOMA	+																											
NEUROFIBROMA	+																											
NEUROFIBROSARCOMA	+																											
RESPIRATORY SYSTEM																												
LUNGS AND BRONCHI	+																											
SQUAMOUS CELL CARCINOMA, METASTAT	+																											
ALVEOLAR/BRONCHIOAL ADENOMA	+																											
ALVEOLAR/BRONCHIOAL CARCINOMA	+																											
C-CELL CARCINOMA, METASTATIC	+																											
FIBROSARCOMA, METASTATIC	+																											
LIPOSARCOMA, METASTATIC	+																											
MESOTHELIOMA, METASTATIC	+																											
OSTEOSARCOMA, METASTATIC	+																											
TRACHEA	+																											
POLLICULAR-CELL CARCINOMA, INVASI	+																											
C-CELL CARCINOMA, METASTATIC	+																											
NASAL CAVITY	+																											
CARCINOMA, NOS	+																											
SQUAMOUS CELL CARCINOMA	+																											
HEMATOPOIETIC SYSTEM																												
BONE MARROW	+																											
LIPOSARCOMA, INVASIVE	+																											
SPLEEN	+																											
MESOTHELIOMA, METASTATIC	+																											
HEMANGIOMA	+																											
HEMANGIOSARCOMA	+																											
MALIG. LYMPHOMA, HISTIOCYTIC TYPE	+																											
LYMPH NODES	+																											
CARCINOMA, NOS, METASTATIC	+																											
SQUAMOUS CELL CARCINOMA, METASTAT	+																											
C-CELL CARCINOMA, METASTATIC	+																											
INTERSTITIAL-CELL TUMOR, METASTAT	+																											
SARCOMA, NOS, INVASIVE	+																											
FIBROSARCOMA, INVASIVE	+																											
MESOTHELIOMA, METASTATIC	+																											
THYROID	+																											
CARCINOMA, NOS	+																											
CIRCULATORY SYSTEM																												
HEART	+																											
CARCINOMA, NOS, INVASIVE	+																											
FIBROSARCOMA, METASTATIC	+																											
DIGESTIVE SYSTEM																												
ORAL CAVITY	+																											
SQUAMOUS CELL PAPILLOMA	+																											
SALIVARY GLAND	+																											
SARCOMA, NOS	+																											
FIBROSARCOMA	+																											
LIVER	+																											
NEOPLASTIC NODULE	+																											
HEPATOCELLULAR CARCINOMA	+																											
C-CELL CARCINOMA, METASTATIC	+																											
FIBROSARCOMA, METASTATIC	+																											
HEMANGIOSARCOMA, METASTATIC	+																											
MONOCYTIC LEUKEMIA	+																											
BILE DUCT	+																											
GALLBLADDER & COMMON BILE DUCT	+																											
PANCREAS	+																											
ACINAR-CELL ADENOMA	+																											
MIXED TUMOR, BENIGN	+																											
ESOPHAGUS	+																											
STOMACH	+																											
CARCINOMA-IN-SITU, NOS	+																											
SQUAMOUS CELL PAPILLOMA	+																											
SQUAMOUS CELL CARCINOMA	+																											
SARCOMA, NOS	+																											
SMALL INTESTINE	+																											
ADENOMATOUS POLYP, NOS	+																											
LARGE INTESTINE	+																											
ADENOMATOUS POLYP, NOS	+																											
LIPOMA	+																											
LEIOMYOSARCOMA	+																											
RECTUM	+																											
LEIOMYOSARCOMA, INVASIVE	+																											

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	687	688	689	690	691	692	693	694	695	696	697	698	699	700	701	702	703	704	705	706	707	708	709	710
WEEKS ON STUDY	10	12	10	6	5	5	5	5	2	7	8	6	6	6	9	5	3	9	9	4	5	3	5	0
ENDOCRINE SYSTEM																								
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS	X	X					X	X	X			X	X			X	X	X	X	X	X	X	X	X
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA							X	X															X	
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA																							X	
C-CELL ADENOMA	X	X	X																					X
C-CELL CARCINOMA				X																				
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																								
ISLET-CELL CARCINOMA																							X	
REPRODUCTIVE SYSTEM																								
MAMMARY GLAND CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS		X																				X		
ADENOCARCINOMA, NOS		X																					X	
PAPILLARY CYSTADENOMA, NOS																								
PAPILLARY CYSTADENOCARCINOMA, NOS														X										
FIBROSARCOMA																								
FIBROADENOMA	X			X										X	X	X		X		X	X	X	X	X
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																						X		
ADENOMA, NOS																								
UTERUS CARCINOMA-IN-SITU, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS																								
ENDOMETRIAL STROMAL POLYP					X			X						X					X					X
CARCINOSARCOMA																								
OVARY THECOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULOSA-CELL TUMOR																							X	
NERVOUS SYSTEM																								
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS, METASTATIC	X ^a	X																						
SPECIAL SENSE ORGANS																								
ZYMBAL'S GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA	X																							
MUSCULOSKELETAL SYSTEM																								
BONE OSTEOSARCOMA	N	+	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
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
CARCINOMA, NOS, INVASIVE																								
SQUAMOUS CELL CARCINOMA, INVASIVE																								
SARCOMA, NOS, INVASIVE																								
SARCOMA, NOS, METASTATIC																								
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																								
MONOCYTIC LEUKEMIA														X	X	X		X		X	X		X	
LEUKEMIA, MONONUCLEAR CELL	X																							
CHEEK NOS																								
SQUAMOUS CELL CARCINOMA, INVASIVE	X																							

^a: MULTIPLE OCCURENCE OF MORPHOLOGY

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30
WEEKS ON STUDY	8	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	7	4	3	2	3	3	8	7	8	3	2	2	4	9	1	2	3	2	4	3	2	2	3	4	2	3	4	3	4	3
ENDOCRINE SYSTEM																														
PITUITARY CARCINOMA, NOS																														
ADENOMA, NOS																														
GANGLIONEUROMA																														
NEUROFIBROSARCOMA																														
ADRENAL CORTICAL ADENOMA																														
PHEOCHROMOCYTOMA																														
PHEOCHROMOCYTOMA, MALIGNANT																														
THYROID FOLLICULAR-CELL ADENOMA																														
FOLLICULAR-CELL CARCINOMA																														
C-CELL ADENOMA																														
C-CELL CARCINOMA																														
CARCINOSARCOMA, INVASIVE																														
PARATHYROID ADENOMA, NOS																														
PANCREATIC ISLETS ISLET-CELL ADENOMA																														
ISLET-CELL CARCINOMA																														
REPRODUCTIVE SYSTEM																														
MAMMARY GLAND ADENOMA, NOS																														
ADENOCARCINOMA, NOS																														
PAPILLARY ADENOCARCINOMA																														
PAPILLARY CYSTADENOMA, NOS																														
FIBROSARCOMA																														
FIBROADENOMA																														
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS																														
SQUAMOUS CELL PAPILLOMA																														
SQUAMOUS CELL CARCINOMA																														
ADENOMA, NOS																														
KERATOCANTHOMA																														
VAGINA SQUAMOUS CELL PAPILLOMA																														
UTERUS CARCINOMA-IN-SITU, NOS																														
ADENOCARCINOMA, NOS																														
ENDOMETRIAL STROMAL POLYP																														
ENDOMETRIAL STROMAL SARCOMA																														
ENDOMETRIAL STROMAL SARCOMA, INVA																														
OVARY GRANULOSA-CELL TUMOR																														
GRANULOSA-CELL CARCINOMA																														
MESOTHELIOMA, NOS																														
NERVOUS SYSTEM																														
BRAIN CARCINOMA, NOS, INVASIVE																														
ASTROCYTOMA																														
MENINGIOMA																														
SPECIAL SENSE ORGANS																														
ZYMBAL'S GLAND SQUAMOUS CELL PAPILLOMA																														
SQUAMOUS CELL CARCINOMA																														
CARCINOSARCOMA																														
MUSCULOSKELETAL SYSTEM																														
BONE SQUAMOUS CELL CARCINOMA, INVASIVE																														
OSTEOSARCOMA																														
BODY CAVITIES																														
PERITONEUM PHEOCHROMOCYTOMA, INVASIVE																														
ALL OTHER SYSTEMS																														
MULTIPLE SITES NOS																														
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																														
MULTIPLE ORGANS NOS																														
SQUAMOUS CELL CARCINOMA, INVASIVE																														
MALIG. LYMPHOMA, UNDIFFER-TYPE																														
MYELOMONOCYTIC LEUKEMIA																														
MONOCYTIC LEUKEMIA																														
LEUKEMIA, MONONUCLEAR CELL																														
LEG NOS																														
OSTEOSARCOMA																														

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE (Continued)

ANIMAL NUMBER	WEEKS ON STUDY																			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
INTEGUMENTARY SYSTEM																				
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL PAPILLOMA																				
SQUAMOUS CELL CARCINOMA																				
BASAL-CELL TUMOR																				
TRICHOEPITHELIOMA																				
KERATOACANTHOMA																				
FIBROSARCOMA																				
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																				
FIBROSARCOMA																				
LIPOMA																				
OSTEOSARCOMA																				
NEUROFIBROMA																				
RESPIRATORY SYSTEM																				
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																				
ALVEOLAR/BRONCHIOLAR CARCINOMA																				
C-CELL CARCINOMA, METASTATIC																				
GRANULOSA-CELL CARCINOMA, METASTATIC																				
PNEUROMYOCYTOMA, METASTATIC																				
CARCINOSARCOMA, METASTATIC																				
OSTEOSARCOMA, METASTATIC																				
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA, INVASIVE																				
NASAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA, INVASIVE																				
HEMATOPOIETIC SYSTEM																				
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																				
C-CELL CARCINOMA, METASTATIC																				
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																				
TERATOMA, BENIGN																				
MALIG. LYMPHOMA, UNDIFFER-TYPE																				
CIRCULATORY SYSTEM																				
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA, METASTATIC																				
DIGESTIVE SYSTEM																				
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL PAPILLOMA																				
SQUAMOUS CELL CARCINOMA																				
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, INVASIVE																				
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL CARCINOMA, METASTATIC																				
NEOPLASTIC NODULE																				
C-CELL CARCINOMA, METASTATIC																				
OSTEOSARCOMA, METASTATIC																				
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
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ACINAR-CELL ADENOMA																				
GRANULOSA-CELL CARCINOMA, METASTATIC																				
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS, METASTATIC																				
SQUAMOUS CELL CARCINOMA																				
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA IN ADENOMATOUS POLYP																				
MUCINOUS CYSTADENOCARCINOMA																				
LEIOMYOMA																				
LEIOMYOSARCOMA																				
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMATOUS POLYP, NOS																				
LEIOMYOSARCOMA																				
URINARY SYSTEM																				
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRANSITIONAL-CELL CARCINOMA																				
PNEUROMYOCYTOMA, METASTATIC																				
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL SARCOMA, INVA																				

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE (Continued)

ANIMAL NUMBER	WEEKS ON STUDY																			
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
ENDOCRINE SYSTEM																				
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																				
GANGLIONEUROMA																				
NEUROFIBROSARCOMA																				
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHENOCYTOPLASIA																				
PHENOCYTOPLASIA, MALIGNANT																				
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA																				
C-CELL ADENOMA																				
C-CELL CARCINOMA																				
CARCINOSARCOMA, INVASIVE																				
PARATHYROID ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS ISLET-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL CARCINOMA																				
REPRODUCTIVE SYSTEM																				
MAMMARY GLAND ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																				
PAPILLARY ADENOCARCINOMA																				
PAPILLARY CYSTADENOMA, NOS																				
FIBROSARCOMA																				
FIBROADENOMA																				
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL PAPILLOMA																				
SQUAMOUS CELL CARCINOMA																				
ADENOMA, NOS																				
KERATOCANTHOMA																				
VAGINA SQUAMOUS CELL PAPILLOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
UTERUS CARCINOMA-IN-SITU, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																				
ENDOMETRIAL STROMAL POLYP																				
ENDOMETRIAL STROMAL SARCOMA																				
ENDOMETRIAL STROMAL SARCOMA, INVA																				
OVARY GRANULOSA-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULOSA-CELL CARCINOMA																				
MESOTHELIOMA, NOS																				
NERVOUS SYSTEM																				
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA																				
MEINGIOMA																				
SPECIAL SENSE ORGANS																				
ZYMBAL'S GLAND SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																				
CARCINOSARCOMA																				
MUSCULOSKELETAL SYSTEM																				
BONE SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
OSTEOSARCOMA																				
BODY CAVITIES																				
PERITONEUM PHENOCYTOPLASIA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ALL OTHER SYSTEMS																				
MULTIPLE SITES NOS MALIG. LYMPHOMA, HISTIOCYTIC TYPE																				
MULTIPLE ORGANS NOS SQUAMOUS CELL CARCINOMA, INVASIVE																				
MALIG. LYMPHOMA, UNDIFFER-TYPE																				
MYELOMONOCYTIC LEUKEMIA																				
MONOCYTIC LEUKEMIA																				
LEUKEMIA, MONONUCLEAR CELL																				
LEG NOS OSTEOSARCOMA																				

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50
WEEKS ON STUDY	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	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50
INTEGUMENTARY SYSTEM																																																		
SKIN	.																																																	
SQUAMOUS CELL PAPILLOMA	.																																																	
SQUAMOUS CELL CARCINOMA	.																																																	
BASAL-CELL TUMOR	.																																																	
TRICHOEPITHELIOMA	.																																																	
KERATOACANTHOMA	.																																																	
FIBROSARCOMA	.																																																	
SUBCUTANEOUS TISSUE																																																		
FIBROMA	.																																																	
FIBROSARCOMA	.																																																	
LIPOMA	.																																																	
OSTEOSARCOMA	.																																																	
NEUROFIBROMA	.																																																	
RESPIRATORY SYSTEM																																																		
LUNGS AND BRONCHI	.																																																	
ADENOCARCINOMA, NOS, METASTATIC	.																																																	
ALVEOLAR/BRONCHIOLAR CARCINOMA	.																																																	
C-CELL CARCINOMA, METASTATIC	.																																																	
GRANULOSA-CELL CARCINOMA, METASTATIC	.																																																	
PNEUMOCYSTOMA, METASTATIC	.																																																	
CARCINOSARCOMA, METASTATIC	.																																																	
OSTEOSARCOMA, METASTATIC	.																																																	
TRACHEA	.																																																	
C-CELL CARCINOMA, INVASIVE	.																																																	
NASAL CAVITY	.																																																	
SQUAMOUS CELL CARCINOMA, INVASIVE	.																																																	
HEMATOPOIETIC SYSTEM																																																		
BONE MARROW	.																																																	
SPLEEN	.																																																	
Lymph nodes	.																																																	
ADENOCARCINOMA, NOS, METASTATIC	.																																																	
C-CELL CARCINOMA, METASTATIC	.																																																	
THYROID	.																																																	
ADENOCARCINOMA, NOS	.																																																	
TERATOMA, BENIGN	.																																																	
MALIG. LYMPHOMA, UNDIFFER-TYPE	.																																																	
CIRCULATORY SYSTEM																																																		
HEART	.																																																	
C-CELL CARCINOMA, METASTATIC	.																																																	
DIGESTIVE SYSTEM																																																		
ORAL CAVITY	.																																																	
SQUAMOUS CELL PAPILLOMA	.																																																	
SQUAMOUS CELL CARCINOMA	.																																																	
SALIVARY GLAND	.																																																	
SQUAMOUS CELL CARCINOMA, INVASIVE	.																																																	
LIVER	.																																																	
ISLET-CELL CARCINOMA, METASTATIC	.																																																	
NEOPLASTIC NODULE	.																																																	
C-CELL CARCINOMA, METASTATIC	.																																																	
OSTEOSARCOMA, METASTATIC	.																																																	
BILE DUCT	.																																																	
GALLBLADDER & COMMON BILE DUCT	.																																																	
PANCREAS	.																																																	
ACINAR-CELL ADENOMA	.																																																	
GRANULOSA-CELL CARCINOMA, METASTATIC	.																																																	
ESOPHAGUS	.																																																	
STOMACH	.																																																	
CARCINOMA, NOS, METASTATIC	.																																																	
SQUAMOUS CELL CARCINOMA	.																																																	
SMALL INTESTINE	.																																																	
ADENOMA IN ADENOMATOUS POLYP	.																																																	
MUCINOUS CYSTADENOCARCINOMA	.																																																	
LEIOMYOMA	.																																																	
LEIOMYOSARCOMA	.																																																	
LARGE INTESTINE	.																																																	
ADENOMATOUS POLYP, NOS	.																																																	
LEIOMYOSARCOMA	.																																																	
URINARY SYSTEM																																																		
KIDNEY	.																																																	
TRANSITIONAL-CELL CARCINOMA	.																																																	
PNEUMOCYSTOMA, METASTATIC	.																																																	
URINARY BLADDER	.																																																	
ENDOMETRIAL STROMAL SARCOMA, INVA	.																																																	

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30	
WEEKS ON STUDY	4	4	2	3	4	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
INTEGUMENTARY SYSTEM																															
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL PAPILLOMA																															
SQUAMOUS CELL CARCINOMA					X																										
BASAL-CELL TUMOR																															
TRICHOEPITHELIOMA																															
KERATOCANTHOMA																															
FIBROSARCOMA																															
SUBCUTANEOUS TISSUE																															
FIBROMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA																															
FIBROSARCOMA																															
LIPOMA																															
OSTEOSARCOMA																															
NEUROFIBROMA																															
RESPIRATORY SYSTEM																															
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOCARCINOMA, NOS, METASTATIC																															
ALVEOLAR/BRONCHIOLAR CARCINOMA																															
C-CELL CARCINOMA, METASTATIC																															
GRANULOSA-CELL CARCINOMA, METASTATIC																															
PNEUMOCYCTOMA, METASTATIC																															
CARCINOSARCOMA, METASTATIC																															
OSTEOSARCOMA, METASTATIC																															
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
C-CELL CARCINOMA, INVASIVE																															
NASAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
SQUAMOUS CELL CARCINOMA, INVASIVE																															
HEMATOPOIETIC SYSTEM																															
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOCARCINOMA, NOS, METASTATIC																															
C-CELL CARCINOMA, METASTATIC																															
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOCARCINOMA, NOS																															
TERATOMA, BENIGN																															
MALIG. LYMPHOMA, UNDIFFER-TYPE																															
CIRCULATORY SYSTEM																															
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
C-CELL CARCINOMA, METASTATIC																															
DIGESTIVE SYSTEM																															
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
SQUAMOUS CELL PAPILLOMA																															
SQUAMOUS CELL CARCINOMA																															
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL CARCINOMA, INVASIVE																															
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ISLET-CELL CARCINOMA, METASTATIC																															
NEOPLASTIC NODULE																															
C-CELL CARCINOMA, METASTATIC																															
OSTEOSARCOMA, METASTATIC																															
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ACINAR-CELL ADENOMA																															
GRANULOSA-CELL CARCINOMA, METASTATIC																															
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
CARCINOMA, NOS, METASTATIC																															
SQUAMOUS CELL CARCINOMA																															
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOMA IN ADENOMATOUS POLYP																															
MUCINOUS CYSTADENOCARCINOMA																															
LEIOMYOMA																															
LEIOMYOSARCOMA																															
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOMATOUS POLYP, NOS																															
LEIOMYOSARCOMA																															
URINARY SYSTEM																															
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
TRANSITIONAL-CELL CARCINOMA																															
PNEUMOCYCTOMA, METASTATIC																															
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ENDOMETRIAL STROMAL SARCOMA, INVA																															

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30	
WEEKS ON STUDY	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	26	27	28	29	30	
ENDOCRINE SYSTEM																															
PITUITARY																															
CARCINOMA, NOS	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
ADENOMA, NOS	X	X	X	X				X			X	X			X	X	X														
ANGLIOMIOMA																															
NEUROFIBROSARCOMA																															
ADRENAL																															
CORTICAL ADENOMA	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
PHEDCHROMOCYTOMA																															
PHEDCHROMOCYTOMA, MALIGNANT	X	X										X		X			X														X
THYROID																															
FOLLICULAR-CELL ADENOMA	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
FOLLICULAR-CELL CARCINOMA																															
C-CELL ADENOMA																															
C-CELL CARCINOMA	X	X																													
CARCINOSARCOMA, INVASIVE																															
PARATHYROID																															
ADENOMA, NOS	-	-	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
PANCREATIC ISLETS																															
ISLET-CELL ADENOMA	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
ISLET-CELL CARCINOMA																															
REPRODUCTIVE SYSTEM																															
MAMMARY GLAND																															
ADENOMA, NOS	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
ADENOCARCINOMA, NOS																															
PAPILLARY ADENOCARCINOMA																															
PAPILLARY CYSTADENOMA, NOS																															
FIBROSARCOMA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
PREPUTIAL/CLITORAL GLAND																															
CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
SQUAMOUS CELL PAPILLOMA																															
SQUAMOUS CELL CARCINOMA																															
ADENOMA, NOS	X																														
KERATOCANTHOMA																															
VAGINA																															
SQUAMOUS CELL PAPILLOMA	N	N	N	N	N	N	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																															
CARCINOMA-IN-SITU, NOS	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
ADENOCARCINOMA, NOS																															
ENDOMETRIAL STROMAL POLYP																															
ENDOMETRIAL STROMAL SARCOMA																															
ENDOMETRIAL STROMAL SARCOMA, INVA	X	X																													
OVARY																															
GRANULOSA-CELL TUMOR	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
GRANULOSA-CELL CARCINOMA																															
THECOMA, NOS																															
NERVOUS SYSTEM																															
BRAIN																															
CARCINOMA, NOS, INVASIVE	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
ASTROCYTOMA																															
MEINGIOMA																															
SPECIAL SENSE ORGANS																															
ZYMBAL'S GLAND																															
SQUAMOUS CELL PAPILLOMA	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
SQUAMOUS CELL CARCINOMA																															
CARCINOSARCOMA																															
MUSCULOSKELETAL SYSTEM																															
BONE																															
SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
OSTEOSARCOMA																															
BODY CAVITIES																															
PERITONEUM																															
PHEDCHROMOCYTOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
ALL OTHER SYSTEMS																															
MULTIPLE SITES NOS																															
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																															
MULTIPLE ORGANS NOS																															
SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
MALIG.LYMPHOMA, UNDIFFER-TYPE																															
MYELOIDIC LEMKEMIA																															
MONOCYTIC LEMKEMIA	X																														
LEUKEMIA, MONONUCLEAR CELL																															
LEG NOS																															
OSTEOSARCOMA																															

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE (Continued)

ANIMAL NUMBER	WEEKS ON STUDY																											
	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	26	27	28
ENDOCRINE SYSTEM																												
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																												
GANGLIONEUROMA																												
NEUROFIBROSARCOMA																												
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA																												
PHEOCHROMOCYTOMA, MALIGNANT	X																											
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA																												
C-CELL ADENOMA																												
C-CELL CARCINOMA	X																											
CARCINOSARCOMA, INVASIVE																												
PARATHYROID ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS ISLET-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL CARCINOMA																												
REPRODUCTIVE SYSTEM																												
MAMMARY GLAND ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																												
PAPILLARY ADENOCARCINOMA																												
PAPILLARY CYSTADENOMA, NOS																												
FIBROSARCOMA																												
FIBROADENOMA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL PAPILLOMA																												
SQUAMOUS CELL CARCINOMA																												
ADENOMA, NOS																												
KERATOCANTHOMA																												
VAGINA SQUAMOUS CELL PAPILLOMA	N	N	N	N	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 CARCINOMA-IN-SITU, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																												
ENDOMETRIAL STROMAL POLYP																												
ENDOMETRIAL STROMAL SARCOMA	X																											
ENDOMETRIAL STROMAL SARCOMA, INVA																												
OVARY GRANULOSA-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULOSA-CELL CARCINOMA																												
MESOTHELIOMA, NOS																												
NERVOUS SYSTEM																												
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA																												
MENINGIOMA																												
SPECIAL SENSE ORGANS																												
ZYMBAL'S GLAND SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																												
CARCINOSARCOMA																												
MUSCULOSKELETAL SYSTEM																												
BONE SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
OSTEOSARCOMA																												
BODY CAVITIES																												
PERITONEUM PHEOCHROMOCYTOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ALL OTHER SYSTEMS																												
MULTIPLE SITES NOS MALIG. LYMPHOMA, HISTIOCYTIC TYPE																												
MULTIPLE ORGANS NOS SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIG. LYMPHOMA, UNDIFFER-TYPE																												
MYELOMONOCYTIC LEUKEMIA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
MONOCYTIC LEUKEMIA																												
LEUKEMIA, NONNUCLEAR CELL																												
LES NOS OSTEOSARCOMA																												

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40			
WEEKS ON STUDY	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	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40		
ENDOCRINE SYSTEM																																											
PITUITARY CARCINOMA, NOS
ADENOMA, NOS
GANGLIOMA
NEUROFIBROSARCOMA
ADRENAL CORTICAL ADENOMA
PHEOCHROMOCYTOMA
PHEOCHROMOCYTOMA, MALIGNANT
THYROID FOLLICULAR-CELL ADENOMA
FOLLICULAR-CELL CARCINOMA
G-CELL ADENOMA
G-CELL CARCINOMA
G-CELL CARCINOMA, INVASIVE
PARATHYROID ADENOMA, NOS	
ADENOMA, NOS
PANCREATIC ISLETS ISLET-CELL ADENOMA	
ISLET-CELL CARCINOMA	
ISLET-CELL CARCINOMA	
REPRODUCTIVE SYSTEM																																											
MAMMARY GLAND ADENOMA, NOS	
ADENOCARCINOMA, NOS	
PAPILLARY ADENOCARCINOMA	
PAPILLARY CYSTADENOMA, NOS	
FIBROSARCOMA	
FIBROADENOMA	
PROLACTIN/CLITORAL GLAND CARCINOMA, NOS		
SQUAMOUS CELL PAPILLOMA		
SQUAMOUS CELL CARCINOMA		
ADENOMA, NOS	
KERATOACANTHOMA	
VAGINA SQUAMOUS CELL PAPILLOMA		
UTERUS CARCINOMA-IN-SITU, NOS		
ADENOCARCINOMA, NOS		
ENDOMETRIAL STROMAL POLYP		
ENDOMETRIAL STROMAL SARCOMA		
ENDOMETRIAL STROMAL SARCOMA, INVA		
OVARY GRANULOSA-CELL TUMOR		
GRANULOSA-CELL CARCINOMA		
MESOTHELIOMA, NOS		
NERVOUS SYSTEM																																											
BRAIN CARCINOMA, NOS, INVASIVE		
ASTROCYTOMA		
MENINGIOMA		
SPECIAL SENSE ORGANS																																											
ZYMBAL'S GLAND SQUAMOUS CELL PAPILLOMA		
SQUAMOUS CELL CARCINOMA		
CARCINOSARCOMA		
MUSCULOSKELETAL SYSTEM																																											
BONE SQUAMOUS CELL CARCINOMA, INVASIVE		
OSTEOSARCOMA		
BODY CAVITIES																																											
PERITONEUM PHEOCHROMOCYTOMA, INVASIVE		
ALL OTHER SYSTEMS																																											
MULTIPLE SITES NOS MALIG. LYMPHOMA, HISTIOCYTIC TYPE		
MULTIPLE ORGANS NOS SQUAMOUS CELL CARCINOMA, INVASIVE		
MALIG. LYMPHOMA, UNDIFFER-TYPE		
MYELOMONOCYTIC LEUKEMIA		
MONOCYTIC LEUKEMIA		
LEUKEMIA, MONONUCLEAR CELL		
LEG NOS OSTEOSARCOMA		

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	
WEEKS ON STUDY	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	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	
TOTAL TISSUES TUMORS																																																																																																					
INTEGUMENTARY SYSTEM																																																																																																					
SKIN	+																																																																																																				250H
SQUAMOUS CELL PAPILLOMA	+																																																																																																				4
SQUAMOUS CELL CARCINOMA	+																																																																																																				1
BASAL-CELL TUMOR	+																																																																																																				1
TRICHOEPITHELIOMA	+																																																																																																				1
KERATOACANTHOMA	+																																																																																																				2
FIBROSARCOMA	+																																																																																																				1
SUBCUTANEOUS TISSUE	+																																																																																																				250H
FIBROMA	+																																																																																																				3
FIBROSARCOMA	+																																																																																																				1
LIPOMA	+																																																																																																				1
OSTEOSARCOMA	+																																																																																																				1
NEUROFIBROMA	+																																																																																																				1
RESPIRATORY SYSTEM																																																																																																					
LUNGS AND BRONCHI	+																																																																																																				245
ADENOCARCINOMA, NOS, METASTATIC	+																																																																																																				2
ALVEOLAR/BRONCHIOLAR CARCINOMA	+																																																																																																				1
C-CELL CARCINOMA, METASTATIC	+																																																																																																				3
GRANULOSA-CELL CARCINOMA, METASTATIC	+																																																																																																				1
PHEOCHROMOCYTOMA, METASTATIC	+																																																																																																				1
CARCINOSARCOMA, METASTATIC	+																																																																																																				1
OSTEOSARCOMA, METASTATIC	+																																																																																																				1
TRACHEA	+																																																																																																				245
C-CELL CARCINOMA, INVASIVE	+																																																																																																				1
NASAL CAVITY	+																																																																																																				250H
SQUAMOUS CELL CARCINOMA, INVASIVE	+																																																																																																				1
HEMATOPOIETIC SYSTEM																																																																																																					
BONE MARROW	+																																																																																																				241
SPLEEN	+																																																																																																				245
LYMPH NODES	+																																																																																																				245
ADENOCARCINOMA, NOS, METASTATIC	+																																																																																																				2
C-CELL CARCINOMA, METASTATIC	+																																																																																																				2
THYROID	+																																																																																																				190
ADENOCARCINOMA, NOS	+																																																																																																				2
TERRATOMA, BENIGN	+																																																																																																				1
MALIG. LYMPHOMA, UNDIFFER-TYPE	+																																																																																																				1
CIRCULATORY SYSTEM																																																																																																					
HEART	+																																																																																																				245
C-CELL CARCINOMA, METASTATIC	+																																																																																																				1
DIGESTIVE SYSTEM																																																																																																					
ORAL CAVITY	+																																																																																																				250H
SQUAMOUS CELL PAPILLOMA	+																																																																																																				1
SQUAMOUS CELL CARCINOMA	+																																																																																																				2
SALIVARY GLAND	+																																																																																																				243
SQUAMOUS CELL CARCINOMA, INVASIVE	+																																																																																																				1
LIVER	+																																																																																																				244
ISLET-CELL CARCINOMA, METASTATIC	+																																																																																																				1
NEOPLASTIC NODULE	+																																																																																																				5
C-CELL CARCINOMA, METASTATIC	+																																																																																																				1
OSTEOSARCOMA, METASTATIC	+																																																																																																				1
BILE DUCT	+																																																																																																				244
GALLBLADDER & COMMON BILE DUCT	+																																																																																																				250H
PANCREAS	+																																																																																																				245
ACINAR-CELL ADENOMA	+																																																																																																				1
GRANULOSA-CELL CARCINOMA, METASTATIC	+																																																																																																				1
ESOPHAGUS	+																																																																																																				244
STOMACH	+																																																																																																				245
CARCINOMA, NOS, METASTATIC	+																																																																																																				1
SQUAMOUS CELL CARCINOMA	+																																																																																																				1
SMALL INTESTINE	+																																																																																																				244
ADENOMA IN ADENOMATOUS POLYP	+																																																																																																				1
MUCINOUS CYSTADENOCARCINOMA	+																																																																																																				1
LEIOMYOMA	+																																																																																																				1
LEIOMYOSARCOMA	+																																																																																																				2
LARGE INTESTINE	+																																																																																																				244
ADENOMATOUS POLYP, NOS	+																																																																																																				3
LEIOMYOSARCOMA	+																																																																																																				1
URINARY SYSTEM																																																																																																					
KIDNEY	+																																																																																																				245
TRANSITIONAL-CELL CARCINOMA	+																																																																																																				1
PHEOCHROMOCYTOMA, METASTATIC	+																																																																																																				1
URINARY BLADDER	+																																																																																																				242
ENDOMETRIAL STROMAL SARCOMA, INVA	+																																																																																																				1

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30	TOTAL TISSUES					
WEEKS ON STUDY	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	26	27	28	29	30						
ENDOCRINE SYSTEM																																				
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	244		
ADENOMA, NOS																																		13		
GANGLIONEUROMA				X	X	X	X	X																										10		
NEUROFIBROSARCOMA																																		1		
ADRENAL																																				
CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	249		
PHENOCROMOCYTOMA																																			30	
PHENOCROMOCYTOMA, MALIGNANT																																				
THYROID																																				
FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	244	
FOLLICULAR-CELL CARCINOMA																																			4	
C-CELL ADENOMA																																			8	
C-CELL CARCINOMA																																			20	
CARCINOSARCOMA, INVASIVE																																			21	
PARATHYROID																																				
ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	222		
PANCREATIC ISLETS																																				
ISLET-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	245	
ISLET-CELL CARCINOMA																																			3	
REPRODUCTIVE SYSTEM																																				
MAMMARY GLAND																																				
ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250H	
ADENOCARCINOMA, NOS																																			14	
PAPILLARY ADENOCARCINOMA																																			19	
PAPILLARY CYSTADENOMA, NOS																																			1	
FIBROSARCOMA																																			3	
FIBROADENOMA																																			1	
PREPUTIAL/CLITORAL GLAND																																				
CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	250H		
SQUAMOUS CELL PAPILLOMA																																			8	
SQUAMOUS CELL CARCINOMA																																				1
KERATOACANTHOMA																																				9
VAGINA																																				
SQUAMOUS CELL PAPILLOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	250H		
UTERUS																																				
CARCINOMA-IN-SITU, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	245	
ADENOCARCINOMA, NOS																																				1
ENDOMETRIAL STROMAL POLYP																																				34
ENDOMETRIAL STROMAL SARCOMA																																				4
ENDOMETRIAL STROMAL SARCOMA, INVA																																				2
OVARY																																				
GRANULOSA-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	245	
GRANULOSA-CELL CARCINOMA																																				3
MESOTHELIOMA, NOS																																				2
NERVOUS SYSTEM																																				
BRAIN																																				
CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	245	
ASTROCYTOMA																																				11
MEINGIOMA																																				4
SPECIAL SENSE ORGANS																																				
ZYMBAL'S GLAND																																				
SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	250H	
SQUAMOUS CELL CARCINOMA																																				1
CARCINOSARCOMA																																				1
MUSCULOSKELETAL SYSTEM																																				
BONE																																				
SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	250H		
OSTEOSARCOMA																																				1
BODY CAVITIES																																				
PERITONEUM																																				
PHENOCROMOCYTOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	250H		
ALL OTHER SYSTEMS																																				
MULTIPLE SITES NOS																																				
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																																			1	
MULTIPLE ORGANS NOS																																				
SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	250H	
MALIG.LYMPHOMA, UNDIFFER-TYPE																																				1
MYELOMONOCYTIC LEUKEMIA																																				1
MONOCYTIC LEUKEMIA																																				99
LEUKEMIA, MONONUCLEAR CELL																																				1
LEG NOS																																				
OSTEOSARCOMA																																				1

H ANIMALS NECROPSIED

APPENDIX B

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
ANIMALS INITIALLY IN STUDY	88	125	250	175	100
ANIMALS NECROPSIED	88	125	250	175	100
ANIMALS EXAMINED HISTOPATHOLOGICALLY	85	125	250	175	100
INTEGUMENTARY SYSTEM					
*HEAD	(88)	(125)	(250)	(175)	(100)
FIBROUS HISTIOCYTOMA, MALIGNANT					1 (1%)
*AXILLA	(88)	(125)	(250)	(175)	(100)
FIBROUS HISTIOCYTOMA, MALIGNANT				1 (1%)	
*SKIN	(88)	(125)	(250)	(175)	(100)
PAPILLOMA, NOS	5 (6%)				
SQUAMOUS CELL PAPILLOMA		2 (2%)	8 (3%)	4 (2%)	3 (3%)
SQUAMOUS CELL CARCINOMA		2 (2%)	3 (1%)	3 (2%)	1 (1%)
BASAL-CELL TUMOR			2 (1%)	2 (1%)	
BASAL-CELL CARCINOMA	2 (2%)		1 (0%)	1 (1%)	
TRICHOEPITHELIOMA		4 (3%)			
SEBACEOUS ADENOMA			2 (1%)	1 (1%)	
SEBACEOUS ADENOCARCINOMA			1 (0%)		
KERATOACANTHOMA	1 (1%)	6 (5%)	†19 (8%)	11 (6%)	7 (7%)
FIBROMA					1 (1%)
FIBROSARCOMA			1 (0%)		
NEUROFIBROSARCOMA				1 (1%)	
*SUBCUT TISSUE	(88)	(125)	(250)	(175)	(100)
CARCINOMA, NOS			1 (0%)		
SQUAMOUS CELL CARCINOMA	3 (3%)	1 (1%)	1 (0%)	1 (1%)	2 (2%)
BASAL-CELL TUMOR	1 (1%)				
BASAL-CELL CARCINOMA			1 (0%)	1 (1%)	
TRICHOEPITHELIOMA		1 (1%)		1 (1%)	1 (1%)
KERATOACANTHOMA					1 (1%)
SARCOMA, NOS	1 (1%)	2 (2%)	3 (1%)	2 (1%)	5 (5%)
FIBROMA	17 (19%)	13 (10%)	51 (20%)	15 (9%)	11 (11%)
FIBROSARCOMA	7 (8%)	3 (2%)	5 (2%)	2 (1%)	1 (1%)
FIBROUS HISTIOCYTOMA, MALIGNANT			2 (1%)	2 (1%)	
LIPOMA		1 (1%)	1 (0%)	2 (1%)	
RHABDOMYOSARCOMA				1 (1%)	1 (1%)
OSTEOSARCOMA			2 (1%)		1 (1%)
AMELOBLASTIC ODONTOMA				1 (1%)	
NEUROFIBROMA					1 (1%)
NEUROFIBROSARCOMA			1 (0%)		
RESPIRATORY SYSTEM					
*NASAL CAVITY	(88)	(125)	(250)	(175)	(100)
ADENOMA, NOS		1 (1%)			
*NASAL TURBINATE	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA, INVASIVE				1 (1%)	
ADENOMA, NOS		1 (1%)			
ADENOCARCINOMA, NOS				1 (1%)	
#TRACHEA	(85)	(124)	(250)	(175)	(99)
SQUAMOUS CELL CARCINOMA, INVASIVE				1 (1%)	
FIBROSARCOMA, INVASIVE	1 (1%)				

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
RESPIRATORY SYSTEM (Continued)					
#LUNG	(85)	(125)	(250)	(175)	(99)
CARCINOMA, NOS, METASTATIC				1 (1%)	
SQUAMOUS CELL CARCINOMA	1 (1%)				1 (1%)
SQUAMOUS CELL CARCINOMA, METASTATIC			1 (0%)	1 (1%)	2 (2%)
ADENOCARCINOMA, NOS, METASTATIC		1 (1%)	2 (1%)		
HEPATOCELLULAR CARCINOMA, METASTATIC				1 (1%)	
ALVEOLAR/BRONCHIOLAR ADENOMA		1 (1%)	4 (2%)	1 (1%)	
ALVEOLAR/BRONCHIOLAR CARCINOMA	2 (2%)		1 (0%)		
C-CELL CARCINOMA, METASTATIC	1 (1%)	1 (1%)			
PHEOCHROMOCYTOMA, METASTATIC	1 (1%)	-	4 (2%)		
SARCOMA, NOS, METASTATIC				2 (1%)	
FIBROSARCOMA, METASTATIC		1 (1%)	1 (0%)		
FIBROUS HISTIOCYTOMA, METASTATIC			1 (0%)		
LIPOSARCOMA, METASTATIC			1 (0%)		
MIXED TUMOR, METASTATIC				1 (1%)	
CARCINOSARCOMA, METASTATIC				1 (1%)	
MESOTHELIOMA, NOS			1 (0%)		
OSTEOSARCOMA, METASTATIC		1 (1%)	1 (0%)	1 (1%)	
MENINGIOMA, METASTATIC			1 (0%)		
HEMATOPOIETIC SYSTEM					
*MULTIPLE ORGANS	(88)	(125)	(250)	(175)	(100)
MALIG.LYMPHOMA, HISTIO- CYTIC TYPE	1 (1%)	2 (2%)	1 (0%)	2 (1%)	3 (3%)
MYELOMONOCYTIC LEUKEMIA			3 (1%)	2 (1%)	
MONOCYTIC LEUKEMIA	28 (32%)	40 (32%)	90 (36%)	65 (37%)	36 (36%)
LEUKEMIA, MONONUCLEAR CELL	3 (3%)	2 (2%)	1 (0%)	2 (1%)	
#SPLEEN	(85)	(125)	(250)	(175)	(99)
INTERSTITIAL-CELL TUMOR, METASTATIC			1 (0%)		
SARCOMA, NOS			1 (0%)		
MALIG.LYMPHOMA, HISTIO- CYTIC TYPE		1 (1%)			
MONOCYTIC LEUKEMIA			2 (1%)	2 (1%)	
#MANDIBULAR L. NODE	(85)	(125)	(250)	(175)	(100)
CARCINOMA, NOS, INVASIVE				1 (1%)	
SQUAMOUS CELL CARCINOMA, METASTATIC		1 (1%)			
SARCOMA, NOS		1 (1%)			
SARCOMA, NOS, INVASIVE			1 (0%)		
#CERVICAL LYMPH NODE	(85)	(125)	(250)	(175)	(100)
CARCINOMA, NOS, METASTATIC				1 (1%)	
C-CELL CARCINOMA, METASTATIC					1 (1%)
SARCOMA, NOS, INVASIVE			1 (0%)		

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
HEMATOPOIETIC SYSTEM (Continued)					
#MEDIASTINAL L. NODE	(85)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA, METASTATIC			1 (0%)		
SARCOMA, NOS, METASTATIC				1 (1%)	
FIBROUS HISTIOCYTOMA, METASTATIC			1 (0%)		
#MESENTERIC L. NODE	(85)	(125)	(250)	(175)	(100)
MUCINOUS CYSTADENO- CARCINOMA, METASTATIC				3 (2%)	
#ILEOCOLIC LYMPH NODE	(85)	(125)	(250)	(175)	(100)
MUCINOUS CYSTADENO- CARCINOMA, METASTATIC		1 (1%)		4 (2%)	
SIGNET RING CARCINOMA, METASTATIC		1 (1%)			
#LIVER	(85)	(125)	(250)	(175)	(100)
MALIG. LYMPHOMA, HISTIO- CYTIC TYPE		1 (1%)			
MONOCYTIC LEUKEMIA					1 (1%)
CIRCULATORY SYSTEM					
#SPLEEN	(85)	(125)	(250)	(175)	(99)
HEMANGIOSARCOMA			3 (1%)		
#LUNG	(85)	(125)	(250)	(175)	(99)
HEMANGIOSARCOMA, METASTATIC		1 (1%)			
#HEART	(85)	(125)	(250)	(175)	(99)
ADENOCARCINOMA, NOS, METASTATIC	1 (1%)		1 (0%)	1 (1%)	
#LIVER	(85)	(125)	(250)	(175)	(100)
HEMANGIOSARCOMA		2 (2%)			
#ASCENDING COLON	(85)	(125)	(250)	(175)	(100)
HEMANGIOSARCOMA	1 (1%)				
DIGESTIVE SYSTEM					
*MOUTH/ORAL CAVITY	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA			1 (0%)		
*HARD PALATE	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL PAPILLOMA KERATOACANTHOMA			1 (0%)		1 (1%)
*TONGUE	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL PAPILLOMA			1 (0%)	1 (1%)	
#SALIVARY GLAND	(84)	(124)	(247)	(173)	(98)
CARCINOMA, NOS				2 (1%)	
SARCOMA, NOS		5 (4%)	3 (1%)	1 (1%)	
FIBROSARCOMA	3 (4%)		2 (1%)		
FIBROSARCOMA, INVASIVE	1 (1%)		1 (0%)		
#PAROTID GLAND	(84)	(124)	(247)	(173)	(98)
SARCOMA, NOS		1 (1%)			
#LIVER	(85)	(125)	(250)	(175)	(100)
NEOPLASTIC NODULE	6 (7%)	12 (10%)	13 (5%)	10 (6%)	5 (5%)
HEPATOCELLULAR CARCINOMA	2 (2%)	17 (14%)	7 (3%)	20 (11%)	1 (1%)
FIBROSARCOMA, METASTATIC					
FIBROUS HISTIOCYTOMA, METASTATIC				1 (1%)	
LIPOMA				1 (1%)	
LIPOSARCOMA				2 (1%)	
LIPOSARCOMA, METASTATIC			1 (0%)		

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
DIGESTIVE SYSTEM (Continued)					
#PANCREAS	(85)	(124)	(249)	(174)	(99)
ACINAR-CELL ADENOMA	3 (4%)	7 (6%)	23 (9%)	14 (8%)	9 (9%)
ACINAR-CELL CARCINOMA	1 (1%)		2 (1%)		
MESOTHELIOMA, METASTATIC					1 (1%)
#PANCREATIC DUCT	(85)	(124)	(249)	(174)	(99)
ADENOCARCINOMA, NOS		1 (1%)			
#ESOPHAGUS	(83)	(125)	(250)	(174)	(98)
FIBROSARCOMA					1 (1%)
#STOMACH	(85)	(124)	(250)	(175)	(100)
ADENOCARCINOMA, NOS			1 (0%)		
#GASTRIC SEROSA	(85)	(124)	(250)	(175)	(100)
MESOTHELIOMA, METASTATIC					1 (1%)
#SMALL INTESTINE	(85)	(125)	(250)	(175)	(100)
LEIOMYOSARCOMA					1 (1%)
#DUODENUM	(85)	(125)	(250)	(175)	(100)
ADENOCARCINOMA, NOS				1 (1%)	
ADENOMATOUS POLYP, NOS			1 (0%)		
MUCINOUS CYSTADENO- CARCINOMA			1 (0%)	1 (1%)	
SIGNET RING CARCINOMA			1 (0%)	1 (1%)	
LEIOMYOMA			1 (0%)		
#JEJUNUM	(85)	(125)	(250)	(175)	(100)
ADENOCARCINOMA, NOS				1 (1%)	
MUCINOUS CYSTADENO- CARCINOMA				1 (1%)	
LEIOMYOSARCOMA			2 (1%)		
#ILEUM	(85)	(125)	(250)	(175)	(100)
LEIOMYOMA	1 (1%)				1 (1%)
#COLONIC SEROSA	(85)	(125)	(250)	(175)	(100)
MESOTHELIOMA, METASTATIC				1 (1%)	
#CECUM	(85)	(125)	(250)	(175)	(100)
ADENOCARCINOMA, NOS		1 (1%)			
ADENOMATOUS POLYP, NOS				1 (1%)	
MUCINOUS CYSTADENO- CARCINOMA		4 (3%)		4 (2%)	
MUCINOUS CYSTADENOCA, METASTATIC				1 (1%)	
#ASCENDING COLON	(85)	(125)	(250)	(175)	(100)
ADENOCARCINOMA, NOS				1 (1%)	
ADENOMATOUS POLYP, NOS		3 (2%)	2 (1%)	3 (2%)	
ADENOCARCINOMA IN ADENOMATOUS POLYP				1 (1%)	
MUCINOUS CYSTADENO- CARCINOMA		3 (2%)		11 (6%)	
MUCINOUS CYSTADENO- CRCINOMA, METASTATIC		1 (1%)			
SIGNET RING CARCINOMA		1 (1%)			
#TRANSVERSE COLON	(85)	(125)	(250)	(175)	(100)
ADENOCARCINOMA, NOS		1 (1%)			
ADENOMATOUS POLYP, NOS		4 (3%)		6 (3%)	
LEIOMYOSARCOMA					1 (1%)
#DESCENDING COLON	(85)	(125)	(250)	(175)	(100)
ADENOMATOUS POLYP, NOS		24 (19%)	7 (3%)	37 (21%)	2 (2%)
ADENOCARCINOMA IN ADENOMATOUS POLYP				2 (1%)	
MUCINOUS CYSTADENO- CARCINOMA				4 (2%)	
SIGNET RING CARCINOMA				1 (1%)	

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
DIGESTIVE SYSTEM (Continued)					
*ANUS	(88)	(125)	(250)	(175)	(100)
ADENOMATOUS POLYP, NOS		1 (1%)			
URINARY SYSTEM					
#KIDNEY	(85)	(125)	(250)	(175)	(100)
TUBULAR-CELL ADENO- CARCINOMA		1 (1%)	1 (0%)		
TUBULAR ADENOCARCINOMA			1 (0%)		
LIPOMA			1 (0%)		
LIPOSARCOMA, INVASIVE			1 (0%)		
MIXED TUMOR, MALIGNANT			1 (0%)	1 (1%)	
#RIGHT KIDNEY	(85)	(125)	(250)	(175)	(100)
MIXED TUMOR, MALIGNANT		1 (1%)			
*RIGHT URETER	(88)	(125)	(250)	(175)	(100)
MIXED TUMOR, MALIGNANT		1 (1%)			
#URINARY BLADDER	(84)	(124)	(249)	(174)	(98)
PAPILLOMA, NOS		1 (1%)			
TRANSITIONAL-CELL PAPILLOMA		1 (1%)	1 (0%)	1 (1%)	
TRANSITIONAL-CELL CARCINOMA			1 (0%)		
ENDOCRINE SYSTEM					
#PITUITARY	(85)	(124)	(246)	(175)	(100)
CARCINOMA, NOS	4 (5%)	3 (2%)	3 (1%)	1 (1%)	1 (1%)
ADENOMA, NOS	14 (16%)	12 (10%)	49 (20%)	16 (9%)	18 (18%)
#ADRENAL	(85)	(125)	(250)	(175)	(100)
CORTICAL ADENOMA			4 (2%)	1 (1%)	1 (1%)
CORTICAL CARCINOMA	2 (2%)				
PHEOCHROMOCYTOMA	14 (16%)	20 (16%)	57 (23%)	31 (18%)	30 (30%)
PHEOCHROMOCYTOMA, MALIGNANT	1 (1%)		4 (2%)		
#ADRENAL MEDULLA	(85)	(125)	(250)	(175)	(100)
PHEOCHROMOCYTOMA	2 (2%)		2 (1%)	3 (2%)	2 (2%)
PHEOCHROMOCYTOMA, MALIGNANT			1 (0%)		
#THYROID	(84)	(124)	(250)	(175)	(99)
FOLLICULAR-CELL ADENOMA	1 (1%)	1 (1%)	12 (5%)	14 (8%)	3 (3%)
FOLLICULAR-CELL CARCINOMA	5 (6%)	8 (6%)	13 (5%)	14 (8%)	2 (2%)
C-CELL ADENOMA	13 (15%)	11 (9%)	29 (12%)	18 (10%)	9 (9%)
C-CELL CARCINOMA	19 (23%)	15 (12%)	38 (15%)	21 (12%)	23 (23%)
SARCOMA, NOS, INVASIVE			1 (0%)		
FIBROSARCOMA, INVASIVE	1 (1%)				
#PARATHYROID	(78)	(119)	(243)	(166)	(93)
ADENOMA, NOS	3 (4%)	1 (1%)	4 (2%)		
C-CELL CARCINOMA, INVASIVE	1 (1%)		1 (0%)		
#PANCREATIC ISLETS	(85)	(124)	(249)	(174)	(99)
ISLET-CELL ADENOMA	5 (6%)	1 (1%)	6 (2%)	5 (3%)	5 (5%)
ISLET-CELL CARCINOMA	3 (4%)	6 (5%)	17 (7%)	4 (2%)	6 (6%)
REPRODUCTIVE SYSTEM					
*MAMMARY GLAND	(88)	(125)	(250)	(175)	(100)
ADENOMA, NOS	1 (1%)	3 (2%)	6 (2%)		1 (1%)
ADENOCARCINOMA, NOS		1 (1%)	1 (0%)		
FIBROMA			1 (0%)		
FIBROUS HISTIOCYTOMA, INVASIVE				1 (1%)	
CARCINOSARCOMA			1 (0%)		
FIBROADENOMA	3 (3%)	1 (1%)	16 (6%)	4 (2%)	7 (7%)

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
REPRODUCTIVE SYSTEM (Continued)					
*PREPUCE	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA			1 (0%)		
*PREPUTIAL GLAND	(88)	(125)	(250)	(175)	(100)
CARCINOMA, NOS	2 (2%)	6 (5%)	10 (4%)	9 (5%)	3 (3%)
SQUAMOUS CELL CARCINOMA	1 (1%)	1 (1%)	1 (0%)	1 (1%)	
ADENOMA, NOS	1 (1%)				
#PROSTATE	(85)	(125)	(249)	(174)	(99)
CARCINOMA, NOS			2 (1%)		
SQUAMOUS CELL CARCINOMA					1 (1%)
ADENOMA, NOS		1 (1%)	3 (1%)	2 (1%)	
MESOTHELIOMA, NOS	1 (1%)				
*SEMINAL VESICLE	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA, INVASIVE					1 (1%)
#TESTIS	(84)	(125)	(250)	(175)	(100)
INTERSTITIAL-CELL TUMOR	79 (94%)	112 (90%)	237 (95%)	160 (91%)	89 (89%)
INTERSTITIAL-CELL TUMOR, MALIGNANT		1 (1%)	1 (0%)		
*EPIDIDYMIS	(88)	(125)	(250)	(175)	(100)
LIPOSARCOMA			1 (0%)		
MESOTHELIOMA, NOS				1 (1%)	
*SCROTUM	(88)	(125)	(250)	(175)	(100)
FIBROMA		1 (1%)			
MESOTHELIOMA, MALIGNANT			2 (1%)		
MESOTHELIOMA, METASTATIC		1 (1%)			
NERVOUS SYSTEM					
#CEREBRUM	(85)	(125)	(250)	(175)	(100)
CARCINOMA, NOS, INVASIVE		1 (1%)			
ASTROCYTOMA	1 (1%)		1 (0%)		1 (1%)
#BRAIN	(85)	(125)	(250)	(175)	(100)
CARCINOMA, NOS, INVASIVE	2 (2%)		1 (0%)	1 (1%)	1 (1%)
OSTEOMA				1 (1%)	
GRANULAR-CELL TUMOR, NOS				1 (1%)	
ASTROCYTOMA			2 (1%)	1 (1%)	
MENINGIOMA			1 (0%)		
#CEREBELLUM	(85)	(125)	(250)	(175)	(100)
GRANULAR-CELL TUMOR, NOS					1 (1%)
*SPINAL CORD	(88)	(125)	(250)	(175)	(100)
NEURILEMOMA, MALIGNANT		1 (1%)			
*PARA AORTIC BODY	(88)	(125)	(250)	(175)	(100)
PARAGANGLIOMA, NOS			2 (1%)		
SPECIAL SENSE ORGANS					
*EYE	(88)	(125)	(250)	(175)	(100)
ADENOCARCINOMA, NOS, INVASIVE				1 (1%)	
SARCOMA, NOS				1 (1%)	
*EYE/IRIS	(88)	(125)	(250)	(175)	(100)
MALIGNANT MELANOMA			1 (0%)		
*HARDERIAN GLAND	(88)	(125)	(250)	(175)	(100)
SARCOMA, NOS, INVASIVE			1 (0%)		
*EAR	(88)	(125)	(250)	(175)	(100)
FIBROSARCOMA		1 (1%)			

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
SPECIAL SENSE ORGANS (Continued)					
*ZYMBAL GLAND	(88)	(125)	(250)	(175)	(100)
CARCINOMA, NOS	1 (1%)	3 (2%)	2 (1%)	2 (1%)	
SQUAMOUS CELL PAPILLOMA		1 (1%)		3 (2%)	
SQUAMOUS CELL CARCINOMA	1 (1%)	15 (12%)	8 (3%)	22 (13%)	3 (3%)
KERATOACANTHOMA			1 (0%)	1 (1%)	
CARCINOSARCOMA			1 (0%)	1 (1%)	
MUSCULOSKELETAL SYSTEM					
*MANDIBLE	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL PAPILLOMA			1 (0%)		
SQUAMOUS CELL CARCINOMA					2 (2%)
*VERTEBRA	(88)	(125)	(250)	(175)	(100)
OSTEOSARCOMA	1 (1%)				
*STERNUM	(88)	(125)	(250)	(175)	(100)
OSTEOSARCOMA				1 (1%)	
*RIB	(88)	(125)	(250)	(175)	(100)
SARCOMA, NOS					1 (1%)
OSTEOSARCOMA	1 (1%)		1 (0%)		
*INTERCHONDRAL JOINT	(88)	(125)	(250)	(175)	(100)
OSTEOSARCOMA			1 (0%)		
*MUSCLE OF LEG	(88)	(125)	(250)	(175)	(100)
RHABDOMYOSARCOMA					1 (1%)
BODY CAVITIES					
*THORACIC CAVITY	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA			1 (0%)		
*MEDIASTINUM	(88)	(125)	(250)	(175)	(100)
ADENOCARCINOMA, NOS,					
METASTATIC			1 (0%)		
MESOTHELIOMA, NOS			1 (0%)		
*ABDOMINAL CAVITY	(88)	(125)	(250)	(175)	(100)
LIPOSARCOMA			1 (0%)		
OSTEOSARCOMA					1 (1%)
CHONDROMA					1 (1%)
*PERITONEUM	(88)	(125)	(250)	(175)	(100)
MESOTHELIOMA, INVASIVE	1 (1%)				
*PLEURA	(88)	(125)	(250)	(175)	(100)
ADENOCARCINOMA, NOS,					
METASTATIC			1 (0%)		
*MESENTERY	(88)	(125)	(250)	(175)	(100)
MUCINOUS CYSTADENOCA,					
METASTATIC				1 (1%)	
SARCOMA, NOS		1 (1%)			
FIBROSARCOMA			1 (0%)		
LIPOMA			1 (0%)		
MESOTHELIOMA, INVASIVE	1 (1%)				
*TUNICA VAGINALIS	(88)	(125)	(250)	(175)	(100)
MESOTHELIOMA, NOS	2 (2%)	1 (1%)	1 (0%)	3 (2%)	1 (1%)
ALL OTHER SYSTEMS					
*MULTIPLE ORGANS	(88)	(125)	(250)	(175)	(100)
ADENOCARCINOMA, NOS,					
INVASIVE		1 (1%)			
ADENOCARCINOMA, NOS,					
METASTATIC		1 (1%)		2 (1%)	
C-CELL CARCINOMA,					
METASTATIC	1 (1%)				

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
ALL OTHER SYSTEMS					
*MULTIPLE ORGANS (Continued)	(88)	(125)	(250)	(175)	(100)
MUCINOUS CYSTADENOMA, METASTATIC		3 (2%)		3 (2%)	
SIGNET RING CARCINOMA, METASTATIC				2 (1%)	
SARCOMA, NOS, INVASIVE	1 (1%)			1 (1%)	
FIBROSARCOMA, INVASIVE			1 (0%)		
FIBROSARCOMA, METASTATIC			1 (0%)		
FIBROUS HISTIOCYTOMA, METASTATIC			1 (0%)	1 (1%)	
CARCINOSARCOMA, METASTATIC			1 (0%)		
MESOTHELIOMA, MALIGNANT	2 (2%)	5 (4%)	13 (5%)	4 (2%)	5 (5%)
MESOTHELIOMA, MALIGNANT			1 (0%)		
MESOTHELIOMA, INVASIVE	1 (1%)				
MESOTHELIOMA, METASTATIC		4 (3%)	13 (5%)	3 (2%)	4 (4%)
OSTEOSARCOMA, METASTATIC	1 (1%)		2 (1%)		3 (3%)
HEAD					
SARCOMA, NOS			1		
ORBITAL REGION					
OSTEOSARCOMA					1
BACK					
RHABDOMYOSARCOMA			1		
LUMBAR REGION					
CHONDROSARCOMA			1		
COCCYGEAL REGION					
NEUROFIBROSARCOMA				1	
BASE OF TAIL					
RHABDOMYOSARCOMA		1			
AXILLA					
FIBROMA					1
LOWER LEG					
OSTEOSARCOMA			1		
ADIPOSE TISSUE					
MUCINOUS CYSTADENO- CARCINOMA, METASTATIC				1	
MIXED MESENCHYMAL TUMOR, MALIGNANT			1		
MESOTHELIOMA, METASTATIC				1	
ANIMAL DISPOSITION SUMMARY					
ANIMALS INITIALLY IN STUDY	88	125	250	175	100
NATURAL DEATH	21	21	29	25	16
MORIBUND SACRIFICE	60	86	191	134	73
TERMINAL SACRIFICE	7	18	29	16	11
ACCIDENTALLY KILLED, NDA			1		

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
TUMOR SUMMARY					
TOTAL ANIMALS WITH PRIMARY TUMORS**	85	122	246	173	95
TOTAL PRIMARY TUMORS	272	411	857	603	320
TOTAL ANIMALS WITH BENIGN TUMORS	80	117	242	163	91
TOTAL BENIGN TUMORS	164	236	555	361	205
TOTAL ANIMALS WITH MALIGNANT TUMORS	65	98	192	145	77
TOTAL MALIGNANT TUMORS	99	162	284	227	108
TOTAL ANIMALS WITH SECONDARY TUMORS##	13	19	39	31	13
TOTAL SECONDARY TUMORS	15	20	47	42	14
TOTAL ANIMALS WITH TUMORS UNCERTAIN--BENIGN OR MALIGNANT	9	12	17	13	7
TOTAL UNCERTAIN TUMORS	9	13	18	15	7

* NUMBER OF ANIMALS NECROPSIED

** PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

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

† MULTIPLE OCCURRENCE OF MORPHOLOGY IN THE SAME ORGAN. TISSUE IS ONLY COUNTED ONCE.

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
ANIMALS INITIALLY IN STUDY	88	125	250	175	100
ANIMALS NECROPSIED	88	125	250	175	100
ANIMALS EXAMINED HISTOPATHOLOGICALLY	87	125	250	175	100
INTEGUMENTARY SYSTEM					
*SKIN	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL PAPILLOMA	3 (3%)		5 (2%)		
SQUAMOUS CELL CARCINOMA			1 (0%)		
BASAL-CELL TUMOR		1 (1%)		1 (1%)	
BASAL-CELL CARCINOMA			2 (1%)	1 (1%)	
KERATOACANTHOMA	1 (1%)		1 (0%)	2 (1%)	
*SUBCUT TISSUE	(88)	(125)	(250)	(175)	(100)
CARCINOMA, NOS				1 (1%)	
SQUAMOUS CELL CARCINOMA	1 (1%)		3 (1%)		
KERATOACANTHOMA				1 (1%)	
SARCOMA, NOS	1 (1%)				1 (1%)
FIBROMA	5 (6%)	2 (2%)	9 (4%)	1 (1%)	3 (3%)
FIBROSARCOMA	1 (1%)	1 (1%)	4 (2%)	1 (1%)	
FIBROUS HISTIOCYTOMA, MALIGNANT	2 (2%)				
LIPOMA			1 (0%)		
RESPIRATORY SYSTEM					
*NOSE	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA				1 (1%)	
*LARYNX	(88)	(125)	(250)	(175)	(100)
FOLLICULAR-CELL CARCINOMA, INVASIVE			1 (0%)		
C-CELL CARCINOMA, INVASIVE			1 (0%)		
#LUNG	(87)	(125)	(250)	(175)	(99)
SQUAMOUS CELL CARCINOMA, METASTATIC			1 (0%)	1 (1%)	
ADENOCARCINOMA, NOS, METASTATIC			2 (1%)		
ALVEOLAR/BRONCHIOLAR ADENOMA		1 (1%)	2 (1%)	1 (1%)	3 (3%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (1%)		1 (0%)		1 (1%)
PAPILLARY ADENOCARCINOMA, METASTATIC					1 (1%)
FOLLICULAR-CELL CARCINOMA, METASTATIC			1 (0%)		
C-CELL CARCINOMA, METASTATIC			4 (2%)		1 (1%)
PHEOCHROMOCYTOMA, METASTATIC	2 (2%)			1 (1%)	2 (2%)
SARCOMA, NOS, METASTATIC	1 (1%)				
FIBROUS HISTIOCYTOMA, METASTATIC	1 (1%)				
LIPOSARCOMA, METASTATIC				1 (1%)	
MIXED TUMOR, METASTATIC				5 (3%)	

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
HEMATOPOIETIC SYSTEM					
*MULTIPLE ORGANS	(88)	(125)	(250)	(175)	(100)
MALIG. LYMPHOMA, UNDIFFER-TYPE				2 (1%)	
MYELOMONOCYTIC LEUKEMIA			2 (1%)	1 (1%)	
MONOCYTIC LEUKEMIA	33 (38%)	66 (53%)	76 (30%)	88 (50%)	26 (26%)
LEUKEMIA, MONONUCLEAR CELL	1 (1%)	4 (3%)	4 (2%)	4 (2%)	3 (3%)
#MANDIBULAR L. NODE	(87)	(125)	(250)	(175)	(99)
SQUAMOUS CELL CARCINOMA, METASTA			3 (1%)		
#CERVICAL LYMPH NODE	(87)	(125)	(250)	(175)	(99)
FOLLICULAR-CELL CARCINOMA, METAS			1 (0%)		
C-CELL CARCINOMA, METASTATIC			2 (1%)		
#MEDIASTINAL L. NODE	(87)	(125)	(250)	(175)	(99)
C-CELL CARCINOMA, METASTATIC		1 (1%)	1 (0%)		1 (1%)
MUCINOUS CYSTADENO- CARCINOMA, METASTATIC				1 (1%)	
#CELIAC LYMPH NODE	(87)	(125)	(250)	(175)	(99)
MUCINOUS CYSTADENO- CARCINOMA, METASTATIC				1 (1%)	
SIGNET RING CARCINOMA, METASTATIC				1 (1%)	
#MESENTERIC L. NODE	(87)	(125)	(250)	(175)	(99)
ADENOCARCINOMA, NOS, METASTATIC				1 (1%)	
MALIG. LYMPHOMA, HISTIOCYTIC TYPE			1 (0%)		
#ILEOCOLIC LYMPH NODE	(87)	(125)	(250)	(175)	(99)
MUCINOUS CYSTADENO- CARCINOMA, METASTATIC		3 (2%)			
#AXILLARY LYMPH NODE	(87)	(125)	(250)	(175)	(99)
ADENOCARCINOMA, NOS, METASTATIC			1 (0%)		
#LIVER	(87)	(125)	(250)	(175)	(99)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE			1 (0%)		
CIRCULATORY SYSTEM					
#SPLEEN	(87)	(125)	(249)	(175)	(99)
HEMANGIOSARCOMA	1 (1%)				
#LUNG	(87)	(125)	(250)	(175)	(99)
HEMANGIOSARCOMA, METASTATIC				1 (1%)	
#HEART	(87)	(125)	(250)	(175)	(99)
ADENOCARCINOMA, NOS, METASTATIC			1 (0%)		
MIXED TUMOR, METASTATIC				1 (1%)	
NEURILEMOMA				1 (1%)	
#MYOCARDIUM	(87)	(125)	(250)	(175)	(99)
PHEOCHROMOCYTOMA, METASTATIC					1 (1%)
#LIVER	(87)	(125)	(250)	(175)	(99)
HEMANGIOSARCOMA				1 (1%)	
#PERIPANCREATIC TISSUE	(87)	(124)	(249)	(175)	(99)
HEMANGIOSARCOMA	1 (1%)				

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
DIGESTIVE SYSTEM					
*MOUTH	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA			1 (0%)		
SQUAMOUS CELL CARCINOMA, INVASIVE		1 (1%)			
*HARD PALATE	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL PAPILLOMA			1 (0%)		
SQUAMOUS CELL CARCINOMA					1 (1%)
*TONGUE	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL PAPILLOMA	1 (1%)	1 (1%)			1 (1%)
SQUAMOUS CELL CARCINOMA		1 (1%)			
#SALIVARY GLAND	(87)	(122)	(248)	(173)	(99)
ADENOCARCINOMA, NOS			1 (0%)		
SARCOMA, NOS					1 (1%)
#LIVER	(87)	(125)	(250)	(175)	(99)
SQUAMOUS CELL CARCINOMA, INVASIVE	1 (1%)				
BILE DUCT ADENOMA				1 (1%)	
NEOPLASTIC NODULE	3 (3%)	12 (10%)	4 (2%)	21 (12%)	1 (1%)
HEPATOCELLULAR CARCINOMA	1 (1%)	12 (10%)	2 (1%)	19 (11%)	
CORTICAL CARCINOMA, METASTATIC			1 (0%)		
MIXED TUMOR, METASTATIC				1 (1%)	
#HEPATIC CAPSULE	(87)	(125)	(250)	(175)	(99)
MIXED TUMOR, METASTATIC				1 (1%)	
#PANCREAS	(87)	(124)	(249)	(175)	(99)
ACINAR-CELL ADENOMA	2 (2%)	1 (1%)	4 (2%)		2 (2%)
ACINAR-CELL CARCINOMA			1 (0%)		
MIXED TUMOR, INVASIVE				1 (1%)	
MIXED TUMOR, METASTATIC				1 (1%)	
#STOMACH	(87)	(124)	(250)	(174)	(99)
SQUAMOUS CELL PAPILLOMA					1 (1%)
SQUAMOUS CELL CARCINOMA	1 (1%)				1 (1%)
ADENOMATOUS POLYP, NOS			1 (0%)		
CARCINOID TUMOR, NOS			2 (1%)		
LEIOMYOSARCOMA			1 (0%)		
ENDOMETRIAL STROMAL SARCOMA, METASTATIC			1 (0%)		
#SMALL INTESTINE	(87)	(125)	(249)	(175)	(99)
MUCINOUS CYSTADENO- CARCINOMA				1 (1%)	
#DUODENUM	(87)	(125)	(249)	(175)	(99)
MUCINOUS CYSTADENO- CARCINOMA		2 (2%)		2 (1%)	
SIGNET RING CARCINOMA				2 (1%)	
LEIOMYOMA	1 (1%)				
#JEJUNUM	(87)	(125)	(249)	(175)	(99)
ADENOMATOUS POLYP, NOS				1 (1%)	
#ILEUM	(87)	(125)	(249)	(175)	(99)
ADENOCARCINOMA IN ADENOMATOUS POLYP				1 (1%)	
#COLON	(87)	(125)	(250)	(175)	(99)
ADENOMATOUS POLYP, NOS		2 (2%)		1 (1%)	
MUCINOUS CYSTADENO- CARCINOMA				1 (1%)	
#COLONIC SEROSA	(87)	(125)	(250)	(175)	(99)
MUCINOUS CYSTADENOCA, METASTATIC		1 (1%)			

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
DIGESTIVE SYSTEM					
#CECUM	(87)	(125)	(250)	(175)	(99)
ADENOCARCINOMA, NOS		1 (1%)			
ADENOMATOUS POLYP, NOS				3 (2%)	
MUCINOUS CYSTADENO- CARCINOMA		8 (6%)		8 (5%)	
SIGNET RING CARCINOMA		1 (1%)			
#ASCENDING COLON	(87)	(125)	(250)	(175)	(99)
ADENOCARCINOMA, NOS				3 (2%)	
ADENOMATOUS POLYP, NOS		2 (2%)		6 (3%)	
MUCINOUS CYSTADENOCARCINOMA		5 (4%)		6 (3%)	
SIGNET RING CARCINOMA		1 (1%)		2 (1%)	
LEIOMYOMA					1 (1%)
LEIOMYOSARCOMA		1 (1%)			
#TRANSVERSE COLON	(87)	(125)	(250)	(175)	(99)
ADENOMATOUS POLYP, NOS		9 (7%)		8 (5%)	
ADENOCARCINOMA IN ADENOMATOUS POLYP				4 (2%)	
MUCINOUS CYSTADENO- CARCINOMA				1 (1%)	
#DESCENDING COLON	(87)	(125)	(250)	(175)	(99)
ADENOMATOUS POLYP, NOS		24 (19%)	1 (0%)	30 (17%)	
ADENOCARCINOMA IN ADENOMATOUS POLYP		2 (2%)		2 (1%)	
MUCINOUS CYSTADENO- CARCINOMA		1 (1%)			
LEIOMYOMA			1 (0%)		
URINARY SYSTEM					
#KIDNEY	(87)	(125)	(250)	(175)	(99)
CARCINOMA, NOS			1 (0%)		
TUBULAR-CELL ADENO- CARCINOMA	1 (1%)				1 (1%)
LIPOMA	1 (1%)				
LIPOSARCOMA			1 (0%)		
MIXED TUMOR, MALIGNANT CARCINOSARCOMA		13 (10%) 1 (1%)		34 (19%)	
#URINARY BLADDER	(85)	(125)	(247)	(175)	(98)
TRANSITIONAL-CELL PAPILOMA			1 (0%)		2 (2%)
ENDOCRINE SYSTEM					
#PITUITARY	(87)	(124)	(249)	(173)	(100)
CARCINOMA, NOS	4 (5%)	1 (1%)	14 (6%)	1 (1%)	1 (1%)
ADENOMA, NOS	49 (56%)	31 (25%)	103 (41%)	51 (29%)	50 (50%)
#PITUITARY INTERMEDIATE ADENOMA, NOS	(87)	(124)	(249)	(173)	(100)
ADENOMA, NOS		1 (1%)			
#ADRENAL	(87)	(124)	(249)	(175)	(99)
CORTICAL ADENOMA	4 (5%)	1 (1%)	10 (4%)	6 (3%)	5 (5%)
CORTICAL CARCINOMA			5 (2%)	1 (1%)	
PHEOCHROMOCYTOMA	8 (9%)	6 (5%)	23 (9%)	8 (5%)	11 (11%)
PHEOCHROMOCYTOMA, MALIGNANT	2 (2%)			1 (1%)	2 (2%)
GANGLIONEUROMA					1 (1%)
#ADRENAL MEDULLA	(87)	(124)	(249)	(175)	(99)
PHEOCHROMOCYTOMA			2 (1%)		
PHEOCHROMOCYTOMA, MALIGNANT		1 (1%)			

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
ENDOCRINE SYSTEM (Continued)					
#THYROID	(87)	(124)	(248)	(174)	(100)
FOLLICULAR-CELL ADENOMA	6 (7%)	7 (6%)	13 (5%)	9 (5%)	6 (6%)
FOLLICULAR-CELL CARCINOMA	1 (1%)	5 (4%)	14 (6%)	7 (4%)	7 (7%)
C-CELL ADENOMA	11 (13%)	9 (7%)	26 (10%)	18 (10%)	20 (20%)
C-CELL CARCINOMA	11 (13%)	9 (7%)	41 (17%)	12 (7%)	12 (12%)
#PARATHYROID	(73)	(119)	(235)	(164)	(97)
ADENOMA, NOS			1 (0%)		1 (1%)
C-CELL CARCINOMA, INVASIVE			3 (1%)		
#PANCREATIC ISLETS	(87)	(124)	(249)	(175)	(99)
ISLET-CELL ADENOMA	2 (2%)	1 (1%)	6 (2%)	1 (1%)	4 (4%)
ISLET-CELL CARCINOMA	4 (5%)	1 (1%)	7 (3%)	1 (1%)	3 (3%)
REPRODUCTIVE SYSTEM					
*MAMMARY GLAND	(88)	(125)	(250)	(175)	(100)
CARCINOMA, NOS	1 (1%)		3 (1%)		1 (1%)
ADENOMA, NOS	6 (7%)	2 (2%)	21 (8%)	5 (3%)	11 (11%)
ADENOCARCINOMA, NOS	5 (6%)		9 (4%)	1 (1%)	4 (4%)
FIBROADENOMA	49 (56%)	36 (29%)	128 (51%)	41 (23%)	58 (58%)
CHONDROMA					1 (1%)
*VULVA	(88)	(125)	(250)	(175)	(100)
FIBROSARCOMA, INVASIVE			1 (0%)		
*CLITORAL GLAND	(88)	(125)	(250)	(175)	(100)
CARCINOMA, NOS		5 (4%)	16 (6%)	4 (2%)	4 (4%)
SQUAMOUS CELL CARCINOMA	1 (1%)		2 (1%)		
*VAGINA	(88)	(125)	(250)	(175)	(100)
FIBROMA		1 (1%)			
FIBROSARCOMA			1 (0%)		
ENDOMETRIAL STROMAL POLYP					1 (1%)
ENDOMETRIAL STROMAL SARCOMA			2 (1%)		
ENDOMETRIAL STROMAL SARCOMA, INVASIVE				1 (1%)	
#UTERUS	(87)	(125)	(249)	(175)	(99)
PAPILLARY ADENOCARCINOMA					1 (1%)
PAPILLARY CYSTADENOMA, NOS					1 (1%)
LEIOMYOMA	2 (2%)		1 (0%)		
ENDOMETRIAL STROMAL POLYP	13 (15%)	7 (6%)	22 (9%)	15 (9%)	10 (10%)
ENDOMETRIAL STROMAL SARCOMA	1 (1%)	2 (2%)	2 (1%)	2 (1%)	1 (1%)
#CERVIX UTERI	(87)	(125)	(249)	(175)	(99)
FIBROMA			1 (0%)		
LEIOMYOSARCOMA				1 (1%)	
ENDOMETRIAL STROMAL POLYP	1 (1%)				1 (1%)
ENDOMETRIAL STROMAL SARCOMA			3 (1%)	1 (1%)	
ENDOMETRIAL STROMAL SARCOMA, INVASIVE				1 (1%)	1 (1%)
#UTERUS/ENDOMETRIUM	(87)	(125)	(249)	(175)	(99)
CARCINOMA, NOS			1 (0%)		
PAPILLARY CARCINOMA				1 (1%)	
ADENOMA, NOS			1 (0%)	4 (2%)	
PAPILLARY ADENOMA				1 (1%)	
#OVARY	(87)	(125)	(249)	(174)	(99)
PAPILLARY ADENOCARCINOMA			1 (0%)		
THECOMA	1 (1%)				
GRANULOSA-CELL TUMOR	1 (1%)		4 (2%)	1 (1%)	2 (2%)
NERVOUS SYSTEM					
#CEREBRUM	(87)	(125)	(250)	(175)	(100)
ASTROCYTOMA	1 (1%)				

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
NERVOUS SYSTEM (Continued)					
*BRAIN	(87)	(125)	(250)	(175)	(100)
CARCINOMA, NOS, INVASIVE	4 (5%)	1 (1%)	13 (5%)	1 (1%)	1 (1%)
GRANULAR-CELL TUMOR, NOS					1 (1%)
GLIOMA, NOS					1 (1%)
ASTROCYTOMA	1 (1%)		5 (2%)	1 (1%)	1 (1%)
*SPINAL CORD	(88)	(125)	(250)	(175)	(100)
OLIGODENDROGLIOMA			1 (0%)		
SPECIAL SENSE ORGANS					
*EYE	(88)	(125)	(250)	(175)	(100)
FIBROMA			1 (0%)		
*EYELID	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA	1 (1%)				
*EAR	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA				1 (1%)	
*ZYMBAL GLAND	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL PAPILLOMA		1 (1%)		2 (1%)	
SQUAMOUS CELL CARCINOMA	1 (1%)	14 (11%)	7 (3%)	26 (15%)	2 (2%)
ADENOMA, NOS				1 (1%)	
SARCOMA, NOS, INVASIVE					1 (1%)
MUSCULOSKELETAL SYSTEM					
*MAXILLA	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA			1 (0%)		
*FEMUR	(88)	(125)	(250)	(175)	(100)
OSTEOSARCOMA	1 (1%)				
*SKELETAL MUSCLE	(88)	(125)	(250)	(175)	(100)
RHABDOMYOSARCOMA					1 (1%)
*ABDOMINAL MUSCLE	(88)	(125)	(250)	(175)	(100)
MIXED TUMOR, INVASIVE				1 (1%)	
BODY CAVITIES					
*MEDIASTINUM	(88)	(125)	(250)	(175)	(100)
MUCINOUS CYSTADENO- CARCINOMA, METASTATIC				1 (1%)	
*ABDOMINAL CAVITY	(88)	(125)	(250)	(175)	(100)
LEIOMYOSARCOMA	1 (1%)				
*ABDOMINAL WALL	(88)	(125)	(250)	(175)	(100)
MIXED TUMOR, INVASIVE				1 (1%)	
*MESENTERY	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA, INVASIVE					1 (1%)
MIXED TUMOR, INVASIVE				1 (1%)	
ALL OTHER SYSTEMS					
*MULTIPLE ORGANS	(88)	(125)	(250)	(175)	(100)
ADENOCARCINOMA, NOS, METASTATIC		1 (1%)			
ALVEOLAR/BRONCHIOLAR CARCINOMA, METASTATIC			1 (0%)		
PAPILLARY ADENOCARCINOMA, METASTATIC			1 (0%)		
CORTICAL CARCINOMA, METASTATIC			2 (1%)		
C-CELL CARCINOMA, METASTATIC	1 (1%)				

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
ALL OTHER SYSTEMS					
*MULTIPLE ORGANS (Continued)	(88)	(125)	(250)	(175)	(100)
MUCINOUS CYSTADENO- CARCINOMA, METASTATIC		6 (5%)		10 (6%)	
SIGNET RING CARCINOMA, METASTATIC		1 (1%)		4 (2%)	
SARCOMA, NOS		1 (1%)			
MIXED TUMOR, METASTATIC		1 (1%)			
CARCINOSARCOMA, METASTATIC		1 (1%)			
OSTEOSARCOMA, METASTATIC	1 (1%)				
THORACOLUMBAR REGION					
OSTEOSARCOMA	1				
PERINEUM					
FIBROSARCOMA			1		
LOWER LEG					
OSTEOSARCOMA	1				
FOOT					
FIBROMA			1		
ADIPOSE TISSUE					
MUCINOUS CYSTADENOCA, METASTATIC				1	
MIXED TUMOR, INVASIVE				3	
BROAD LIGAMENT					
LEIOMYOMA			1		
ANIMAL DISPOSITION SUMMARY					
ANIMALS INITIALLY IN STUDY	88	125	250	175	100
NATURAL DEATH	19	26	39	32	14
MORIBUND SACRIFICE	60	83	186	117	77
TERMINAL SACRIFICE	9	16	25	26	9
TUMOR SUMMARY					
TOTAL ANIMALS WITH PRIMARY TUMORS**					
TOTAL PRIMARY TUMORS	86	123	239	168	93
TOTAL ANIMALS WITH BENIGN TUMORS	253	317	637	488	274
TOTAL ANIMALS WITH MALIGNANT TUMORS	78	79	201	123	88
TOTAL ANIMALS WITH BENIGN TUMORS	166	146	388	219	194
TOTAL ANIMALS WITH MALIGNANT TUMORS	64	108	172	157	56
TOTAL ANIMALS WITH SECONDARY TUMORS###	83	159	239	247	76
TOTAL ANIMALS WITH SECONDARY TUMORS###	10	16	32	35	8
TOTAL ANIMALS WITH TUMORS	11	17	42	43	10
UNCERTAIN--BENIGN OR MALIGNANT	4	12	9	22	4
TOTAL UNCERTAIN TUMORS	4	12	10	22	4

* NUMBER OF ANIMALS NECROPSIED

** PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

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

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291	292	293	294	295	296	297	298	299	300
WEEKS ON STUDY	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
ENDOCRINE SYSTEM																															
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS			X	X					X		X	X																			
ADRENAL CORTICAL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA																															
PHEOCHROMOCYTOMA, MALIGNANT									X		X																				
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA				X			X		X		X		X	X	X																
C-CELL ADENOMA	X																														
C-CELL CARCINOMA								X	X	X				X																	
FIBROSARCOMA, INVASIVE																															
PARATHYROID ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA, INVASIVE			X																												
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																															
ISLET-CELL CARCINOMA																															
REPRODUCTIVE SYSTEM																															
MAMMARY GLAND ADENOMA, NOS	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROADENOMA																															
TESTIS INTERSTITIAL-CELL TUMOR	X	+	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PROSTATE MESOTHELIOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																															
ADENOMA, NOS																															
NERVOUS SYSTEM																															
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA																															
SPECIAL SENSE ORGANS																															
ZYMBAL GLAND CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																															
MUSCULOSKELETAL SYSTEM																															
BONE OSTEOSARCOMA	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
BODY CAVITIES																															
PERITONEUM MESOTHELIOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TUNICA VAGINALIS MESOTHELIOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, MALIGNANT																															
MESENTERY MESOTHELIOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	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	N	N	N	N
C-CELL CARCINOMA, METASTATIC																															
SARCOMA, NOS, INVASIVE																															
MESOTHELIOMA, INVASIVE																															
OSTEOSARCOMA, METASTATIC																															
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																															
MONOCYTIC LEUKEMIA																															
LEUKEMIA, MONONUCLEAR CELL					X	X			X	X	X																				

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

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	3021	3022	3023	3024	3025	3026	3027	3028	3029	3030	3031	3032	3033	3034	3035	3036	3037	3038	3039	3040	3041	3042	3043	3044	3045	3046	3047	3048	3049	3050
WEEKS ON STUDY	0	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
INTEGUMENTARY SYSTEM																														
SKIN PAPILLOMA, NOS BASAL-CELL CARCINOMA KERATOACANTHOMA	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SUBCUTANEOUS TISSUE SQUAMOUS CELL CARCINOMA BASAL-CELL TUMOR SARCOMA, NOS FIBROMA FIBROSARCOMA	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																														
LUNGS AND BRONCHI SQUAMOUS CELL CARCINOMA ALVEOLAR/BRONCHIOLAR CARCINOMA C-CELL CARCINOMA, METASTATIC PNEUMOCYTOMA, METASTATIC	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA FIBROSARCOMA, INVASIVE	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																														
BONE MARROW	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	C	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																														
HEART ADENOCARCINOMA, NOS, METASTATIC	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																														
SALIVARY GLAND FIBROSARCOMA FIBROSARCOMA, INVASIVE	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER NEOPLASTIC NODULE HEPATOCELLULAR CARCINOMA	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS ACINAR-CELL ADENOMA ACINAR-CELL CARCINOMA	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE LEIOMYOMA	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE HEMANGIOSARCOMA	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																														
KIDNEY	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	TOTAL TISSUES TUMORS
WEEKS ON STUDY	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
ENDOCRINE SYSTEM																																							
PITUITARY CARCINOMA, NOS	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	85	
ADENOMA, NOS	X																																						4
ADRENAL CORTICAL CARCINOMA	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	85	
PHEOCHROMOCYTOMA																																							2
PHEOCHROMOCYTOMA, MALIGNANT				X																																			16
THYROID FOLLICULAR-CELL ADENOMA	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	84	
FOLLICULAR-CELL CARCINOMA																																							5
C-CELL ADENOMA																																							13
C-CELL CARCINOMA																																							19
FIBROSARCOMA, INVASIVE																																							1
PARATHYROID ADENOMA, NOS	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	78	
C-CELL CARCINOMA, INVASIVE																																							3
PANCREATIC ISLETS	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	85	
ISLET-CELL ADENOMA																																							5
ISLET-CELL CARCINOMA																																							3
REPRODUCTIVE SYSTEM																																							
MAMMARY GLAND ADENOMA, NOS	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	88*	
FIBROADENOMA																																							1
TESTIS INTERSTITIAL-CELL TUMOR	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	84	
	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	79	
PROSTATE MESOTHELIOMA, NOS	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	85	
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	88*	
SQUAMOUS CELL CARCINOMA																																							2
ADENOMA, NOS																																							1
NERVOUS SYSTEM																																							
BRAIN CARCINOMA, NOS, INVASIVE	C	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	85	
ASTROCYTOMA	X																																						2
SPECIAL SENSE ORGANS																																							
ZYMBAL GLAND CARCINOMA, NOS	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	88*	
SQUAMOUS CELL CARCINOMA																																							1
MUSCULOSKELETAL SYSTEM																																							
BONE OSTEOSARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	88*	
BODY CAVITIES																																							2
PERITONEUM MESOTHELIOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	88*	
TUNICA VAGINALIS MESOTHELIOMA, NOS	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	88*	
MESOTHELIOMA, MALIGNANT																																							2
MESENTERY MESOTHELIOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	88*	
ALL OTHER SYSTEMS																																							
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	88*	
C-CELL CARCINOMA, METASTATIC																																							1
SARCOMA, NOS, INVASIVE																																							1
MESOTHELIOMA, INVASIVE																																							1
OSTEOSARCOMA, METASTATIC																																							1
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																																							1
MONOCYTIC LEUKEMIA																																							1
LEUKEMIA, MONONUCLEAR CELL																																							28
																																							3

* ANIMALS NECROPSIED

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	471	472	473	474	475	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	
WEEKS ON STUDY	7	8	2	9	2	2	9	1	8	4	9	8	1	2	1	7	5	2	2	7	7	1	2	1	1	0
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL PAPILLOMA																										
SQUAMOUS CELL CARCINOMA																										
TRICHOEPITHELIOMA																										
KERATOACANTHOMA																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																										
TRICHOEPITHELIOMA																										
SARCOMA, NOS																										
FIBROMA																										
FIBROSARCOMA																										
LIPOMA																										
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																										
ALVEOLAR/BRONCHIOLAR ADENOMA																										
C-CELL CARCINOMA, METASTATIC																										
FIBROSARCOMA, METASTATIC																										
HEMANGIOSARCOMA, METASTATIC																										
OSTEOSARCOMA, METASTATIC																										
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NASAL CAVITY																										
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
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																										
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, METASTATIC																										
MUCINOUS CYSTADENOMA, METASTATIC																										
SIGNET RING CARCINOMA, METASTATIC																										
SARCOMA, NOS																										
THYMUS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																										
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																										
HEPATOCELLULAR CARCINOMA																										
HEMANGIOSARCOMA																										
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																										
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																										
ACINAR-CELL ADENOMA																										
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																										
ADENOMATOUS POLYP, NOS																										
MUCINOUS CYSTADENOCARCINOMA																										
MUCINOUS CYSTADENOMA, METASTATIC																										
SIGNET RING CARCINOMA																										
RECTUM	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMATOUS POLYP, NOS																										

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30			
WEEKS ON STUDY	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1			
INTEGUMENTARY SYSTEM																																	
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
SQUAMOUS CELL PAPILLOMA																																	
SQUAMOUS CELL CARCINOMA																																	
BASAL-CELL TUMOR																																	
BASAL-CELL CARCINOMA																																	
SEBACEOUS ADEHOMA																																	
SEBACEOUS ADENOCARCINOMA																																	
KERATOACANTHOMA																																	
FIBROSARCOMA																																	
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
CARCINOMA, NOS																																	
SQUAMOUS CELL CARCINOMA																																	
BASAL-CELL CARCINOMA																																	
SARCOMA, NOS																																	
FIBROMA																																	
FIBROSARCOMA																																	
FIBROUS HISTIOCYTOMA, MALIGNANT																																	
OSTEOSARCOMA																																	
NEUROFIBROSARCOMA																																	
RESPIRATORY SYSTEM																																	
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL CARCINOMA, METASTATIC																																	
ADENOCARCINOMA, NOS, METASTATIC																																	
ALVEOLAR/BRONCHIOLAR ADENOMA																																	
ALVEOLAR/BRONCHIOLAR CARCINOMA																																	
PNEUMOCYTOMA, METASTATIC																																	
FIBROSARCOMA, METASTATIC																																	
FIBROUS HISTIOCYTOMA, METASTATIC																																	
LIPOSARCOMA, METASTATIC																																	
MESOTHELIOMA, NOS																																	
OSTEOSARCOMA, METASTATIC																																	
MENINGIOMA, METASTATIC																																	
TRACHEA																																	
HEMATOPOIETIC SYSTEM																																	
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
INTERSTITIAL-CELL TUMOR, METASTATIC																																	
SARCOMA, NOS																																	
HEMANGIOSARCOMA																																	
MONOCYTTIC LEUKEMIA																																	
Lymph Nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL CARCINOMA, METASTATIC																																	
SARCOMA, NOS, INVASIVE																																	
FIBROUS HISTIOCYTOMA, METASTATIC																																	
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
CIRCULATORY SYSTEM																																	
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOCARCINOMA, NOS, METASTATIC																																	
DIGESTIVE SYSTEM																																	
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
SQUAMOUS CELL PAPILLOMA																																	
SQUAMOUS CELL CARCINOMA																																	
KERATOACANTHOMA																																	
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SARCOMA, NOS																																	
FIBROSARCOMA																																	
FIBROSARCOMA, INVASIVE																																	
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
NEOPLASTIC NODULE																																	
HEPATOCELLULAR CARCINOMA																																	
FIBROSARCOMA, METASTATIC																																	
LIPOSARCOMA, METASTATIC																																	
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ACINAR-CELL ADENOMA																																	
ACINAR-CELL CARCINOMA																																	
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOCARCINOMA, NOS																																	
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOMATOUS POLYP, NOS																																	
MUCINOUS CYSTADENOCARCINOMA																																	
SIGNET RING CARCINOMA																																	
LEIOMYOMA																																	
LEIOMYOSARCOMA																																	
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOMATOUS POLYP, NOS																																	
URINARY SYSTEM																																	
KIDNEY	+																																

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30	
WEEKS ON STUDY	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	26	27	28	29	30
ENDOCRINE SYSTEM																															
PITUITARY CARCINOMA, NOS																															
ADRENAL CORTICAL ADENOMA PHEOCHROMOCYTOMA PHEOCHROMOCYTOMA, MALIGNANT																															
PARAGANGLION PARAGANGLIOMA, NOS																															
THYROID FOLLICULAR-CELL ADENOMA FOLLICULAR-CELL CARCINOMA C-CELL ADENOMA C-CELL CARCINOMA SARCOMA, NOS, INVASIVE																															
PARATHYROID ADENOMA, NOS C-CELL CARCINOMA, INVASIVE																															
PANCREATIC ISLETS ISLET-CELL ADENOMA ISLET-CELL CARCINOMA																															
REPRODUCTIVE SYSTEM																															
MAMMARY GLAND ADENOMA, NOS ADENOCARCINOMA, NOS FIBROMA CARCINOSARCOMA FIBROADENOMA																															
TESTIS INTERSTITIAL-CELL TUMOR INTERSTITIAL-CELL TUMOR, MALIGNANT																															
PROSTATE CARCINOMA, NOS ADENOMA, NOS																															
PENIS SQUAMOUS CELL CARCINOMA																															
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS SQUAMOUS CELL CARCINOMA																															
EPIDIDYMIS LIPOSARCOMA																															
NERVOUS SYSTEM																															
BRAIN CARCINOMA, NOS, INVASIVE ASTROCYTOMA MENINGIOMA																															
SPECIAL SENSE ORGANS																															
EYE MALIGNANT MELANOMA																															
HARDERIAN GLAND SARCOMA, NOS, INVASIVE																															
ZYMBAL GLAND CARCINOMA, NOS SQUAMOUS CELL CARCINOMA KERATOCARCINOMA CARCINOSARCOMA																															
MUSCULOSKELETAL SYSTEM																															
BONE SQUAMOUS CELL PAPILLOMA OSTEOSARCOMA																															
JOINT OSTEOSARCOMA																															
BODY CAVITIES																															
PLEURA SQUAMOUS CELL CARCINOMA ADENOCARCINOMA, NOS, METASTATIC																															
MEDIASTINUM ADENOCARCINOMA, NOS, METASTATIC MESOTHELIOMA, NOS																															
PERITONEUM LIPOSARCOMA																															
TUNICA VAGINALIS MESOTHELIOMA, NOS MESOTHELIOMA, MALIGNANT																															
MESENTERY FIBROSARCOMA LIPOMA																															
ALL OTHER SYSTEMS																															
MULTIPLE ORGANS NOS FIBROSARCOMA, INVASIVE FIBROSARCOMA, METASTATIC FIBROUS HISTIOCYTOMA, METASTATIC CARCINOSARCOMA, METASTATIC MESOTHELIOMA, MALIGNANT MESOTHELIOMA, METASTATIC OSTEOSARCOMA, METASTATIC MALIG. LYMPHOMA, HISTIOCYTIC TYPE MYELOMONOCYTIC LEUKEMIA MONOCYTIC LEUKEMIA LEUKEMIA, MONONUCLEAR CELL																															
HEAD NOS SARCOMA, NOS																															
BACK NOS RHABDOMYOSARCOMA																															
LUMBAR REGION CHONDROSARCOMA																															
LOWER LEG NOS OSTEOSARCOMA																															
ADIPOSE TISSUE MIXED MESENCHYMAL TUMOR, MALIGNANT																															
SCROTUM NOS MESOTHELIOMA, MALIGNANT																															

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50
WEEKS ON STUDY	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	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50
ENDOCRINE SYSTEM																																																		
PITUITARY CARCINOMA, NOS																																																		
ADENOMA, NOS																																																		
ADRENAL CORTICAL ADENOMA																																																		
PHEOCHROMOCYTOMA																																																		
PHEOCHROMOCYTOMA, MALIGNANT																																																		
PARAGANGLION PARAGANGLIOMA, NOS																																																		
THYROID FOLLICULAR-CELL ADENOMA																																																		
FOLLICULAR-CELL CARCINOMA																																																		
C-CELL ADENOMA																																																		
C-CELL CARCINOMA																																																		
SARCOMA, NOS, INVASIVE																																																		
PARATHYROID ADENOMA, NOS																																																		
C-CELL CARCINOMA, INVASIVE																																																		
PANCREATIC ISLETS ISLET-CELL ADENOMA																																																		
ISLET-CELL CARCINOMA																																																		
REPRODUCTIVE SYSTEM																																																		
MAMMARY GLAND ADENOMA, NOS																																																		
ADENOCARCINOMA, NOS																																																		
FIBROMA																																																		
CARCINOSARCOMA																																																		
FIBROADENOMA																																																		
TESTIS INTERSTITIAL-CELL TUMOR																																																		
INTERSTITIAL-CELL TUMOR, MALIGNANT																																																		
PROSTATE CARCINOMA, NOS																																																		
ADENOMA, NOS																																																		
PENIS SQUAMOUS CELL CARCINOMA																																																		
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS																																																		
SQUAMOUS CELL CARCINOMA																																																		
EPIDIDYMIOS LIPOSARCOMA																																																		
NERVOUS SYSTEM																																																		
BRAIN CARCINOMA, NOS, INVASIVE																																																		
ASTROCYTOMA																																																		
MENINGEOMA																																																		
SPECIAL SENSE ORGANS																																																		
EYE MALIGNANT MELANOMA																																																		
HARDERIAN GLAND SARCOMA, NOS, INVASIVE																																																		
ZYMBAL GLAND CARCINOMA, NOS																																																		
SQUAMOUS CELL CARCINOMA																																																		
KERATOACANTHOMA																																																		
CARCINOSARCOMA																																																		
MUSCULOSKELETAL SYSTEM																																																		
BONE SQUAMOUS CELL PAPILLOMA																																																		
OSTEOSARCOMA																																																		
JOINT OSTEOSARCOMA																																																		
BODY CAVITIES																																																		
PLEURA SQUAMOUS CELL CARCINOMA																																																		
ADENOCARCINOMA, NOS, METASTATIC																																																		
MEDIASTINUM ADENOCARCINOMA, NOS, METASTATIC																																																		
MESOTHELIOMA, NOS																																																		
PERITONEUM LIPOSARCOMA																																																		
TUNICA VAGINALIS MESOTHELIOMA, NOS																																																		
MESOTHELIOMA, MALIGNANT																																																		
MESENTERY FIBROSARCOMA																																																		
LIPOMA																																																		
ALL OTHER SYSTEMS																																																		
MULTIPLE ORGANS NOS																																																		
FIBROSARCOMA, INVASIVE																																																		
FIBROSARCOMA, METASTATIC																																																		
FIBROUS HISTIOCYTOMA, METASTATIC																																																		
CARCINOSARCOMA, METASTATIC																																																		
MESOTHELIOMA, MALIGNANT																																																		
MESOTHELIOMA, METASTATIC																																																		
OSTEOSARCOMA, METASTATIC																																																		
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																																																		
MYELOMONOCYTIC LEUKEMIA																																																		
MONOCYTIC LEUKEMIA																																																		
LEUKEMIA, MONONUCLEAR CELL																																																		
HEAD NOS SARCOMA, NOS																																																		
BACK NOS RHABDOMYOSARCOMA																																																		
LUMBAR REGION CHONDROSARCOMA																																																		
LOWER LEG NOS OSTEOSARCOMA																																																		
ADIPOSE TISSUE MIXED MESENCHYMAL TUMOR, MALIGNANT																																																		
SCROTUM NOS MESOTHELIOMA, MALIGNANT																																																		

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE (Continued)

ANIMAL NUMBER	WEEKS ON STUDY																											
	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	26	27	28
ENDOCRINE SYSTEM																												
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																												
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA																												
PHEOCHROMOCYTOMA, MALIGNANT	X	X	X					X																				X
PARAGANGLION PARAGANGLIOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA																												
C-CELL ADENOMA																												
C-CELL CARCINOMA																												
SARCOMA, NOS, INVASIVE																												
PARATHYROID ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA, INVASIVE																												
PANCREATIC ISLETS ISLET-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL CARCINOMA																												
REPRODUCTIVE SYSTEM																												
MAMMARY GLAND ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																												
FIBROMA																												
CARCINOSARCOMA																												
FIBROADENOMA																												
TESTIS INTERSTITIAL-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR, MALIGNANT	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PROSTATE CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																												
PENIS SQUAMOUS CELL CARCINOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																												
EPIDIDYMS LIPOSARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
NERVOUS SYSTEM																												
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA																												
MEINGIOMA																												
SPECIAL SENSE ORGANS																												
EYE MALIGNANT MELANOMA	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
HARDERIAN GLAND SARCOMA, NOS, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ZYMBAL GLAND CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																												
KERATOACANTHOMA																												
CARCINOSARCOMA																												
MUSCULOSKELETAL SYSTEM																												
BONE SQUAMOUS CELL PAPILLOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
OSTEOSARCOMA																												
JOINT 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
BODY CAVITIES																												
PLEURA SQUAMOUS CELL CARCINOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOCARCINOMA, NOS, METASTATIC																												
MEDIASTINUM ADENOCARCINOMA, NOS, METASTATIC	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, NOS																												
PERITONEUM LIPOSARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TUNICA VAGINALIS MESOTHELIOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, MALIGNANT																												
MESENTERY 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	N
LIPOMA																												
ALL OTHER SYSTEMS																												
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
FIBROSARCOMA, INVASIVE																												
FIBROSARCOMA, METASTATIC																												
FIBROUS HISTIOCYTOMA, METASTATIC																												
CARCINOSARCOMA, METASTATIC																												
MESOTHELIOMA, MALIGNANT																												
MESOTHELIOMA, METASTATIC																												
OSTEOSARCOMA, METASTATIC																												
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																												
MYELOMONOCYTIC LEUKEMIA																												
MONOCYTIC LEUKEMIA																												
LEUKEMIA, MONONUCLEAR CELL	X		X				X	X	X		X					X					X						X	
HEAD NOS SARCOMA, NOS																												
BACK NOS RHABDOMYOSARCOMA																												
LUMBAR REGION CHONDROSARCOMA																												
LOWER LEG NOS OSTEOSARCOMA																												
ADIPOSE TISSUE MIXED MESENCHYMAL TUMOR, MALIGN.																												
SCROTUM NOS MESOTHELIOMA, MALIGNANT																												

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	WEEKS ON STUDY																											
	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	26	27	28
INTEGUMENTARY SYSTEM																												
SKIN																												
SQUAMOUS CELL PAPILLOMA																												
SQUAMOUS CELL CARCINOMA																												
BASAL-CELL TUMOR																												
BASAL-CELL CARCINOMA																												
SEBACEOUS ADENOMA																												
KERATOCARCINOMA																												
NEUROFIBROSARCOMA																												
SUBCUTANEOUS TISSUE																												
SQUAMOUS CELL CARCINOMA																												
BASAL-CELL CARCINOMA																												
TRICHOPHYTHALIOSIS																												
SARCOMA, NOS																												
FIBROSARCOMA																												
FIBROSARCOMA																												
FIBROUS HISTIOCYTOMA, MALIGNANT																												
LIPOMA																												
RHABDYOSARCOMA																												
AMELOBLASTIC ODONTOMA																												
RESPIRATORY SYSTEM																												
LUNGS AND BRONCHI																												
CARCINOMA, NOS, METASTATIC																												
SQUAMOUS CELL CARCINOMA, METASTAT																												
HEPATOCELLULAR CARCINOMA, METASTAT																												
ALVEOLAR-BRONCHIOLAR ADENOMA																												
SARCOMA, NOS, METASTATIC																												
MIXED TUMOR, METASTATIC																												
CARCINOSARCOMA, METASTATIC																												
OSTEOSARCOMA, METASTATIC																												
TRACHEA																												
SQUAMOUS CELL CARCINOMA, INVASIVE																												
NASAL CAVITY																												
SQUAMOUS CELL CARCINOMA, INVASIVE																												
ADENOCARCINOMA, NOS																												
HEMATOPOIETIC SYSTEM																												
BONE MARROW																												
SPLEEN																												
MONOCYTTIC LEUKEMIA																												
LYMPH NODES																												
CARCINOMA, NOS, INVASIVE																												
CARCINOMA, NOS, METASTATIC																												
MUCINOUS CYSTADENOMA, METASTATIC																												
SARCOMA, NOS, METASTATIC																												
THYMUS																												
CIRCULATORY SYSTEM																												
HEART																												
ADENOCARCINOMA, NOS, METASTATIC																												
DIGESTIVE SYSTEM																												
ORAL CAVITY																												
SQUAMOUS CELL PAPILLOMA																												
SALIVARY GLAND																												
CARCINOMA, NOS																												
SARCOMA, NOS																												
LIVER																												
NEOPLASTIC NODULE																												
HEPATOCELLULAR CARCINOMA																												
FIBROUS HISTIOCYTOMA, METASTATIC																												
LIPOMA																												
LIPOSARCOMA																												
BILE DUCT																												
GALLBLADDER & COMMON BILE DUCT																												
PANCREAS																												
ACINAR-CELL ADENOMA																												
ESOPHAGUS																												
STOMACH																												
SMALL INTESTINE																												
ADENOCARCINOMA, NOS																												
MUCINOUS CYSTADENOCARCINOMA																												
SIGNET RING CARCINOMA																												
LARGE INTESTINE																												
ADENOCARCINOMA, NOS																												
ADENOMATOUS POLYP, NOS																												
ADENOMA IN ADENOMATOUS POLYP																												
MUCINOUS CYSTADENOCARCINOMA																												
MUCINOUS CYSTADENOMA, METASTATIC																												
SIGNET RING CARCINOMA																												
MESOTHELIOMA, METASTATIC																												
URINARY SYSTEM																												
KIDNEY																												
MIXED TUMOR, MALIGNANT																												
URINARY BLADDER																												
TRANSITIONAL-CELL PAPILLOMA																												

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30		
WEEKS ON STUDY	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
ENDOCRINE SYSTEM																																
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOMA, NOS																																
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
PHEOCHROMOCYTOMA	X	X																														
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
FOLLICULAR-CELL CARCINOMA																																
C-CELL ADENOMA	X	X																														
C-CELL CARCINOMA																																
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ISLET-CELL ADENOMA																																
ISLET-CELL CARCINOMA																																
REPRODUCTIVE SYSTEM																																
MAMMARY GLAND FIBROUS HISTIOCYTOMA, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
FIBROADENOMA																																
TESTIS INTERSTITIAL-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
PROSTATE ADENOMA, NOS																																
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
SQUAMOUS CELL CARCINOMA																																
EPIDIDYMS MESOTHELIOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
NERVOUS SYSTEM																																
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
OSTEOMA																																
GRANULAR-CELL TUMOR, NOS																																
ASTROCYTOMA																																
SPECIAL SENSE ORGANS																																
EYE ADENOCARCINOMA, NOS, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
SARCOMA, NOS																																
ZYMBAL GLAND CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL PAPILLOMA																																
SQUAMOUS CELL CARCINOMA																																
KERATOCANTHOMA																																
CARCINOSARCOMA																																
MUSCULOSKELETAL SYSTEM																																
BONE OSTEOSARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
BODY CAVITIES																																
TUNICA VAGINALIS MESOTHELIOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
MESOTHELIOMA, MALIGNANT																																
MESENTERY MUCINOUS CYSTADENOMA, METASTATIC	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	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	N	N	N	N	
ADENOCARCINOMA, NOS, METASTATIC																																
MUCINOUS CYSTADENOMA, METASTATIC																																
SIGNET RING CARCINOMA, METASTATIC																																
SARCOMA, NOS, INVASIVE																																
FIBROUS HISTIOCYTOMA, METASTATIC																																
MESOTHELIOMA, METASTATIC	X																															
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																																
MYELOMONOCYTIC LEUKEMIA																																
HOMOCYTIC LEUKEMIA	X	X																														
LEUKEMIA, MONONUCLEAR CELL																																
COCCYGEAL REGION NEUROFIBROSARCOMA																																
AXILLA NOS FIBROUS HISTIOCYTOMA, MALIGNANT																																
ADIPOSE TISSUE MUCINOUS CYSTADENOMA, METASTATIC																																
MESOTHELIOMA, METASTATIC																																

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																							
WEEKS ON STUDY	1	8	15	22	29	36	43	50	57	64	71	78	85	92	99	106	113	120	127	134	141	148	155	162	169	176	183	190	197	204	211	218	225	232	239	246	253	260	267	274	281	288	295	302	309	316	323	330	337	344	351	358	365	372	379	386	393	400	407	414	421	428	435	442	449	456	463	470	477	484	491	498	505	512	519	526	533	540	547	554	561	568	575	582	589	596	603	610	617	624	631	638	645	652	659	666	673	680	687	694	701	708	715	722	729	736	743	750	757	764	771	778	785	792	799	806	813	820	827	834	841	848	855	862	869	876	883	890	897	904	911	918	925	932	939	946	953	960	967	974	981	988	995	1002	1009	1016	1023	1030	1037	1044	1051	1058	1065	1072	1079	1086	1093	1100	1107	1114	1121	1128	1135	1142	1149	1156	1163	1170	1177	1184	1191	1198	1205	1212	1219	1226	1233	1240	1247	1254	1261	1268	1275	1282	1289	1296	1303	1310	1317	1324	1331	1338	1345	1352	1359	1366	1373	1380	1387	1394	1401	1408	1415	1422	1429	1436	1443	1450	1457	1464	1471	1478	1485	1492	1499	1506	1513	1520	1527	1534	1541	1548	1555	1562	1569	1576	1583	1590	1597	1604	1611	1618	1625	1632	1639	1646	1653	1660	1667	1674	1681	1688	1695	1702	1709	1716	1723	1730	1737	1744	1751	1758	1765	1772	1779	1786	1793	1800	1807	1814	1821	1828	1835	1842	1849	1856	1863	1870	1877	1884	1891	1898	1905	1912	1919	1926	1933	1940	1947	1954	1961	1968	1975	1982	1989	1996	2003	2010	2017	2024	2031	2038	2045	2052	2059	2066	2073	2080	2087	2094	2101	2108	2115	2122	2129	2136	2143	2150	2157	2164	2171	2178	2185	2192	2199	2206	2213	2220	2227	2234	2241	2248	2255	2262	2269	2276	2283	2290	2297	2304	2311	2318	2325	2332	2339	2346	2353	2360	2367	2374	2381	2388	2395	2402	2409	2416	2423	2430	2437	2444	2451	2458	2465	2472	2479	2486	2493	2500	2507	2514	2521	2528	2535	2542	2549	2556	2563	2570	2577	2584	2591	2598	2605	2612	2619	2626	2633	2640	2647	2654	2661	2668	2675	2682	2689	2696	2703	2710	2717	2724	2731	2738	2745	2752	2759	2766	2773	2780	2787	2794	2801	2808	2815	2822	2829	2836	2843	2850	2857	2864	2871	2878	2885	2892	2899	2906	2913	2920	2927	2934	2941	2948	2955	2962	2969	2976	2983	2990	2997	3004	3011	3018	3025	3032	3039	3046	3053	3060	3067	3074	3081	3088	3095	3102	3109	3116	3123	3130	3137	3144	3151	3158	3165	3172	3179	3186	3193	3200	3207	3214	3221	3228	3235	3242	3249	3256	3263	3270	3277	3284	3291	3298	3305	3312	3319	3326	3333	3340	3347	3354	3361	3368	3375	3382	3389	3396	3403	3410	3417	3424	3431	3438	3445	3452	3459	3466	3473	3480	3487	3494	3501	3508	3515	3522	3529	3536	3543	3550	3557	3564	3571	3578	3585	3592	3599	3606	3613	3620	3627	3634	3641	3648	3655	3662	3669	3676	3683	3690	3697	3704	3711	3718	3725	3732	3739	3746	3753	3760	3767	3774	3781	3788	3795	3802	3809	3816	3823	3830	3837	3844	3851	3858	3865	3872	3879	3886	3893	3900	3907	3914	3921	3928	3935	3942	3949	3956	3963	3970	3977	3984	3991	3998	4005	4012	4019	4026	4033	4040	4047	4054	4061	4068	4075	4082	4089	4096	4103	4110	4117	4124	4131	4138	4145	4152	4159	4166	4173	4180	4187	4194	4201	4208	4215	4222	4229	4236	4243	4250	4257	4264	4271	4278	4285	4292	4299	4306	4313	4320	4327	4334	4341	4348	4355	4362	4369	4376	4383	4390	4397	4404	4411	4418	4425	4432	4439	4446	4453	4460	4467	4474	4481	4488	4495	4502	4509	4516	4523	4530	4537	4544	4551	4558	4565	4572	4579	4586	4593	4600	4607	4614	4621	4628	4635	4642	4649	4656	4663	4670	4677	4684	4691	4698	4705	4712	4719	4726	4733	4740	4747	4754	4761	4768	4775	4782	4789	4796	4803	4810	4817	4824	4831	4838	4845	4852	4859	4866	4873	4880	4887	4894	4901	4908	4915	4922	4929	4936	4943	4950	4957	4964	4971	4978	4985	4992	4999	5006	5013	5020	5027	5034	5041	5048	5055	5062	5069	5076	5083	5090	5097	5104	5111	5118	5125	5132	5139	5146	5153	5160	5167	5174	5181	5188	5195	5202	5209	5216	5223	5230	5237	5244	5251	5258	5265	5272	5279	5286	5293	5300	5307	5314	5321	5328	5335	5342	5349	5356	5363	5370	5377	5384	5391	5398	5405	5412	5419	5426	5433	5440	5447	5454	5461	5468	5475	5482	5489	5496	5503	5510	5517	5524	5531	5538	5545	5552	5559	5566	5573	5580	5587	5594	5601	5608	5615	5622	5629	5636	5643	5650	5657	5664	5671	5678	5685	5692	5699	5706	5713	5720	5727	5734	5741	5748	5755	5762	5769	5776	5783	5790	5797	5804	5811	5818	5825	5832	5839	5846	5853	5860	5867	5874	5881	5888	5895	5902	5909	5916	5923	5930	5937	5944	5951	5958	5965	5972	5979	5986	5993	6000	6007	6014	6021	6028	6035	6042	6049	6056	6063	6070	6077	6084	6091	6098	6105	6112	6119	6126	6133	6140	6147	6154	6161	6168	6175	6182	6189	6196	6203	6210	6217	6224	6231	6238	6245	6252	6259	6266	6273	6280	6287	6294	6301	6308	6315	6322	6329	6336	6343	6350	6357	6364	6371	6378	6385	6392	6399	6406	6413	6420	6427	6434	6441	6448	6455	6462	6469	6476	6483	6490	6497	6504	6511	6518	6525	6532	6539	6546	6553	6560	6567	6574	6581	6588	6595	6602	6609	6616	6623	6630	6637	6644	6651	6658	6665	6672	6679	6686	6693	6700	6707	6714	6721	6728	6735	6742	6749	6756	6763	6770	6777	6784	6791	6798	6805	6812	6819	6826	6833	6840	6847	6854	6861	6868	6875	6882	6889	6896	6903	6910	6917	6924	6931	6938	6945	6952	6959	6966	6973	6980	6987	6994	7001	7008	7015	7022	7029	7036	7043	7050	7057	7064	7071	7078	7085	7092	7099	7106	7113	7120	7127	7134	7141	7148	7155	7162	7169	7176	7183	7190	7197	7204	7211	7218	7225	7232	7239	7246	7253	7260	7267	7274	7281	7288	7295	7302	7309	7316	7323	7330	7337	7344	7351	7358	7365	7372	7379	7386	7393	7400	7407	7414	7421	7428	7435	7442	7449	7456	7463	7470	7477	7484	7491	7498	7505	7512	7519	7526	7533	7540	7547	7554	7561	7568	7575	7582	7589	7596	7603	7610	7617	7624	7631	7638	7645	7652	7659	7666	7673	7680	7687	7694	7701	7708	7715	7722	7729	7736	7743	7750	7757	7764	7771	7778	7785	7792	7799	7806	7813	7820	7827	7834	7841	7848	7855	7862	7869	7876	7883	7890	7897	7904	7911	7918	7925	7932	7939	7946	7953	7960	7967	7974	7981	7988	7995	8002	8009	8016	8023	8030	8037	8044	8051	8058	8065	8072	8079	8086	8093	8100	8107	8114	8121	8128	8135	8142	8149	8156	8163	8170	8177	8184	8191	8198	8205	8212	8219	8226	8233	8240	8247	8254	8261	8268	8275	8282	8289	8296	8303	8310	8317	8324	8331	8338	8345	8352	8359	8366	8373	8380	8387	8394	8401	8408	8415	8422	8429	8436	8443	8450	8457	8464	8471	8478	8485	8492	8499	8506	8513	8520	8527	8534	8541	8548	8555	8562	8569	8576	8583	8590	8597	8604	8611	8618	8625	8632	8639	8646	8653	8660	8667	8674	8681	8688	8695	8702	8709	8716	8723	8730	8737	8744	8751	8758	8765	8772	8779	8786	8793	8800	8807	8814	8821	8828	8835	8842	8849	8856	8863	8870	8877	8884	8891	8898	8905	8912	8919	8926	8933	8940	8947	8954	8961	8968	8975	8982	8989	8996	9003	9010	9017	9024	9031	9038	9045	9052	9059	9066	9073	9080	9087	9094	9101	9108	9115	9122	9129	9136	9143	9150	9157	9164	9171	9178	9185	9192	9199	9206	9213	9220	9227	9234	9241	9248	9255	9262	9269	9276	9283	9290	9297	9304	9311	9318	9325	9332	9339	9346	9353	9360	9367	9374	9381	9388	9395

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																							
WEEKS ON STUDY	2	9	16	23	30	37	44	51	58	65	72	79	86	93	100	107	114	121	128	135	142	149	156	163	170	177	184	191	198	205	212	219	226	233	240	247	254	261	268	275	282	289	296	303	310	317	324	331	338	345	352	359	366	373	380	387	394	401	408	415	422	429	436	443	450	457	464	471	478	485	492	499	506	513	520	527	534	541	548	555	562	569	576	583	590	597	604	611	618	625	632	639	646	653	660	667	674	681	688	695	702	709	716	723	730	737	744	751	758	765	772	779	786	793	800	807	814	821	828	835	842	849	856	863	870	877	884	891	898	905	912	919	926	933	940	947	954	961	968	975	982	989	996	1003	1010	1017	1024	1031	1038	1045	1052	1059	1066	1073	1080	1087	1094	1101	1108	1115	1122	1129	1136	1143	1150	1157	1164	1171	1178	1185	1192	1199	1206	1213	1220	1227	1234	1241	1248	1255	1262	1269	1276	1283	1290	1297	1304	1311	1318	1325	1332	1339	1346	1353	1360	1367	1374	1381	1388	1395	1402	1409	1416	1423	1430	1437	1444	1451	1458	1465	1472	1479	1486	1493	1500	1507	1514	1521	1528	1535	1542	1549	1556	1563	1570	1577	1584	1591	1598	1605	1612	1619	1626	1633	1640	1647	1654	1661	1668	1675	1682	1689	1696	1703	1710	1717	1724	1731	1738	1745	1752	1759	1766	1773	1780	1787	1794	1801	1808	1815	1822	1829	1836	1843	1850	1857	1864	1871	1878	1885	1892	1899	1906	1913	1920	1927	1934	1941	1948	1955	1962	1969	1976	1983	1990	1997	2004	2011	2018	2025	2032	2039	2046	2053	2060	2067	2074	2081	2088	2095	2102	2109	2116	2123	2130	2137	2144	2151	2158	2165	2172	2179	2186	2193	2200	2207	2214	2221	2228	2235	2242	2249	2256	2263	2270	2277	2284	2291	2298	2305	2312	2319	2326	2333	2340	2347	2354	2361	2368	2375	2382	2389	2396	2403	2410	2417	2424	2431	2438	2445	2452	2459	2466	2473	2480	2487	2494	2501	2508	2515	2522	2529	2536	2543	2550	2557	2564	2571	2578	2585	2592	2599	2606	2613	2620	2627	2634	2641	2648	2655	2662	2669	2676	2683	2690	2697	2704	2711	2718	2725	2732	2739	2746	2753	2760	2767	2774	2781	2788	2795	2802	2809	2816	2823	2830	2837	2844	2851	2858	2865	2872	2879	2886	2893	2900	2907	2914	2921	2928	2935	2942	2949	2956	2963	2970	2977	2984	2991	2998	3005	3012	3019	3026	3033	3040	3047	3054	3061	3068	3075	3082	3089	3096	3103	3110	3117	3124	3131	3138	3145	3152	3159	3166	3173	3180	3187	3194	3201	3208	3215	3222	3229	3236	3243	3250	3257	3264	3271	3278	3285	3292	3299	3306	3313	3320	3327	3334	3341	3348	3355	3362	3369	3376	3383	3390	3397	3404	3411	3418	3425	3432	3439	3446	3453	3460	3467	3474	3481	3488	3495	3502	3509	3516	3523	3530	3537	3544	3551	3558	3565	3572	3579	3586	3593	3600	3607	3614	3621	3628	3635	3642	3649	3656	3663	3670	3677	3684	3691	3698	3705	3712	3719	3726	3733	3740	3747	3754	3761	3768	3775	3782	3789	3796	3803	3810	3817	3824	3831	3838	3845	3852	3859	3866	3873	3880	3887	3894	3901	3908	3915	3922	3929	3936	3943	3950	3957	3964	3971	3978	3985	3992	3999	4006	4013	4020	4027	4034	4041	4048	4055	4062	4069	4076	4083	4090	4097	4104	4111	4118	4125	4132	4139	4146	4153	4160	4167	4174	4181	4188	4195	4202	4209	4216	4223	4230	4237	4244	4251	4258	4265	4272	4279	4286	4293	4300	4307	4314	4321	4328	4335	4342	4349	4356	4363	4370	4377	4384	4391	4398	4405	4412	4419	4426	4433	4440	4447	4454	4461	4468	4475	4482	4489	4496	4503	4510	4517	4524	4531	4538	4545	4552	4559	4566	4573	4580	4587	4594	4601	4608	4615	4622	4629	4636	4643	4650	4657	4664	4671	4678	4685	4692	4699	4706	4713	4720	4727	4734	4741	4748	4755	4762	4769	4776	4783	4790	4797	4804	4811	4818	4825	4832	4839	4846	4853	4860	4867	4874	4881	4888	4895	4902	4909	4916	4923	4930	4937	4944	4951	4958	4965	4972	4979	4986	4993	5000	5007	5014	5021	5028	5035	5042	5049	5056	5063	5070	5077	5084	5091	5098	5105	5112	5119	5126	5133	5140	5147	5154	5161	5168	5175	5182	5189	5196	5203	5210	5217	5224	5231	5238	5245	5252	5259	5266	5273	5280	5287	5294	5301	5308	5315	5322	5329	5336	5343	5350	5357	5364	5371	5378	5385	5392	5399	5406	5413	5420	5427	5434	5441	5448	5455	5462	5469	5476	5483	5490	5497	5504	5511	5518	5525	5532	5539	5546	5553	5560	5567	5574	5581	5588	5595	5602	5609	5616	5623	5630	5637	5644	5651	5658	5665	5672	5679	5686	5693	5700	5707	5714	5721	5728	5735	5742	5749	5756	5763	5770	5777	5784	5791	5798	5805	5812	5819	5826	5833	5840	5847	5854	5861	5868	5875	5882	5889	5896	5903	5910	5917	5924	5931	5938	5945	5952	5959	5966	5973	5980	5987	5994	6001	6008	6015	6022	6029	6036	6043	6050	6057	6064	6071	6078	6085	6092	6099	6106	6113	6120	6127	6134	6141	6148	6155	6162	6169	6176	6183	6190	6197	6204	6211	6218	6225	6232	6239	6246	6253	6260	6267	6274	6281	6288	6295	6302	6309	6316	6323	6330	6337	6344	6351	6358	6365	6372	6379	6386	6393	6400	6407	6414	6421	6428	6435	6442	6449	6456	6463	6470	6477	6484	6491	6498	6505	6512	6519	6526	6533	6540	6547	6554	6561	6568	6575	6582	6589	6596	6603	6610	6617	6624	6631	6638	6645	6652	6659	6666	6673	6680	6687	6694	6701	6708	6715	6722	6729	6736	6743	6750	6757	6764	6771	6778	6785	6792	6799	6806	6813	6820	6827	6834	6841	6848	6855	6862	6869	6876	6883	6890	6897	6904	6911	6918	6925	6932	6939	6946	6953	6960	6967	6974	6981	6988	6995	7002	7009	7016	7023	7030	7037	7044	7051	7058	7065	7072	7079	7086	7093	7100	7107	7114	7121	7128	7135	7142	7149	7156	7163	7170	7177	7184	7191	7198	7205	7212	7219	7226	7233	7240	7247	7254	7261	7268	7275	7282	7289	7296	7303	7310	7317	7324	7331	7338	7345	7352	7359	7366	7373	7380	7387	7394	7401	7408	7415	7422	7429	7436	7443	7450	7457	7464	7471	7478	7485	7492	7499	7506	7513	7520	7527	7534	7541	7548	7555	7562	7569	7576	7583	7590	7597	7604	7611	7618	7625	7632	7639	7646	7653	7660	7667	7674	7681	7688	7695	7702	7709	7716	7723	7730	7737	7744	7751	7758	7765	7772	7779	7786	7793	7800	7807	7814	7821	7828	7835	7842	7849	7856	7863	7870	7877	7884	7891	7898	7905	7912	7919	7926	7933	7940	7947	7954	7961	7968	7975	7982	7989	7996	8003	8010	8017	8024	8031	8038	8045	8052	8059	8066	8073	8080	8087	8094	8101	8108	8115	8122	8129	8136	8143	8150	8157	8164	8171	8178	8185	8192	8199	8206	8213	8220	8227	8234	8241	8248	8255	8262	8269	8276	8283	8290	8297	8304	8311	8318	8325	8332	8339	8346	8353	8360	8367	8374	8381	8388	8395	8402	8409	8416	8423	8430	8437	8444	8451	8458	8465	8472	8479	8486	8493	8500	8507	8514	8521	8528	8535	8542	8549	8556	8563	8570	8577	8584	8591	8598	8605	8612	8619	8626	8633	8640	8647	8654	8661	8668	8675	8682	8689	8696	8703	8710	8717	8724	8731	8738	8745	8752	8759	8766	8773	8780	8787	8794	8801	8808	8815	8822	8829	8836	8843	8850	8857	8864	8871	8878	8885	8892	8899	8906	8913	8920	8927	8934	8941	8948	8955	8962	8969	8976	8983	8990	8997	9004	9011	9018	9025	9032	9039	9046	9053	9060	9067	9074	9081	9088	9095	9102	9109	9116	9123	9130	9137	9144	9151	9158	9165	9172	9179	9186	9193	9200	9207	9214	9221	9228	9235	9242	9249	9256	9263	9270	9277	9284	9291	9298	9305	9312	9319	9326	9333	9340	9347	9354	9361	9368	9375	9382	9389	9396

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE AND PREWEANING GAVAGE (Continued)

ANIMAL NUMBER	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		
WEEKS ON STUDY	4	1	1	2	2	3	4	4	9	4	2	4	8	9	0	1	1	0	4	9	2	4	7	3	3	0	
INTEGUMENTARY SYSTEM																											
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL PAPILLOMA							X																				
SQUAMOUS CELL CARCINOMA																X	X										
KERATOACANTHOMA																											
FIBROMA																											
SUBCUTANEOUS TISSUE																											
SQUAMOUS CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
TRICHOEPITHELIOMA																											
KERATOACANTHOMA																											
SARCOMA, NOS																											
FIBROMA																											
FIBROSARCOMA									X							X											
RHABDOMYOSARCOMA																											
OSTEOSARCOMA																											
NEUROFIBROMA																											
RESPIRATORY SYSTEM																											
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL CARCINOMA																											
SQUAMOUS CELL CARCINOMA, METASTAT																											
HEMATOPOIETIC SYSTEM																											
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
C-CELL CARCINOMA, METASTATIC							X																				
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
CIRCULATORY SYSTEM																											
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
DIGESTIVE SYSTEM																											
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
SQUAMOUS CELL PAPILLOMA																											
SALIVARY GLAND																											
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
NEOPLASTIC NODULE																											
HEPATOCELLULAR CARCINOMA																											
MONOCYTIC LEUKEMIA																											
BILE DUCT																											
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
PANCREAS																											
ACINAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
MESOTHELIOMA, METASTATIC						X	X																				
ESOPHAGUS																											
FIBROSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
STOMACH																											
MESOTHELIOMA, METASTATIC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SMALL INTESTINE																											
LEIOMYOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LEIOMYOSARCOMA																											
LARGE INTESTINE																											
ADENOMATOUS POLYP, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LEIOMYOSARCOMA																											
URINARY SYSTEM																											
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE AND PREWEANING GAVAGE (Continued)

ANIMAL NUMBER	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	
WEEKS ON STUDY	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	0	0	0	0	0	0	0	0	0	0
ENDOCRINE SYSTEM																										
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS										X	X				X			X			X					X
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA	X		X		X			X				X	X		X											
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA								X																		
C-CELL ADENOMA													X													
C-CELL CARCINOMA	X	X	X										X													
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																										
ISLET-CELL CARCINOMA								X																		X
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND ADENOMA, NOS	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROADENOMA																										
TESTIS INTERSTITIAL-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PROSTATE SQUAMOUS CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SEMINAL VESICLE SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	+	N	+	+	+	+	+	+	N	+	+	+	N	+	N	+	N	+	+	+	+	+	N	+
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
NERVOUS SYSTEM																										
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULAR-CELL TUMOR, NOS																										
ASTROCYTOMA																										
SPECIAL SENSE ORGANS																										
ZYMBAL GLAND SQUAMOUS CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUSCULOSKELETAL SYSTEM																										
BONE SQUAMOUS CELL CARCINOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SARCOMA, NOS																										
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
BODY CAVITIES																										
PERITONEUM 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
CHONDROMA																										
TUNICA VAGINALIS MESOTHELIOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, MALIGNANT																										
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, METASTATIC																										
OSTEOSARCOMA, METASTATIC																										
MALIG. LYMPHOMA, HISTIOCYTIC TYPE																										
MONOCYTIC LEUKEMIA	X				X	X	X	X	X					X					X				X	X		
HEAD NOS																										
FIBROUS HISTIOCYTOMA, MALIGNANT																										
ORBITAL REGION OSTEOSARCOMA																										
AXILLA NOS																										
FIBROMA																										

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE AND PREWEANING GAVAGE (Continued)

ANIMAL NUMBER	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
WEEKS ON STUDY	3	7	11	15	19	23	27	31	35	39	43	47	51	55	59	63	67	71	
INTEGUMENTARY SYSTEM																			
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL PAPILLOMA																			
SQUAMOUS CELL CARCINOMA																			
KERATOACANTHOMA																			
FIBROMA																			
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL CARCINOMA																			
TRICHOEPITHELIOMA																			
KERATOACANTHOMA																			
SARCOMA, NOS																			
FIBROMA																			
FIBROSARCOMA																			
RHABDOMYOSARCOMA																			
OSTEOSARCOMA																			
NEUROFIBROMA																			
RESPIRATORY SYSTEM																			
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL CARCINOMA																			
SQUAMOUS CELL CARCINOMA, METASTAT																			
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMATOPOIETIC SYSTEM																			
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
C-CELL CARCINOMA, METASTATIC																			
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
CIRCULATORY SYSTEM																			
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
DIGESTIVE SYSTEM																			
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
SQUAMOUS CELL PAPILLOMA																			
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
NEOPLASTIC NODULE																			
HEPATOCELLULAR CARCINOMA																			
MONOCYTTIC LEUKEMIA																			
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ACINAR-CELL ADENOMA																			
MESOTHELIOMA, METASTATIC																			
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
FIBROSARCOMA																			
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
MESOTHELIOMA, METASTATIC																			
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LEIOMYOMA																			
LEIOMYOSARCOMA																			
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOMATOUS POLYP, NOS																			
LEIOMYOSARCOMA																			
URINARY SYSTEM																			
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	383	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407		
WEEKS ON STUDY	0	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	0	1	1	0	
ENDOCRINE SYSTEM																											
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOMA, NOS			X	X	X	X	X	X			X	X	X	X	X			X	X	X							
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
PHEOCHROMOCYTOMA							X															X					
PHEOCHROMOCYTOMA, MALIGNANT																											
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
FOLLICULAR-CELL CARCINOMA				X																		X					
C-CELL ADENOMA																											
C-CELL CARCINOMA	X			X																				X			
PARATHYROID	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ISLET-CELL ADENOMA																											
ISLET-CELL CARCINOMA										X												X					
REPRODUCTIVE SYSTEM																											
MAMMARY GLAND CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOMA, NOS																											
ADENOCARCINOMA, NOS											X																
FIBROADENOMA			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PREPUTIAL/CLITORAL GLAND SQUAMOUS CELL CARCINOMA	N	N	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 LEIOMYOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ENDOMETRIAL STROMAL POLYP				X					X										X	X		X		X	X	X	
ENDOMETRIAL STROMAL SARCOMA																											
OVARY THECOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
GRANULOSA-CELL TUMOR																						X					
NERVOUS SYSTEM																											
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ASTROCYTOMA																						X					
SPECIAL SENSE ORGANS																											
EYE APPENDAGES SQUAMOUS CELL CARCINOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
ZYMBAL GLAND SQUAMOUS CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
MUSCULOSKELETAL SYSTEM																											
BONE OSTEOSARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
							X																				
BODY CAVITIES																											
PERITONEUM LEIOMYOSARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
								X																			
ALL OTHER SYSTEMS																											
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
C-CELL CARCINOMA, METASTATIC																											
OSTEOSARCOMA, METASTATIC																											
MONOCYTTIC LEUKEMIA				X	X	X						X	X									X	X		X	X	
LEUKEMIA, MONONUCLEAR CELL																											
THORACOLUMBAR REGION OSTEOSARCOMA	X																										
LOWER LEG NOS OSTEOSARCOMA																											

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	408	409	410	411	412	413	414	415	416	417	418	419	420	421	422	423	424	425	426	427	428	429	430	431	432	433	434	435	436	437	438	439	440			
WEEKS ON STUDY	22	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4			
ENDOCRINE SYSTEM																																				
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
ADENOMA, NOS	X	X	X	X	X				X			X		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
PHEOCHROMOCYTOMA		X			X							X						X					X													
PHEOCHROMOCYTOMA, MALIGNANT																																				
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
FOLLICULAR-CELL CARCINOMA		X										X																							X	
C-CELL ADENOMA											X																									
C-CELL CARCINOMA		X									X																								X	
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ISLET-CELL ADENOMA																																				
ISLET-CELL CARCINOMA																																				X
REPRODUCTIVE SYSTEM																																				
MAMMARY GLAND CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOMA, NOS											X																									
ADENOCARCINOMA, NOS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
FIBROADENOMA																																				
PREPUTIAL/CLITORAL GLAND SQUAMOUS CELL CARCINOMA	N	N	N	N	N	N	N	N	N	N	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 LEIOMYOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ENDOMETRIAL STROMAL POLYP											X																									
ENDOMETRIAL STROMAL SARCOMA			X								X																									
OVARY THECOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
GRANULOSA-CELL TUMOR																																				
NERVOUS SYSTEM																																				
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ASTROCYTOMA																																				X
SPECIAL SENSE ORGANS																																				
EYE APPENDAGES SQUAMOUS CELL CARCINOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
ZYMBAL GLAND SQUAMOUS CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUSCULOSKELETAL SYSTEM																																				
BONE OSTEOSARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
BODY CAVITIES																																				
PERITONEUM LEIOMYOSARCOMA	N	N	N	N	N	N	N	N	N	N	N	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	N	N	N	N	N	N	N	N	
C-CELL CARCINOMA, METASTATIC																																				
OSTEOSARCOMA, METASTATIC																																				
MONOCYTTIC LEUKEMIA																																				
LEUKEMIA, MONONUCLEAR CELL																																				
THORACOLUMBAR REGION OSTEOSARCOMA																																				
LOWER LEG NOS OSTEOSARCOMA																																				

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE

ANIMAL NUMBER	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		
WEEKS ON STUDY	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
INTEGUMENTARY SYSTEM																											
SKIN BASAL-CELL TUMOR	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	
SUBCUTANEOUS TISSUE FIBROMA FIBROSARCOMA	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	
RESPIRATORY SYSTEM																											
LUNGS AND BRONCHI ALVEOLAR/BRONCHIOLAR ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMATOPOIETIC SYSTEM																											
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LYMPH NODES C-CELL CARCINOMA, METASTATIC MUCINOUS CYSTADENOCA, METASTATIC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	
CIRCULATORY SYSTEM																											
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
DIGESTIVE SYSTEM																											
ORAL CAVITY SQUAMOUS CELL PAPILOMA SQUAMOUS CELL CARCINOMA SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	
LIVER NEOPLASTIC NODULE HEPATOCELLULAR CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
PANCREAS ACINAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SMALL INTESTINE MUCINOUS CYSTADENOCARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LARGE INTESTINE ADENOCARCINOMA, NOS ADENOMATOUS POLYP, NOS ADEHOCA IN ADENOMATOUS POLYP MUCINOUS CYSTADENOCARCINOMA MUCINOUS CYSTADENOCA, METASTATIC SIGNET RING CARCINOMA LEIOMYOSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
URINARY SYSTEM																											
KIDNEY MIXED TUMOR, MALIGNANT CARCINOSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	

2: MULTIPLE OCCURENCE OF MORPHOLOGY

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	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
WEEKS ON STUDY	0	1	0	1	1	1	0	0	1	0	1	0	1	0	1	0	1	0	1	0	1	0	1	0	1	0	1	0	1	0
ENDOCRINE SYSTEM																														
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS				X					X						X				X		X		X							
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA																														
PHEOCHROMOCYTOMA, MALIGNANT																														X
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA																														
C-CELL ADENOMA																														
C-CELL CARCINOMA	X				X																									
PARATHYROID	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																														
ISLET-CELL CARCINOMA																														
REPRODUCTIVE SYSTEM																														
MAMMARY GLAND ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROADENOMA			X		X		X		X		X		X		X		X		X		X		X		X		X		X	
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
VAGINA FIBROMA																														
UTERUS ENDOMETRIAL STROMAL POLYP	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL SARCOMA																														X
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																														
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																														
ZYMBAL GLAND SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA	X																													
ALL OTHER SYSTEMS																														
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOCARCINOMA, NOS, METASTATIC																														
MUCINOUS CYSTADENOMA, METASTATIC																														
SIGNET RING CARCINOMA, METASTATIC																														
SARCOMA, NOS																														
MIXED TUMOR, METASTATIC																														
CARCINOSARCOMA, METASTATIC																														
MONOCYTIC LEUKEMIA	X				X		X						X				X	X		X	X	X	X		X	X	X	X	X	
LEUKEMIA, MONONUCLEAR CELL						X							X																	

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

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	5966	5977	5988	5999	6000	6011	6022	6033	6044	6055	6066	6077	6088	6099	6100	6111	6122	6133	6144	6155	6166	6177	6188	6199	6200
WEEKS ON STUDY	1001	0811	0616	0606	0111	0111	0844	0844	0888	0888	0933	0888	0666	0900	0111	0111	0111	0111	0111	0111	0111	0833	0833	0899	0000
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BASAL-CELL TUMOR	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SUBCUTANEOUS TISSUE	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																									
FIBROSARCOMA																						X			
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA, METASTATIC																									
MUCINOUS CYSTADENOMA, METASTATIC																									
THYMUS	+	+	-	+	-	-	+	+	+	+	-	-	-	+	+	-	-	-	+	-	+	-	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL PAPILOMA																									
SQUAMOUS CELL CARCINOMA																									
SQUAMOUS CELL CARCINOMA, INVASIVE																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																									
HEPATOCELLULAR CARCINOMA																									X
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ACINAR-CELL ADENOMA																									
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUCINOUS CYSTADENOCARCINOMA																									
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																									
ADENOMATOUS POLYP, NOS																									
ADENOMA IN ADENOMATOUS POLYP																									
MUCINOUS CYSTADENOCARCINOMA																									
MUCINOUS CYSTADENOMA, METASTATIC																									
SIGNET RING CARCINOMA																									
LEIOMYOSARCOMA																									
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MIXED TUMOR, MALIGNANT																									
CARCINOSARCOMA					X			X		X															
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: 1,3-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	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	
WEEKS ON STUDY	070	066	011	002	011	000	000	000	001	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	
INTEGUMENTARY SYSTEM																										
SKIN BASAL-CELL TUMOR	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SUBCUTANEOUS TISSUE FIBROMA FIBROSARCOMA	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI ALVEOLAR/BRONCHIOLAR ADENOMA	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LYMPH NODES C-CELL CARCINOMA, METASTATIC MUCINOUS CYSTADENOMA, METASTATIC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
THYMUS	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
DIGESTIVE SYSTEM																										
ORAL CAVITY SQUAMOUS CELL PAPILOMA SQUAMOUS CELL CARCINOMA SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LIVER NEOPLASTIC NODULE HEPATOCELLULAR CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	X	+	+	+	
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
PANCREAS ACINAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SMALL INTESTINE MUCINOUS CYSTADENOCARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
LARGE INTESTINE ADENOCARCINOMA, NOS ADENOMATOUS POLYP, NOS ADENOMA IN ADENOMATOUS POLYP MUCINOUS CYSTADENOCARCINOMA MUCINOUS CYSTADENOMA, METASTATIC SIGNET RING CARCINOMA LEIOMYOSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
URINARY SYSTEM																										
KIDNEY MIXED TUMOR, MALIGNANT CARCINOSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	

2: MULTIPLE OCCURENCE OF MORPHOLOGY

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: 1,9-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	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		
WEEKS ON STUDY	0.7	0.6	1.1	0.8	1.1	0.0	0.7	0.0	0.9	1.1	1.1	1.1	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8		
ENDOCRINE SYSTEM																											
PITUITARY CARCINOMA, NOS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ADENOMA, NOS				X					X											X	X						
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
PHEOCHROMOCYTOMA							X																				
PHEOCHROMOCYTOMA, MALIGNANT																										X	
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
FOLLICULAR-CELL CARCINOMA			X																								
C-CELL ADENOMA			X																								
C-CELL CARCINOMA					X					X																X	
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ISLET-CELL ADENOMA							X																				
ISLET-CELL CARCINOMA																											
REPRODUCTIVE SYSTEM																											
MAMMARY GLAND ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
FIBROADENOMA			X		X		X		X		X																
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
VAGINA 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	
UTERUS ENDOMETRIAL STROMAL POLYP	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ENDOMETRIAL STROMAL SARCOMA																										X	
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
NERVOUS SYSTEM																											
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SPECIAL SENSE ORGANS																											
ZYMBAL GLAND SQUAMOUS CELL PAPILLOMA	+	+	+	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	
SQUAMOUS CELL CARCINOMA													X													X	
ALL OTHER SYSTEMS																											
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
ADENOCARCINOMA, NOS, METASTATIC																											
MUCINOUS CYSTADENOMA, METASTATIC																											
SIGNET RING CARCINOMA, METASTATIC																										X	
SARCOMA, NOS																											
MIXED TUMOR, METASTATIC																											
CARCINOSARCOMA, METASTATIC																											
MONOCYTIC LEUKEMIA	X		X	X	X				X		X	X	X		X		X		X		X		X		X		
LEUKEMIA, MONONUCLEAR CELL																											

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																											
WEEKS ON STUDY	0	5	11	17	23	29	35	41	47	53	59	65	71	77	83	89	95	101	107	113	119	125	131	137	143	149	155	161	167	173	179	185	191	197	203	209	215	221	227	233	239	245	251	257	263	269	275	281	287	293	299	305	311	317	323	329	335	341	347	353	359	365	371	377	383	389	395	401	407	413	419	425	431	437	443	449	455	461	467	473	479	485	491	497	503	509	515	521	527	533	539	545	551	557	563	569	575	581	587	593	599	605	611	617	623	629	635	641	647	653	659	665	671	677	683	689	695	701	707	713	719	725	731	737	743	749	755	761	767	773	779	785	791	797	803	809	815	821	827	833	839	845	851	857	863	869	875	881	887	893	899	905	911	917	923	929	935	941	947	953	959	965	971	977	983	989	995	1001	1007	1013	1019	1025	1031	1037	1043	1049	1055	1061	1067	1073	1079	1085	1091	1097	1103	1109	1115	1121	1127	1133	1139	1145	1151	1157	1163	1169	1175	1181	1187	1193	1199	1205	1211	1217	1223	1229	1235	1241	1247	1253	1259	1265	1271	1277	1283	1289	1295	1301	1307	1313	1319	1325	1331	1337	1343	1349	1355	1361	1367	1373	1379	1385	1391	1397	1403	1409	1415	1421	1427	1433	1439	1445	1451	1457	1463	1469	1475	1481	1487	1493	1499	1505	1511	1517	1523	1529	1535	1541	1547	1553	1559	1565	1571	1577	1583	1589	1595	1601	1607	1613	1619	1625	1631	1637	1643	1649	1655	1661	1667	1673	1679	1685	1691	1697	1703	1709	1715	1721	1727	1733	1739	1745	1751	1757	1763	1769	1775	1781	1787	1793	1799	1805	1811	1817	1823	1829	1835	1841	1847	1853	1859	1865	1871	1877	1883	1889	1895	1901	1907	1913	1919	1925	1931	1937	1943	1949	1955	1961	1967	1973	1979	1985	1991	1997	2003	2009	2015	2021	2027	2033	2039	2045	2051	2057	2063	2069	2075	2081	2087	2093	2099	2105	2111	2117	2123	2129	2135	2141	2147	2153	2159	2165	2171	2177	2183	2189	2195	2201	2207	2213	2219	2225	2231	2237	2243	2249	2255	2261	2267	2273	2279	2285	2291	2297	2303	2309	2315	2321	2327	2333	2339	2345	2351	2357	2363	2369	2375	2381	2387	2393	2399	2405	2411	2417	2423	2429	2435	2441	2447	2453	2459	2465	2471	2477	2483	2489	2495	2501	2507	2513	2519	2525	2531	2537	2543	2549	2555	2561	2567	2573	2579	2585	2591	2597	2603	2609	2615	2621	2627	2633	2639	2645	2651	2657	2663	2669	2675	2681	2687	2693	2699	2705	2711	2717	2723	2729	2735	2741	2747	2753	2759	2765	2771	2777	2783	2789	2795	2801	2807	2813	2819	2825	2831	2837	2843	2849	2855	2861	2867	2873	2879	2885	2891	2897	2903	2909	2915	2921	2927	2933	2939	2945	2951	2957	2963	2969	2975	2981	2987	2993	2999	3005	3011	3017	3023	3029	3035	3041	3047	3053	3059	3065	3071	3077	3083	3089	3095	3101	3107	3113	3119	3125	3131	3137	3143	3149	3155	3161	3167	3173	3179	3185	3191	3197	3203	3209	3215	3221	3227	3233	3239	3245	3251	3257	3263	3269	3275	3281	3287	3293	3299	3305	3311	3317	3323	3329	3335	3341	3347	3353	3359	3365	3371	3377	3383	3389	3395	3401	3407	3413	3419	3425	3431	3437	3443	3449	3455	3461	3467	3473	3479	3485	3491	3497	3503	3509	3515	3521	3527	3533	3539	3545	3551	3557	3563	3569	3575	3581	3587	3593	3599	3605	3611	3617	3623	3629	3635	3641	3647	3653	3659	3665	3671	3677	3683	3689	3695	3701	3707	3713	3719	3725	3731	3737	3743	3749	3755	3761	3767	3773	3779	3785	3791	3797	3803	3809	3815	3821	3827	3833	3839	3845	3851	3857	3863	3869	3875	3881	3887	3893	3899	3905	3911	3917	3923	3929	3935	3941	3947	3953	3959	3965	3971	3977	3983	3989	3995	4001	4007	4013	4019	4025	4031	4037	4043	4049	4055	4061	4067	4073	4079	4085	4091	4097	4103	4109	4115	4121	4127	4133	4139	4145	4151	4157	4163	4169	4175	4181	4187	4193	4199	4205	4211	4217	4223	4229	4235	4241	4247	4253	4259	4265	4271	4277	4283	4289	4295	4301	4307	4313	4319	4325	4331	4337	4343	4349	4355	4361	4367	4373	4379	4385	4391	4397	4403	4409	4415	4421	4427	4433	4439	4445	4451	4457	4463	4469	4475	4481	4487	4493	4499	4505	4511	4517	4523	4529	4535	4541	4547	4553	4559	4565	4571	4577	4583	4589	4595	4601	4607	4613	4619	4625	4631	4637	4643	4649	4655	4661	4667	4673	4679	4685	4691	4697	4703	4709	4715	4721	4727	4733	4739	4745	4751	4757	4763	4769	4775	4781	4787	4793	4799	4805	4811	4817	4823	4829	4835	4841	4847	4853	4859	4865	4871	4877	4883	4889	4895	4901	4907	4913	4919	4925	4931	4937	4943	4949	4955	4961	4967	4973	4979	4985	4991	4997	5003	5009	5015	5021	5027	5033	5039	5045	5051	5057	5063	5069	5075	5081	5087	5093	5099	5105	5111	5117	5123	5129	5135	5141	5147	5153	5159	5165	5171	5177	5183	5189	5195	5201	5207	5213	5219	5225	5231	5237	5243	5249	5255	5261	5267	5273	5279	5285	5291	5297	5303	5309	5315	5321	5327	5333	5339	5345	5351	5357	5363	5369	5375	5381	5387	5393	5399	5405	5411	5417	5423	5429	5435	5441	5447	5453	5459	5465	5471	5477	5483	5489	5495	5501	5507	5513	5519	5525	5531	5537	5543	5549	5555	5561	5567	5573	5579	5585	5591	5597	5603	5609	5615	5621	5627	5633	5639	5645	5651	5657	5663	5669	5675	5681	5687	5693	5699	5705	5711	5717	5723	5729	5735	5741	5747	5753	5759	5765	5771	5777	5783	5789	5795	5801	5807	5813	5819	5825	5831	5837	5843	5849	5855	5861	5867	5873	5879	5885	5891	5897	5903	5909	5915	5921	5927	5933	5939	5945	5951	5957	5963	5969	5975	5981	5987	5993	5999	6005	6011	6017	6023	6029	6035	6041	6047	6053	6059	6065	6071	6077	6083	6089	6095	6101	6107	6113	6119	6125	6131	6137	6143	6149	6155	6161	6167	6173	6179	6185	6191	6197	6203	6209	6215	6221	6227	6233	6239	6245	6251	6257	6263	6269	6275	6281	6287	6293	6299	6305	6311	6317	6323	6329	6335	6341	6347	6353	6359	6365	6371	6377	6383	6389	6395	6401	6407	6413	6419	6425	6431	6437	6443	6449	6455	6461	6467	6473	6479	6485	6491	6497	6503	6509	6515	6521	6527	6533	6539	6545	6551	6557	6563	6569	6575	6581	6587	6593	6599	6605	6611	6617	6623	6629	6635	6641	6647	6653	6659	6665	6671	6677	6683	6689	6695	6701	6707	6713	6719	6725	6731	6737	6743	6749	6755	6761	6767	6773	6779	6785	6791	6797	6803	6809	6815	6821	6827	6833	6839	6845	6851	6857	6863	6869	6875	6881	6887	6893	6899	6905	6911	6917	6923	6929	6935	6941	6947	6953	6959	6965	6971	6977	6983	6989	6995	7001	7007	7013	7019	7025	7031	7037	7043	7049	7055	7061	7067	7073	7079	7085	7091	7097	7103	7109	7115	7121	7127	7133	7139	7145	7151	7157	7163	7169	7175	7181	7187	7193	7199	7205	7211	7217	7223	7229	7235	7241	7247	7253	7259	7265	7271	7277	7283	7289	7295	7301	7307	7313	7319	7325	7331	7337	7343	7349	7355	7361	7367	7373	7379	7385	7391	7397	7403	7409	7415	7421	7427	7433	7439	7445	7451	7457	7463	7469	7475	7481	7487	7493	7499	7505	7511	7517	7523	7529	7535	7541	7547	7553	7559	7565	7571	7577	7583	7589	7595	7601	7607	7613	7619	7625	7631	7637	7643	7649	7655	7661	7667	7673	7679	7685	7691	7697	7703	7709	7715	7721	7727	7733	7739	7745	7751	7757	7763	7769	7775	7781	7787	7793	7799	7805	7811	7817	7823	7829	7835	7841	7847	7853	7859	7865	7871	7877	7883	7889	7895	7901	7907	7913	7919	7925	7931	7937	7943	7949	7955	7961	7967	7973	7979	7985	7991	7997	8003	8009	8015	8021	8027	8033	8039

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE (Continued)

ANIMAL NUMBER	WEEKS ON STUDY																			
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
URINARY SYSTEM																				
KIDNEY CARCINOMA, NOS LIPOSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER TRANSITIONAL-CELL PAPILOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																				
PITUITARY CARCINOMA, NOS ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADRENAL CORTICAL ADENOMA CORTICAL CARCINOMA PHEOCHROMOCYTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID FOLLICULAR-CELL ADENOMA FOLLICULAR-CELL CARCINOMA C-CELL ADENOMA C-CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID ADENOMA, NOS C-CELL CARCINOMA, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS ISLET-CELL ADENOMA ISLET-CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																				
MAMMARY GLAND CARCINOMA, NOS ADENOMA, NOS ADENOCARCINOMA, NOS FIBROADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS SQUAMOUS CELL CARCINOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
FEMALE EXTERNAL GENITALIA FIBROSARCOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
VAGINA FIBROSARCOMA ENDOMETRIAL STROMAL SARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
UTERUS CARCINOMA, NOS ADENOMA, NOS FIBROMA LEIOMYOMA ENDOMETRIAL STROMAL POLYP ENDOMETRIAL STROMAL SARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
OVARY PAPILLARY ADENOCARCINOMA GRANULOSA-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																				
BRAIN CARCINOMA, NOS, INVASIVE ASTROCYTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPINAL CORD OLIGODENDROGLIOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SPECIAL SENSE ORGANS																				
EYE FIBROMA	N	N	N	+	N	N	N	N	N	+	N	N	+	+	+	N	N	N	N	N
ZYMBAL GLAND SQUAMOUS CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUSCULOSKELETAL SYSTEM																				
BONE SQUAMOUS CELL CARCINOMA	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 ALVEOLAR/BRONCHIOLAR CA, METASTAT PAPILLARY ADENOCARCINOMA, METASTAT CORTICAL CARCINOMA, METASTATIC MYELOMONOCYTTIC LEUKEMIA MONOCYTTIC LEUKEMIA LEUKEMIA, MONONUCLEAR CELL	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PERINEUM NOS FIBROSARCOMA																				
FOOT NOS FIBROMA																				

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE (Continued)

ANIMAL NUMBER	0300	0301	0302	0303	0304	0305	0306	0307	0308	0309	0310	0311	0312	0313	0314	0315	0316	0317	0318	0319	0320	0321	0322	0323	0324	
WEEKS ON STUDY	0	1	1	2	2	4	6	1	2	3	4	0	6	8	0	8	3	4	6	8	1	1	1	1	1	1
INTEGUMENTARY SYSTEM																										
SKIN																										
SQUAMOUS CELL PAPILLOMA	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA			X																							
BASAL-CELL CARCINOMA																										
KERATOACANTHOMA																										
SUBCUTANEOUS TISSUE																										
SQUAMOUS CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																										
FIBROSARCOMA																										
LIPOMA																										X
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI																										
SQUAMOUS CELL CARCINOMA, METASTAT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																										
ALVEOLAR/BRONCHIOLAR ADENOMA																										
ALVEOLAR/BRONCHIOLAR CARCINOMA																										
FOLLICULAR-CELL CARCINOMA, METAST																										
C-CELL CARCINOMA, METASTATIC																										
TRACHEA																										
LARYNX																										
FOLLICULAR-CELL CARCINOMA, INVASI	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
C-CELL CARCINOMA, INVASIVE																										
HEMATOPOIETIC SYSTEM																										
BONE MARROW																										
SPLEEN																										
LYMPH NODES																										
SQUAMOUS CELL CARCINOMA, METASTAT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																										
FOLLICULAR-CELL CARCINOMA, METAST																										
C-CELL CARCINOMA, METASTATIC																										
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																										
HEART																										
ADENOCARCINOMA, NOS, METASTATIC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																										
ORAL CAVITY																										
SQUAMOUS CELL PAPILLOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																										
SALIVARY GLAND																										
ADENOCARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER																										
NEOPLASTIC NODULE																										
HEPATOCYLLULAR CARCINOMA																										
CORTICAL CARCINOMA, METASTATIC																										
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										
BILE DUCT																										
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS																										
ACINAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ACINAR-CELL CARCINOMA																										
ESOPHAGUS																										
STOMACH																										
ADENOMATOUS POLYP, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOID TUMOR, NOS																										
LEIOMYOSARCOMA																										
ENDOMETRIAL STROMAL SARCOMA, META																										
SMALL INTESTINE																										
LARGE INTESTINE																										
ADENOMATOUS POLYP, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LEIOMYOMA																										

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE (Continued)

ANIMAL NUMBER	WEEKS ON STUDY																				
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
URINARY SYSTEM																					
KIDNEY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
KIDNEY LIPOSARCOMA																					
URINARY BLADDER TRANSITIONAL-CELL PAPILLOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																					
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PITUITARY ADENOMA, NOS						X			X	X	X			X	X		X		X		X
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADRENAL CORTICAL CARCINOMA									X									X			
ADRENAL PHEOCHROMOCYTOMA						X														X	
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID FOLLICULAR-CELL CARCINOMA						X												X			
THYROID C-CELL ADENOMA																					X
THYROID C-CELL CARCINOMA			X	X				X	X	X									X		
PARATHYROID ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID C-CELL CARCINOMA, INVASIVE									-												
PANCREATIC ISLETS ISLET-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS ISLET-CELL CARCINOMA																		X	X		
REPRODUCTIVE SYSTEM																					
MAMMARY GLAND CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MAMMARY GLAND ADENOMA, NOS																					X
MAMMARY GLAND ADENOCARCINOMA, NOS																					
MAMMARY GLAND FIBROADENOMA	X					X	X			X	X			X		X	X	X		X	X
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PREPUTIAL/CLITORAL GLAND SQUAMOUS CELL CARCINOMA																					X
FEMALE EXTERNAL GENITALIA FIBROSARCOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
VAGINA FIBROSARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
VAGINA ENDOMETRIAL STROMAL SARCOMA																					
UTERUS CARCINOMA, NOS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
UTERUS ADENOMA, NOS																					
UTERUS FIBROMA																					
UTERUS LEIOMYOMA																					
UTERUS ENDOMETRIAL STROMAL POLYP																		X		X	
UTERUS ENDOMETRIAL STROMAL SARCOMA																				X	
OVARY PAPILLARY ADENOCARCINOMA	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
OVARY GRANULOSA-CELL TUMOR																					
NERVOUS SYSTEM																					
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BRAIN ASTROCYTOMA																					X
SPINAL CORD OLIGODENDROGLIOMA	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			X																		
SPECIAL SENSE ORGANS																					
EYE FIBROMA	N	N	N	+	N	N	N	+	+	N	N	+	N	+	N	+	N	N	+	+	N
								X													
ZYMBAL GLAND SQUAMOUS CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
																		X			
MUSCULOSKELETAL SYSTEM																					
BONE SQUAMOUS CELL CARCINOMA	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
ALVEOLAR/BRONCHIOLAR CA, METASTAT																					
PAPILLARY ADENOCARCINOMA, METASTAT																					
CORTICAL CARCINOMA, METASTATIC																					
MYELOMONOCYTTIC LEUKEMIA																					
MONOCYTTIC LEUKEMIA	X	X			X			X		X	X	X							X		X
LEUKEMIA, MONONUCLEAR CELL																			X		
PERINEUM NOS FIBROSARCOMA																					
FOOT NOS FIBROMA																					

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE (Continued)

ANIMAL NUMBER	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					
WEEKS ON STUDY	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	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49
INTEGUMENTARY SYSTEM																																																		
SKIN	+																																																	
SQUAMOUS CELL PAPILLOMA																																																		
SQUAMOUS CELL CARCINOMA																																																		
BASAL-CELL CARCINOMA																																																		
KERATOACANTHOMA																																																		
SUBCUTANEOUS TISSUE	+																																																	
SQUAMOUS CELL CARCINOMA																																																		
FIBROMA																																																		
FIBROSARCOMA																																																		
LIPOMA	X																																																	
RESPIRATORY SYSTEM																																																		
LUNGS AND BRONCHI	+																																																	
SQUAMOUS CELL CARCINOMA, METASTAT																																																		
ADENOCARCINOMA, NOS, METASTATIC																																																		
ALVEOLAR/BRONCHIOLAR ADENOMA																																																		
ALVEOLAR/BRONCHIOLAR CARCINOMA																																																		
FOLLICULAR-CELL CARCINOMA, METAST																																																		
C-CELL CARCINOMA, METASTATIC																																																		
TRACHEA	+																																																	
LARYNX	N																																																	
FOLLICULAR-CELL CARCINOMA, INVASI																																																		
C-CELL CARCINOMA, INVASIVE																																																		
HEMATOPOIETIC SYSTEM																																																		
BONE MARROW	+																																																	
SPLEEN	+																																																	
LYMPH NODES	+																																																	
SQUAMOUS CELL CARCINOMA, METASTAT																																																		
ADENOCARCINOMA, NOS, METASTATIC																																																		
FOLLICULAR-CELL CARCINOMA, METAST																																																		
C-CELL CARCINOMA, METASTATIC																																																		
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																																																		
THYMUS	+																																																	
CIRCULATORY SYSTEM																																																		
HEART	+																																																	
ADENOCARCINOMA, NOS, METASTATIC																																																		
DIGESTIVE SYSTEM																																																		
ORAL CAVITY	N																																																	
SQUAMOUS CELL PAPILLOMA																																																		
SQUAMOUS CELL CARCINOMA																																																		
SALIVARY GLAND	+																																																	
ADENOCARCINOMA, NOS																																																		
LIVER	+																																																	
NEOPLASTIC NODULE																																																		
HEPATOCELLULAR CARCINOMA																																																		
CORTICAL CARCINOMA, METASTATIC																																																		
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	X																																																	
BILE DUCT	+																																																	
GALLBLADDER & COMMON BILE DUCT	N																																																	
PANCREAS	+																																																	
ACINAR-CELL ADENOMA																																																		
ACINAR-CELL CARCINOMA																																																		
ESOPHAGUS	+																																																	
STOMACH	+																																																	
ADENOMATOUS POLYP, NOS																																																		
CARCINOID TUMOR, NOS																																																		
LEIOMYOSARCOMA																																																		
ENDOMETRIAL STROMAL SARCOMA, META																																																		
SMALL INTESTINE	+																																																	
LARGE INTESTINE	+																																																	
ADENOMATOUS POLYP, NOS																																																		
LEIOMYOMA																																																		

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	4466	4467	4468	4469	4470	4471	4472	4473	4474	4475	4476	4477	4478	4479	4480	4481	4482	4483	4484	4485	4486	4487	4488	4489	4490
WEEKS ON STUDY	073	119	093	093	090	091	092	093	094	095	096	097	098	099	100	101	102	103	104	105	106	107	108	109	110
ENDOCRINE SYSTEM																									
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS		X			X						X										X				X
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL CARCINOMA		X																			X				
PHEOCHROMOCYTOMA																									
PHEOCHROMOCYTOMA, MALIGNANT																						X			
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA																									X
C-CELL ADENOMA																									
C-CELL CARCINOMA																									
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																									
ISLET-CELL CARCINOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND ADENOMA, NOS	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																									
FIBROADENOMA																									X
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
VAGINA ENDOMETRIAL STROMAL SARCOMA, INVA	N	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 PAPILLARY CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																									
PAPILLARY ADENOMA-LEIOMYOSARCOMA																									
ENDOMETRIAL STROMAL POLYP																									
ENDOMETRIAL STROMAL SARCOMA																									
ENDOMETRIAL STROMAL SARCOMA, INVA																									
OVARY GRANULOSA-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA																									
SPECIAL SENSE ORGANS																									
EAR SQUAMOUS CELL CARCINOMA	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ZYMBAL GLAND SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
ADENOMA, NOS							X																		X
MUSCULOSKELETAL SYSTEM																									
MUSCLE MIXED TUMOR, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
BODY CAVITIES																									
MEDIASTINUM MUCINOUS CYSTADENOCA, METASTATIC	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PERITONEUM MIXED TUMOR, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESENTERY MIXED TUMOR, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
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
MUCINOUS CYSTADENOCA, METASTATIC																									
SIGNET RING CARCINOMA, METASTATIC																									
MALIG. LYMPHOMA, UNDIFFER-TYPE																									
MYELOMONOCYTTIC LEUKEMIA																									
MONOCYTTIC LEUKEMIA																									
LEUKEMIA, MONONUCLEAR CELL		X		X	X		X	X	X	X	X										X	X			X
ADIPOSE TISSUE MUCINOUS CYSTADENOCA, METASTATIC																									
MIXED TUMOR, INVASIVE	X																								

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	471	472	473	474	475	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495		
WEEKS ON STUDY	117	108	106	114	100	107	107	107	109	108	108	108	108	108	108	108	108	108	108	108	108	108	108	108	108		
ENDOCRINE SYSTEM																											
PITUITARY CARCINOMA, NOS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
ADENOMA, NOS	X		X	X						X	X		X	X						X	X		X	X			
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
CORTICAL CARCINOMA																											
PHEOCHROMOCYTOMA																							X		X		
PHEOCHROMOCYTOMA, MALIGNANT																											
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
FOLLICULAR-CELL CARCINOMA	X			X						X				X													
C-CELL ADENOMA								X				X															
C-CELL CARCINOMA	X																										
PARATHYROID	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	-		
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
ISLET-CELL ADENOMA																											
ISLET-CELL CARCINOMA																											
REPRODUCTIVE SYSTEM																											
MAMMARY GLAND ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
ADENOCARCINOMA, NOS																											
FIBROADENOMA				X				X			X														X		
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
VAGINA ENDOMETRIAL STROMAL SARCOMA, INVA	N	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 PAPILLARY CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
ADENOMA, NOS																									X		
PAPILLARY ADENOMA																											
LEIOMYOSARCOMA																											
ENDOMETRIAL STROMAL POLYP																											
ENDOMETRIAL STROMAL SARCOMA																											
ENDOMETRIAL STROMAL SARCOMA, INVA																											
OVARY GRANULOSA-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
NERVOUS SYSTEM																											
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
ASTROCYTOMA																											
SPECIAL SENSE ORGANS																											
EAR SQUAMOUS CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+		
ZYMBAL GLAND SQUAMOUS CELL PAPILOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+		
SQUAMOUS CELL CARCINOMA																											
ADENOMA, NOS			X	X		X		X																	X		
MUSCULOSKELETAL SYSTEM																											
MUSCLE MIXED TUMOR, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
BODY CAVITIES																											
MEDIASTINUM MUCINOUS CYSTADENOCA, METASTATIC	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
PERITONEUM MIXED TUMOR, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
MESENTERY MIXED TUMOR, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
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		
MUCINOUS CYSTADENOCA, METASTATIC																											
SIGNET RING CARCINOMA, METASTATIC																											
MALIG. LYMPHOMA, UNDIFFER-TYPE																											
MYELOMONOCYTIC LEUKEMIA																											
MONOCYTIC LEUKEMIA	X	X		X			X	X		X	X	X								X		X	X		X		
LEUKEMIA, MONONUCLEAR CELL																											
ADIPOSE TISSUE MUCINOUS CYSTADENOCA, METASTATIC																											
MIXED TUMOR, INVASIVE																											

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

ANIMAL NUMBER	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	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	TOTAL TISSUES TUMORS																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																					
WEEKS ON 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9216	9225	9234	9243	9252	9261	9270	9279	9288	9297	9306	9315	9324	9333	9342	9351	9360	9369	9378	9387	9396	9405	9414	9423	9432	9441	9450	9459	9468	9477	9486	9495	9504	9513	9522	9531	9540	9549	9558	9567	9576	9585	9594	9603	9612	9621	9630	9639	9648	9657	9666	9675	9684	9693	9702	9711	9720	9729	9738	9747	9756	9765	9774	9783	9792	9801	9810	9819	9828	9837	9846	9855	9864	9873	9882	9891	9900	9909	9918	9927	9936	9945	9954	9963	9972	9981	9990	10000
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TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE AND PREWEANING GAVAGE (Continued)

ANIMAL NUMBER	6444	6447	6448	6449	6450	6451	6452	6453	6454	6455	6456	6457	6458	6459	6460	6461	6462	6463	6464	6465	6466	6467
WEEKS ON STUDY	17	14	11	12	11	10	9	7	6	8	9	11	12	13	14	14	11	14	10	12	13	13
ENDOCRINE SYSTEM																						
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS	X	X					X		X	X	X				X	X	X		X	X	X	X
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHOCHROMOCYTOA		X																				
PHOCHROMOCYTOA, MALIGNANT																						
GANGLIONEUROMA																						
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA		X					X															
C-CELL ADENOMA						X									X	X			X			
C-CELL CARCINOMA		X						X													X	X
PARATHYROID ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																						
ISLET-CELL CARCINOMA																						X
REPRODUCTIVE SYSTEM																						
MAMMARY GLAND CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																					X	X
ADENOCARCINOMA, NOS							X															X
FIBROADENOMA	X	X		X	X	X	X	X	X						X	X	X	X		X	X	X
CHONDROMA																						
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
VAGINA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ENDOMETRIAL STROMAL POLYP																						
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLARY ADENOCARCINOMA																						
PAPILLARY CYSTADENOMA, NOS																						
ENDOMETRIAL STROMAL POLYP																						
ENDOMETRIAL STROMAL SARCOMA																						
ENDOMETRIAL STROMAL SARCOMA, INV								X							X	X						
OVARY GRANULOSA-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																						
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULAR-CELL TUMOR, NOS																						
GLIOMA, NOS																						X
ASTROCYTOMA															X						X	
SPECIAL SENSE ORGANS																						
ZYMBAL GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																						
SARCOMA, NOS, INVAS																						
MUSCULOSKELETAL SYSTEM																						
MUSCLE RHABDOMYOSARCOMA																						
BODY CAVITIES																						
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA, INVASIV																						
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
MONOCYTTIC LEUKEMIA	X																					
LEUKEMIA, MONONUCLEAR CELL		X				X																X
															X	X						

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE AND PREWEANING GAVAGE (Continued)

ANIMAL NUMBER	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		
WEEKS ON STUDY	1	1	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	0	1	1	1		
	2	3	4	8	1	3	2	2	2	1	4	0	9	1	2	2	1	2	3	0	2	5	9	1	1		
	1	3	4	5	8	3	1	5	9	8	6	5	6	5	2	2	1	4	3	0	5	8	0	1	6		
INTEGUMENTARY SYSTEM																											
SUBCUTANEOUS TISSUE SARCOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
FIBROMA																											
RESPIRATORY SYSTEM																											
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
ALVEOLAR/BRONCHIOLAR ADENOMA																											
ALVEOLAR/BRONCHIOLAR CARCINOMA																											
PAPILLARY ADENOCARCINOMA, METASTATIC																											
C-CELL CARCINOMA, METASTATIC																											
PHEOCHROMOCYTOMA, METASTATIC																											
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
HEMATOPOIETIC SYSTEM																											
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
C-CELL CARCINOMA, METASTATIC																											
THYMUS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
CIRCULATORY SYSTEM																											
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
PHEOCHROMOCYTOMA, METASTATIC																											
DIGESTIVE SYSTEM																											
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
SQUAMOUS CELL PAPILOMA																											
SQUAMOUS CELL CARCINOMA																											
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
SARCOMA, NOS																											
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
NEOPLASTIC NODULE																											
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
ACINAR-CELL ADENOMA																											
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
SQUAMOUS CELL PAPILOMA																											
SQUAMOUS CELL CARCINOMA																											
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
LEIOMYOMA																											
URINARY SYSTEM																											
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
TUBULAR-CELL ADENOCARCINOMA																											
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
TRANSITIONAL-CELL PAPILOMA																											

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE AND PREWEANING GAVAGE (Continued)

ANIMAL NUMBER	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		
WEEKS ON STUDY	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1		
	2	3	4	8	1	3	2	2	2	1	4	0	9	1	2	2	2	1	2	3	0	2	0	0	1		
	1	3	4	5	8	3	1	3	9	8	6	5	6	5	2	2	1	4	3	0	9	8	0	1	4		
ENDOCRINE SYSTEM																											
PITUITARY CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
ADENOMA, NOS						X	X	X	X		X									X							
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
PHEOCHROMOCYTOMA																				X							
PHEOCHROMOCYTOMA, MALIGNANT																				X							
GANGLIONEUROMA				X																							
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
FOLLICULAR-CELL CARCINOMA					X			X																			
C-CELL ADENOMA	X	X				X		X													X						
C-CELL CARCINOMA																											
PARATHYROID ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
PANCREATIC ISLETS ISLET-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
ISLET-CELL CARCINOMA																											
REPRODUCTIVE SYSTEM																											
MAMMARY GLAND CARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
ADENOMA, NOS										X																	
ADENOCARCINOMA, NOS																											
FIBROADENOMA	X	X	X		X	X	X	X			X									X	X	X					
CHONDROMA																											
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
VAGINA ENDOMETRIAL STROMAL POLYP																											
UTERUS PAPILLARY ADENOCARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
PAPILLARY CYSTADENOMA, NOS																											
ENDOMETRIAL STROMAL POLYP																											
ENDOMETRIAL STROMAL SARCOMA																											
ENDOMETRIAL STROMAL SARCOMA, INVA																											
OVARY GRANULOSA-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
NERVOUS SYSTEM																											
BRAIN CARCINOMA, NOS, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
GRANULAR-CELL TUMOR, NOS																											
GLIOMA, NOS																											
ASTROCYTOMA																											
SPECIAL SENSE ORGANS																											
ZYMBAL GLAND SQUAMOUS CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
SARCOMA, NOS, INVASIVE																											
MUSCULOSKELETAL SYSTEM																											
MUSCLE RHABDOMYOSARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		
BODY CAVITIES																											
MESENTERY SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	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		
MONOCYTIC LEUKEMIA					X	X	X			X				X	X												
LEUKEMIA, MONONUCLEAR CELL																											

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE-RANGE AND PREWEANING GAVAGE (Continued)

ANIMAL NUMBER	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	TOTAL TISSUES TUMORS
WEEKS ON STUDY	3	2	2	2	2	1	3	4	3	3	4	1	4	1	4	0	0	0	0	0	1	1	1	1	1	0	0	1	0	0	
ENDOCRINE SYSTEM																															
PITUITARY CARCINOMA, NOS ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100 1 50	
ADRENAL CORTICAL ADENOMA PHEOCHROMOCYTOMA PHEOCHROMOCYTOMA, MALIGNANT GANGLIONEUROMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	99 5 11 2 1	
THYROID FOLLICULAR-CELL ADENOMA FOLLICULAR-CELL CARCINOMA C-CELL ADENOMA C-CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100 6 7 20 12	
PARATHYROID ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	97 1	
PANCREATIC ISLETS ISLET-CELL ADENOMA ISLET-CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	99 4 3	
REPRODUCTIVE SYSTEM																															
MAMMARY GLAND CARCINOMA, NOS ADENOMA, NOS ADENOCARCINOMA, NOS FIBROADENOMA CHONDROMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100* 1 11 4 58 1	
PREPUTIAL/CLITORAL GLAND CARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	100* 4	
VAGINA ENDOMETRIAL STROMAL POLYP	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	100* 1	
UTERUS PAPILLARY ADENOCARCINOMA PAPILLARY CYSTADENOMA, NOS ENDOMETRIAL STROMAL POLYP ENDOMETRIAL STROMAL SARCOMA ENDOMETRIAL STROMAL SARCOMA, INVA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	99 1 1 11 1	
OVARY GRANULOSA-CELL TUMOR	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	99 2	
NERVOUS SYSTEM																															
BRAIN CARCINOMA, NOS, INVASIVE GRANULAR-CELL TUMOR, NOS GLIOMA, NOS ASTROCYTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100 1 1 1 1	
SPECIAL SENSE ORGANS																															
ZYMBAL GLAND SQUAMOUS CELL CARCINOMA SARCOMA, NOS, INVASIVE	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100* 2 1	
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	N	N	100* 1	
BODY CAVITIES																															
MESENTERY SQUAMOUS CELL CARCINOMA, INVASIVE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	100* 1	
ALL OTHER SYSTEMS																															
MULTIPLE ORGANS NOS MONOCYTTIC LEUKEMIA LEUKEMIA, MONONUCLEAR CELL	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	100* 26 3	

* ANIMALS NECROPSIED

APPENDIX C

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS

	CONTROL (UNTR)	SHORT RANGE
ANIMALS INITIALLY IN STUDY	88	250
ANIMALS NECROPSIED	88	250
ANIMALS EXAMINED HISTOPATHOLOGICALLY	88	248
INTEGUMENTARY SYSTEM		
*SKIN	(88)	(250)
CYST, NOS		1 (0%)
EPIDERMAL INCLUSION CYST	4 (5%)	5 (2%)
ABSCESS, NOS	2 (2%)	1 (0%)
GRANULOMA, NOS	1 (1%)	
FIBROSIS, FOCAL		1 (0%)
HYPERKERATOSIS		4 (2%)
ACANTHOSIS	1 (1%)	5 (2%)
*SUBCUT TISSUE	(88)	(250)
HEMORRHAGIC CYST		2 (1%)
ABSCESS, NOS	2 (2%)	1 (0%)
RESPIRATORY SYSTEM		
*NASAL TURBINATE	(88)	(250)
INFLAMMATION, ACUTE		1 (0%)
INFLAMMATION, ACUTE DIFFUSE		1 (0%)
HYPERKERATOSIS		1 (0%)
METAPLASIA, SQUAMOUS		1 (0%)
#TRACHEA	(87)	(248)
FIBROSIS, DIFFUSE		1 (0%)
#LUNG	(88)	(247)
MINERALIZATION		1 (0%)
CONGESTION, NOS	2 (2%)	4 (2%)
EDEMA, NOS	1 (1%)	2 (1%)
HEMORRHAGE	6 (7%)	13 (5%)
INFLAMMATION, INTERSTITIAL	1 (1%)	10 (4%)
INFLAMMATION, ACUTE FOCAL	1 (1%)	1 (0%)
INFLAMMATION, ACUTE DIFFUSE		1 (0%)
INFLAMMATION, CHRONIC	80 (91%)	208 (84%)
GRANULOMA, NOS		6 (2%)
FIBROSIS, DIFFUSE	2 (2%)	
NECROSIS, FOCAL		1 (0%)
PIGMENTATION, NOS	3 (3%)	7 (3%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (1%)	10 (4%)
#LUNG/ALVEOLI	(88)	(247)
HISTIOCYTOSIS		5 (2%)
HEMATOPOIETIC SYSTEM		
*MULTIPLE ORGANS	(88)	(250)
HEMATOPOIESIS	1 (1%)	
#BONE MARROW	(88)	(247)
HEMORRHAGE	1 (1%)	
NECROSIS, DIFFUSE	1 (1%)	
HYPOPLASIA, NOS	4 (5%)	3 (1%)
HYPERPLASIA, NOS	3 (3%)	6 (2%)
MYELOFIBROSIS	1 (1%)	
#SPLEEN	(88)	(247)
CONGESTION, NOS		1 (0%)
HEMORRHAGE	3 (3%)	3 (1%)
FIBROSIS, FOCAL	3 (3%)	16 (6%)
FIBROSIS, MULTIFOCAL	2 (2%)	7 (3%)
FIBROSIS, DIFFUSE	1 (1%)	4 (2%)
NECROSIS, NOS		1 (0%)
NECROSIS, FOCAL	3 (3%)	6 (2%)
METAMORPHOSIS FATTY		1 (0%)
PIGMENTATION, NOS	3 (3%)	2 (1%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
HEMATOPOIETIC SYSTEM		
#SPLEEN (Continued)		
HEMOSIDEROSIS	11 (13%)	34 (14%)
ANGIECTASIS		2 (1%)
HEMATOPOIESIS	19 (22%)	41 (17%)
#SPLENIC CAPSULE	(88)	(247)
FIBROSIS, FOCAL	1 (1%)	
#SPLENIC FOLLICLES	(88)	(247)
ATROPHY, NOS	1 (1%)	5 (2%)
#LYMPH NODE	(88)	(248)
INFLAMMATION, CHRONIC		1 (0%)
#MANDIBULAR L. NODE	(88)	(248)
CONGESTION, NOS		1 (0%)
HEMORRHAGE	3 (3%)	
FIBROSIS, FOCAL	1 (1%)	
PIGMENTATION, NOS		1 (0%)
HYPERPLASIA, RETICULUM CELL		1 (0%)
HYPERPLASIA, LYMPHOID	4 (5%)	34 (14%)
#CERVICAL LYMPH NODE	(88)	(248)
PIGMENTATION, NOS		1 (0%)
ERYTHROPHAGOCYTOSIS		1 (0%)
#MEDIASTINAL L.NODE	(88)	(248)
CONGESTION, NOS	2 (2%)	1 (0%)
HEMORRHAGE	3 (3%)	11 (4%)
INFLAMMATION, ACUTE DIFFUSE		1 (0%)
NECROSIS, FOCAL	1 (1%)	1 (0%)
PIGMENTATION, NOS	10 (11%)	32 (13%)
ERYTHROPHAGOCYTOSIS	2 (2%)	4 (2%)
HYPERPLASIA, RETICULUM CELL		1 (0%)
HYPERPLASIA, LYMPHOID		4 (2%)
#PANCREATIC L.NODE	(88)	(248)
PIGMENTATION, NOS	3 (3%)	4 (2%)
HYPERPLASIA, RETICULUM CELL	3 (3%)	8 (3%)
HYPERPLASIA, LYMPHOID		1 (0%)
#MESENTERIC L. NODE	(88)	(248)
INFLAMMATION, ACUTE DIFFUSE		2 (1%)
ABSCCESS, NOS		1 (0%)
NECROSIS, FOCAL	1 (1%)	1 (0%)
PIGMENTATION, NOS		1 (0%)
ERYTHROPHAGOCYTOSIS		5 (2%)
HYPERPLASIA, RETICULUM CELL	38 (43%)	81 (33%)
HYPERPLASIA, LYMPHOID	1 (1%)	2 (1%)
#ILEOCOLIC LYMPH NODE	(88)	(248)
HYPERPLASIA, LYMPHOID		1 (0%)
#RENAL LYMPH NODE	(88)	(248)
PIGMENTATION, NOS	2 (2%)	2 (1%)
#LIVER	(88)	(248)
LEUKOCYTOSIS, NOS	2 (2%)	6 (2%)
HEMATOPOIESIS	1 (1%)	
#PANCREAS	(86)	(247)
HYPERPLASIA, RETICULUM CELL		1 (0%)
#THYMUS	(76)	(197)
CYST, NOS		1 (1%)
HEMORRHAGE		1 (1%)
CIRCULATORY SYSTEM		
#MANDIBULAR LYMPH NODE	(88)	(248)
LYMPHANGIECTASIS		3 (1%)
#MEDIASTINAL LYMPH NODE	(88)	(248)
LYMPHANGIECTASIS		1 (0%)
#MESENTERIC LYMPH NODE	(88)	(248)
LYMPHANGIECTASIS	1 (1%)	5 (2%)
#ILEOCOLIC LYMPH NODE	(88)	(248)
LYMPHANGIECTASIS		6 (2%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
CIRCULATORY SYSTEM (Continued)		
#RENAL LYMPH NODE	(88)	(248)
LYMPHANGIECTASIS	1 (1%)	1 (0%)
#HEART	(88)	(247)
THROMBOSIS, NOS		2 (1%)
INFLAMMATION, CHRONIC DIFFUSE		1 (0%)
#HEART/ATRIUM	(88)	(247)
THROMBOSIS, NOS	1 (1%)	
#MYOCARDIUM	(88)	(247)
MINERALIZATION	1 (1%)	3 (1%)
INFLAMMATION, CHRONIC	1 (1%)	
INFLAMMATION, CHRONIC FOCAL	38 (43%)	91 (37%)
INFLAMMATION, CHRONIC DIFFUSE	32 (36%)	86 (35%)
FIBROSIS, FOCAL	1 (1%)	
PIGMENTATION, NOS		1 (0%)
#CARDIAC VALVE	(88)	(247)
INFLAMMATION, CHRONIC FOCAL	1 (1%)	
*AORTA	(88)	(250)
MINERALIZATION	2 (2%)	
#SALIVARY GLAND	(87)	(243)
LYMPHANGIECTASIS		1 (0%)
#LIVER	(88)	(248)
THROMBOSIS, NOS	1 (1%)	2 (1%)
THROMBUS, ORGANIZED		1 (0%)
#PANCREAS	(86)	(247)
PERIARTERITIS	4 (5%)	2 (1%)
#TESTIS	(87)	(246)
PERIARTERITIS	1 (1%)	2 (1%)
#ADRENAL	(88)	(248)
THROMBOSIS, NOS	1 (1%)	2 (1%)
DIGESTIVE SYSTEM		
*TONGUE	(88)	(250)
EDEMA, NOS		2 (1%)
#SALIVARY GLAND	(87)	(243)
FIBROSIS, DIFUSE		2 (1%)
NECROSIS, FOCAL		1 (0%)
ATROPHY, DIFFUSE		1 (0%)
HYPERPLASIA, DIFFUSE		1 (0%)
#LIVER	(88)	(248)
CONGESTION, NOS	1 (1%)	1 (0%)
HEMORRHAGE	2 (2%)	
INFLAMMATION, ACUTE FOCAL		1 (0%)
GRANULOMA, NOS	8 (9%)	15 (6%)
CHOLANGIOFIBROSIS	3 (3%)	
ADHESION, NOS		2 (1%)
HEPATITIS, TOXIC	12 (14%)	36 (15%)
DEGENERATION, NOS	18 (20%)	42 (17%)
NECROSIS, FOCAL	7 (8%)	22 (9%)
NECROSIS, DIFFUSE	1 (1%)	
METAMORPHOSIS FATTY	14 (16%)	44 (18%)
PIGMENTATION, NOS	11 (13%)	29 (12%)
FOCAL CELLULAR CHANGE	29 (33%)	74 (30%)
ANGIECTASIS	2 (2%)	4 (2%)
#HEPATIC CAPSULE	(88)	(248)
FIBROSIS		1 (0%)
#LIVER/CENTRILOBULAR	(88)	(248)
NECROSIS, NOS		2 (1%)
#BILE DUCT	(88)	(248)
INFLAMMATION, CHRONIC	11 (13%)	47 (19%)
GRANULOMA, NOS		1 (0%)
FIBROSIS	1 (1%)	4 (2%)
HYPERPLASIA, NOS	26 (30%)	53 (21%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
DIGESTIVE SYSTEM (Continued)		
#PANCREAS	(86)	(247)
ECTOPIA	1 (1%)	5 (2%)
HEMORRHAGE		1 (0%)
INFLAMMATION, CHRONIC FOCAL		1 (0%)
INFLAMMATION, CHRONIC DIFFUSE	1 (1%)	
FIBROSIS, FOCAL		1 (0%)
ATROPHY, NOS	1 (1%)	
ATROPHY, FOCAL	8 (9%)	24 (10%)
ATROPHY, DIFFUSE	3 (3%)	10 (4%)
#PANCREATIC DUCT	(86)	(247)
HYPERPLASIA, NOS		1 (0%)
#PANCREATIC ACINUS	(86)	(247)
HYPERPLASIA, FOCAL	6 (7%)	8 (3%)
#ESOPHAGUS	(86)	(247)
INFLAMMATION, ACUTE DIFFUSE	1 (1%)	
NECROSIS, FOCAL	1 (1%)	
HYPERKERATOSIS	6 (7%)	16 (6%)
#STOMACH	(88)	(248)
MINERALIZATION	3 (3%)	2 (1%)
EDEMA, NOS		1 (0%)
HEMORRHAGE		2 (1%)
INFLAMMATION, ACUTE FOCAL	1 (1%)	3 (1%)
INFLAMMATION, ACUTE DIFFUSE	1 (1%)	1 (0%)
INFLAMMATION, CHRONIC FOCAL	4 (5%)	6 (2%)
INFLAMMATION, CHRONIC DIFFUSE	6 (7%)	25 (10%)
ULCER, PERFORATED	4 (5%)	10 (4%)
FIBROSIS, FOCAL		1 (0%)
ADHESION, NOS	1 (1%)	1 (0%)
NECROSIS, FOCAL	13 (15%)	35 (14%)
NECROSIS, DIFFUSE		5 (2%)
CALCIFICATION, NOS	1 (1%)	
HYPERPLASIA, EPITHELIAL	3 (3%)	
HYPERKERATOSIS	8 (9%)	29 (12%)
ACANTHOSIS	11 (13%)	36 (15%)
#GASTRIC MUCOSA	(88)	(248)
HYPERTROPHY, NOS	1 (1%)	
HYPERPLASIA, DIFFUSE	1 (1%)	
#GASTRIC MUSCULARIS	(88)	(248)
DEGENERATION, NOS	2 (2%)	
#GASTRIC FUNDUS	(88)	(248)
HYPERPLASIA, EPITHELIAL		1 (0%)
#DUODENUM	(88)	(248)
HEMORRHAGE		1 (0%)
INFLAMMATION, ACUTE FOCAL		1 (0%)
NECROSIS, FOCAL		2 (1%)
#JEJUNUM	(88)	(248)
CYST, NOS	1 (1%)	
INFLAMMATION, ACUTE DIFFUSE		1 (0%)
NECROSIS, FOCAL		1 (0%)
#COLON	(87)	(248)
INFLAMMATION, CHRONIC DIFFUSE		1 (0%)
PARASITISM	13 (15%)	22 (9%)
NECROSIS, FOCAL		1 (0%)
NECROSIS, DIFFUSE		1 (0%)
#COLONIC MUSCULARIS PROPRIA	(87)	(248)
DEGENERATION, NOS		1 (0%)
#CECUM	(87)	(248)
MINERALIZATION	1 (1%)	
CYST, NOS		1 (0%)
INFLAMMATION, ACUTE FOCAL		2 (1%)
INFLAMMATION, CHRONIC FOCAL		2 (1%)
INFLAMMATION, CHRONIC DIFFUSE		2 (1%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
DIGESTIVE SYSTEM		
#CECUM (Continued)	(87)	(248)
PARASITISM		2 (1%)
NECROSIS, NOS		1 (0%)
NECROSIS, FOCAL		4 (2%)
#TRANSVERSE COLON	(87)	(248)
CYST, NOS		1 (0%)
URINARY SYSTEM		
#KIDNEY	(88)	(248)
HAMARTOMA		1 (0%)
MINERALIZATION	5 (6%)	13 (5%)
HYDRONEPHROSIS	1 (1%)	3 (1%)
ABSCESS, NOS	1 (1%)	3 (1%)
INFLAMMATION, CHRONIC	77 (88%)	237 (96%)
INFLAMMATION, CHRONIC DIFFUSE	1 (1%)	
INFARCT, NOS		1 (0%)
INFARCT, HEALED	2 (2%)	1 (0%)
HYPERPLASIA, TUBULAR CELL		4 (2%)
METAPLASIA, OSSEOUS		1 (0%)
#KIDNEY/CORTEX	(88)	(248)
CYST, NOS	4 (5%)	15 (6%)
#RENAL PAPILLA	(88)	(248)
INFLAMMATION, ACUTE FOCAL		1 (0%)
NECROSIS, NOS		1 (0%)
NECROSIS, FOCAL		3 (1%)
#KIDNEY/TUBULE	(88)	(248)
CYST, NOS	1 (1%)	
PIGMENTATION, NOS	25 (28%)	74 (30%)
#KIDNEY/PELVIS	(88)	(248)
HEMORRHAGE		1 (0%)
INFLAMMATION, ACUTE FOCAL		1 (0%)
NECROSIS, FOCAL		1 (0%)
#URINARY BLADDER	(85)	(247)
HEMORRHAGE	2 (2%)	5 (2%)
INFLAMMATION, ACUTE FOCAL		2 (1%)
INFLAMMATION, ACUTE DIFFUSE	2 (2%)	3 (1%)
INFLAMMATION, ACUTE/CHRONIC		1 (0%)
INFLAMMATION, CHRONIC FOCAL	1 (1%)	1 (0%)
INFLAMMATION, CHRONIC DIFFUSE	2 (2%)	2 (1%)
NECROSIS, FOCAL		3 (1%)
NECROSIS, DIFFUSE	1 (1%)	3 (1%)
HYPERPLASIA, EPITHELIAL		1 (0%)
HYPERPLASIA, DIFFUSE	1 (1%)	3 (1%)
HYPERPLASIA, PAPILLARY		1 (0%)
POLYP, INFLAMMATORY		1 (0%)
#U. BLADDER/MUCOSA	(85)	(247)
HYPERPLASIA, PAPILLARY		1 (0%)
ENDOCRINE SYSTEM		
#PITUITARY	(87)	(247)
CYST, NOS		10 (4%)
HEMORRHAGE	2 (2%)	1 (0%)
HEMORRHAGIC CYST		1 (0%)
PIGMENTATION, NOS		1 (0%)
HYPERPLASIA, FOCAL	10 (11%)	13 (5%)
ANGIECTASIS	9 (10%)	14 (6%)
#ADRENAL	(88)	(248)
HEMORRHAGE	1 (1%)	1 (0%)
NECROSIS, FOCAL	1 (1%)	
PIGMENTATION, NOS	2 (2%)	

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
ENDOCRINE SYSTEM		
#ADRENAL (Continued)	(88)	(248)
ATROPHY, NOS	1 (1%)	
HYPERPLASIA, FOCAL		1 (0%)
ANGIECTASIS		7 (3%)
#ADRENAL/CAPSULE	(88)	(248)
FIBROSIS, DIFFUSE		1 (0%)
#ADRENAL CORTEX	(88)	(248)
CONGESTION, NOS	1 (1%)	
DEGENERATION, NOS		2 (1%)
NECROSIS, FOCAL	2 (2%)	
METAMORPHOSIS FATTY	18 (20%)	42 (17%)
HYPERTROPHY, FOCAL	1 (1%)	
HYPERPLASIA, FOCAL	1 (1%)	10 (4%)
#ADRENAL MEDULLA	(88)	(248)
HYPERPLASIA, FOCAL	32 (36%)	74 (30%)
#THYROID	(86)	(246)
CYST, NOS	1 (1%)	
CYSTIC FOLLICLES	1 (1%)	5 (2%)
FOLLICULAR CYST, NOS	5 (6%)	27 (11%)
PIGMENTATION, NOS		1 (0%)
HYPERPLASIA, C-CELL	16 (19%)	45 (18%)
#PARATHYROID	(83)	(229)
HYPERPLASIA, NOS	8 (10%)	16 (7%)
#PANCREATIC ISLETS	(86)	(247)
HYPERPLASIA, FOCAL	4 (5%)	4 (2%)
HYPERPLASIA, DIFFUSE	1 (1%)	
REPRODUCTIVE SYSTEM		
*MAMMARY GLAND	(88)	(250)
GALACTOCELE		5 (2%)
CYST, NOS	1 (1%)	
CYSTIC DUCTS	7 (8%)	9 (4%)
FIBROSIS, DIFFUSE		1 (0%)
HYPERPLASIA, NOS		3 (1%)
HYPERPLASIA, FOCAL	1 (1%)	1 (0%)
HYPERPLASIA, DIFFUSE	5 (6%)	13 (5%)
*PREPUTIAL GLAND	(88)	(250)
CYSTIC DUCTS	6 (7%)	7 (3%)
INFLAMMATION, ACUTE		1 (0%)
INFLAMMATION, ACUTE DIFFUSE		2 (1%)
ABSCESS, NOS	2 (2%)	5 (2%)
INFLAMMATION, CHRONIC		1 (0%)
INFLAMMATION, CHRONIC FOCAL		1 (0%)
INFLAMMATION, CHRONIC DIFFUSE		1 (0%)
NECROSIS, NOS		1 (0%)
HYPERPLASIA, FOCAL		1 (0%)
HYPERPLASIA, DIFFUSE		1 (0%)
HYPERKERATOSIS	4 (5%)	2 (1%)
#PROSTATE	(87)	(247)
CYST, NOS	1 (1%)	4 (2%)
CYSTIC DUCTS	1 (1%)	
HEMORRHAGE	1 (1%)	1 (0%)
INFLAMMATION, DIFFUSE	1 (1%)	
INFLAMMATION, ACUTE DIFFUSE		5 (2%)
ABSCESS, NOS	8 (9%)	19 (8%)
INFLAMMATION, ACUTE/CHRONIC	1 (1%)	1 (0%)
INFLAMMATION, CHRONIC FOCAL	21 (24%)	55 (22%)
INFLAMMATION, CHRONIC DIFFUSE	6 (7%)	15 (6%)
HYPERPLASIA, FOCAL	11 (13%)	28 (11%)
HYPERPLASIA, DIFFUSE		2 (1%)
HYPERKERATOSIS		1 (0%)
METAPLASIA, SQUAMOUS		1 (0%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
REPRODUCTIVE SYSTEM (Continued)		
*SEMINAL VESICLE	(88)	(250)
CYST, NOS	1 (1%)	12 (5%)
INFLAMMATION, ACUTE DIFFUSE	1 (1%)	1 (0%)
ABSCESS, NOS	2 (2%)	1 (0%)
INFLAMMATION, CHRONIC FOCAL	1 (1%)	
HYPERPLASIA, FOCAL	1 (1%)	1 (0%)
HYPERPLASIA, DIFFUSE	2 (2%)	9 (4%)
HYPERPLASIA, PAPILLARY		1 (0%)
#TESTIS	(87)	(246)
CYST, NOS		1 (0%)
DEGENERATION, NOS	10 (11%)	26 (11%)
HYPERPLASIA, INTERSTITIAL CELL	32 (37%)	92 (37%)
*EPIDIDYMIS	(88)	(250)
HEMORRHAGE		1 (0%)
INFLAMMATION, ACUTE DIFFUSE	1 (1%)	
GRANULOMA, SPERMATIC		1 (0%)
FIBROSIS, FOCAL		1 (0%)
NECROSIS, FAT	2 (2%)	3 (1%)
NERVOUS SYSTEM		
#BRAIN/MENINGES	(88)	(248)
INFLAMMATION, ACUTE DIFFUSE	1 (1%)	
#CEREBRUM	(88)	(248)
HEMORRHAGE		3 (1%)
GLIOSIS		1 (0%)
NECROSIS, FOCAL	1 (1%)	
#BRAIN	(88)	(248)
HEMORRHAGE		3 (1%)
NECROSIS, FOCAL		1 (0%)
#CEREBELLUM	(88)	(248)
HEMORRHAGE	2 (2%)	2 (1%)
NECROSIS, FOCAL	2 (2%)	
#MEDULLA OBLONGATA	(88)	(248)
NECROSIS, FOCAL		1 (0%)
*SPINAL CORD	(88)	(250)
DEGENERATION, NOS	1 (1%)	
SPECIAL SENSE ORGANS		
*EYE	(88)	(250)
HEMORRHAGE	3 (3%)	4 (2%)
EMPHYEMA	1 (1%)	1 (0%)
SYNECHIA, ANTERIOR		1 (0%)
SYNECHIA, POSTERIOR	1 (1%)	2 (1%)
CATARACT	7 (8%)	11 (4%)
*VITREOUS BODY	(88)	(250)
VASCULARIZATION		1 (0%)
*EYE/CORNEA	(88)	(250)
INFLAMMATION, ACUTE FOCAL	2 (2%)	1 (0%)
INFLAMMATION, CHRONIC FOCAL	1 (1%)	1 (0%)
NECROSIS, FOCAL	2 (2%)	1 (0%)
*EYE/IRIS	(88)	(250)
INFLAMMATION, CHRONIC FOCAL	1 (1%)	
*EYE/RETINA	(88)	(250)
DEGENERATION, NOS	18 (20%)	47 (19%)
*HARDERIAN GLAND	(88)	(250)
INFLAMMATION, ACUTE/CHRONIC		1 (0%)
INFLAMMATION, CHRONIC DIFFUSE		1 (0%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
SPECIAL SENSE ORGANS (Continued)		
*ZYMBAL GLAND	(88)	(250)
CYST, NOS		1 (0%)
CYSTIC DUCTS	9 (10%)	20 (8%)
ABSCISS, NOS	1 (1%)	
INFLAMMATION, CHRONIC DIFFUSE	1 (1%)	
HYPERKERATOSIS	1 (1%)	5 (2%)
MUSCULOSKELETAL SYSTEM		
*SKULL	(88)	(250)
OSTEOPETROSIS	2 (2%)	2 (1%)
FIBROUS OSTEODYSTROPHY	1 (1%)	
*STERNUM	(88)	(250)
FIBROUS OSTEODYSTROPHY	1 (1%)	
*RIB	(88)	(250)
DEGENERATION, NOS		3 (1%)
BODY CAVITIES		
*MEDIASTINUM	(88)	(250)
ECTOPIA	1 (1%)	
INFLAMMATION, ACUTE DIFFUSE	1 (1%)	
*ABDOMINAL CAVITY	(88)	(250)
CONGESTION, NOS		1 (0%)
HEMORRHAGE		1 (0%)
INFLAMMATION, CHRONIC		1 (0%)
NECROSIS, FAT	2 (2%)	9 (4%)
*PLEURA	(88)	(250)
INFLAMMATION, FIBRINOUS		1 (0%)
INFLAMMATION, CHRONIC DIFFUSE		1 (0%)
*PERICARDIUM	(88)	(250)
INFLAMMATION, FIBRINOUS		1 (0%)
*MESENTERY	(88)	(250)
INFLAMMATION, ACUTE FOCAL		1 (0%)
INFLAMMATION, CHRONIC FOCAL		1 (0%)
INFLAMMATION, CHRONIC DIFFUSE		1 (0%)
ALL OTHER SYSTEMS		
*MULTIPLE ORGANS	(88)	(250)
MINERALIZATION	5 (6%)	1 (0%)
CYST, NOS	1 (1%)	
HEMORRHAGE		1 (0%)
INFLAMMATION, ACUTE DIFFUSE		1 (0%)
INFLAMMATION, CHRONIC	3 (3%)	8 (3%)
PIGMENTATION, NOS		1 (0%)
DIAPHRAGM		
HERNIA, NOS		3
HEMORRHAGE		1
INFLAMMATION, ACUTE DIFFUSE		1
INFLAMMATION, CHRONIC FOCAL	1	
NECROSIS, DIFFUSE		1
MESENTERY OF COLON		
INFLAMMATION, FIBRINOUS		1
SPECIAL MORPHOLOGY SUMMARY		
NECROPSY PERF/NO HISTO PERFORMED		2

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

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS

	CONTROL (UNTR)	SHORT RANGE
ANIMALS INITIALLY IN STUDY	88	250
ANIMALS NECROPSIED	88	250
ANIMALS EXAMINED HISTOPATHOLOGICALLY	88	248
INTEGUMENTARY SYSTEM		
*SKIN	(88)	(250)
EPIDERMAL INCLUSION CYST	1 (1%)	1 (0%)
ULCER, NOS		1 (0%)
ABSCESS, NOS		4 (2%)
INFLAMMATION, CHRONIC FOCAL		1 (0%)
FIBROSIS, FOCAL	1 (1%)	
HYPERKERATOSIS		1 (0%)
ACANTHOSIS		3 (1%)
*SUBCUT TISSUE	(88)	(250)
ABSCESS, NOS		1 (0%)
INFLAMMATION, CHRONIC FOCAL		1 (0%)
RESPIRATORY SYSTEM		
#LUNG/BRONCHUS	(87)	(245)
BRONCHIECTASIS		1 (0%)
#LUNG	(87)	(245)
CONGESTION, NOS	2 (2%)	5 (2%)
HEMORRHAGE	1 (1%)	3 (1%)
INFLAMMATION, INTERSTITIAL	1 (1%)	3 (1%)
PNEUMONIA, ASPIRATION		2 (1%)
INFLAMMATION, ACUTE FOCAL	1 (1%)	2 (1%)
INFLAMMATION, CHRONIC	79 (91%)	229 (93%)
PNEUMONIA INTERSTITIAL CHRONIC	1 (1%)	
GRANULOMA, NOS		2 (1%)
NECROSIS, FOCAL	1 (1%)	
PIGMENTATION, NOS		4 (2%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	5 (6%)	3 (1%)
#LUNG/ALVEOLI	(87)	(245)
HISTIOCYTOSIS		3 (1%)
HEMATOPOIETIC SYSTEM		
#BONE MARROW	(84)	(241)
HYPOPLASIA, NOS	1 (1%)	8 (3%)
HYPERPLASIA, NOS	1 (1%)	1 (0%)
MYELOPOIESIS		1 (0%)
#SPLEEN	(87)	(245)
HEMORRHAGE	2 (2%)	4 (2%)
INFLAMMATION, CHRONIC FOCAL		1 (0%)
FIBROSIS, FOCAL	4 (5%)	7 (3%)
FIBROSIS, MULTIFOCAL	1 (1%)	
FIBROSIS, DIFFUSE	1 (1%)	4 (2%)
NECROSIS, NOS		1 (0%)
NECROSIS, FOCAL	2 (2%)	5 (2%)
NECROSIS, DIFFUSE	1 (1%)	
METAMORPHOSIS FATTY		1 (0%)
HEMOSIDEROSIS	27 (31%)	65 (27%)
METAPLASIA, OSSEOUS		1 (0%)
HYPERPLASIA, MEGAKARYOCYTIC		1 (0%)
HEMATOPOIESIS	24 (28%)	72 (29%)
#SPLENIC CAPSULE	(87)	(245)
FIBROSIS, FOCAL		1 (0%)
FIBROSIS, MULTIFOCAL		2 (1%)
#SPLENIC FOLLICLES	(87)	(245)
ATROPHY, NOS	2 (2%)	3 (1%)

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
HEMATOPOIETIC SYSTEM (Continued)		
#LYMPH NODE	(87)	(245)
INFLAMMATION, ACUTE FIBRINOUS		1 (0%)
NECROSIS, DIFFUSE		1 (0%)
HYPERPLASIA, LYMPHOID		2 (1%)
#MANDIBULAR L. NODE	(87)	(245)
HEMORRHAGE	1 (1%)	1 (0%)
INFLAMMATION, FIBRINOUS		1 (0%)
PIGMENTATION, NOS	1 (1%)	
ERYTHROPHAGOCYTOSIS		3 (1%)
HYPERPLASIA, LYMPHOID	15 (17%)	38 (16%)
#CERVICAL LYMPH NODE	(87)	(245)
HYPERPLASIA, LYMPHOID		2 (1%)
#MEDIASTINAL LYMPH NODE	(87)	(245)
CONGESTION, NOS		3 (1%)
HEMORRHAGE	2 (2%)	3 (1%)
INFLAMMATION, FIBRINOUS		1 (0%)
INFLAMMATION, ACUTE		1 (0%)
PIGMENTATION, NOS	3 (3%)	26 (11%)
ERYTHROPHAGOCYTOSIS	2 (2%)	5 (2%)
HYPERPLASIA, RETICULUM CELL	1 (1%)	2 (1%)
HYPERPLASIA, LYMPHOID	1 (1%)	10 (4%)
#HEPATIC LYMPH NODE	(87)	(245)
PIGMENTATION, NOS		1 (0%)
HYPERPLASIA, RETICULUM CELL		1 (0%)
#PANCREATIC LYMPH NODE	(87)	(245)
INFLAMMATION, ACUTE DIFFUSE		1 (0%)
PIGMENTATION, NOS	2 (2%)	12 (5%)
ATROPHY, NOS	1 (1%)	
HYPERPLASIA, RETICULUM CELL	4 (5%)	13 (5%)
HYPERPLASIA, LYMPHOID		2 (1%)
#MESENTERIC LYMPH NODE	(87)	(245)
HEMORRHAGE	2 (2%)	
INFLAMMATION, ACUTE		1 (0%)
PIGMENTATION, NOS	2 (2%)	3 (1%)
ATROPHY, NOS		1 (0%)
ERYTHROPHAGOCYTOSIS		3 (1%)
HYPERPLASIA, RETICULUM CELL	43 (49%)	90 (37%)
HYPERPLASIA, LYMPHOID	4 (5%)	4 (2%)
#ILEOCOLIC LYMPH NODE	(87)	(245)
HYPERPLASIA, RETICULUM CELL	1 (1%)	
#RENAL LYMPH NODE	(87)	(245)
INFLAMMATION, ACUTE DIFFUSE		1 (0%)
#ILIAC LYMPH NODE	(87)	(245)
HYPERPLASIA, LYMPHOID	1 (1%)	
#LIVER	(87)	(244)
LEUKOCYTOSIS, NOS		2 (1%)
HEMATOPOIESIS		3 (1%)
#CECUM	(87)	(244)
HEMATOPOIESIS		1 (0%)
CIRCULATORY SYSTEM		
*MEDIASTINUM	(88)	(250)
PERIARTERITIS		1 (0%)
#LYMPH NODE	(87)	(245)
LYMPHANGIECTASIS		1 (0%)
#MEDIASTINAL L. NODE	(87)	(245)
LYMPHANGIECTASIS		1 (0%)
#HEPATIC LYMPH NODE	(87)	(245)
LYMPHANGIECTASIS	1 (1%)	
#PANCREATIC L. NODE	(87)	(245)
LYMPHANGIECTASIS		1 (0%)

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
CIRCULATORY SYSTEM (Continued)		
#MESENTERIC L. NODE	(87)	(245)
LYMPHANGIECTASIS	1 (1%)	1 (0%)
#ILEOCOLIC LYMPH NODE	(87)	(245)
LYMPHANGIECTASIS	1 (1%)	1 (0%)
#ILIAC LYMPH NODE	(87)	(245)
LYMPHANGIECTASIS	1 (1%)	
*ADIPOSE TISSUE	(88)	(250)
PERIARTERITIS		1 (0%)
#HEART	(87)	(245)
THROMBOSIS, NOS		1 (0%)
INFLAMMATION, CHRONIC FOCAL	1 (1%)	
#HEART/ATRIUM	(87)	(245)
THROMBOSIS, NOS	1 (1%)	1 (0%)
#MYOCARDIUM	(87)	(245)
INFLAMMATION, CHRONIC FOCAL	33 (38%)	72 (29%)
INFLAMMATION, CHRONIC DIFFUSE	22 (25%)	65 (27%)
DEGENERATION, NOS		1 (0%)
#PANCREAS	(86)	(245)
PERIARTERITIS		1 (0%)
*MESENTERY	(88)	(250)
PERIARTERITIS		2 (1%)
#UTERUS	(87)	(245)
THROMBOSIS, NOS		1 (0%)
#PITUITARY	(87)	(244)
THROMBOSIS, NOS	1 (1%)	
DIGESTIVE SYSTEM		
*TONGUE	(88)	(250)
ABSCCESS, NOS		1 (0%)
ACANTHOSIS		2 (1%)
#SALIVARY GLAND	(87)	(243)
ABSCCESS, NOS		1 (0%)
INFLAMMATION, CHRONIC DIFFUSE		1 (0%)
ATROPHY, FOCAL	1 (1%)	
#LIVER	(87)	(244)
HEMORRHAGE	2 (2%)	6 (2%)
INFLAMMATION, FIBRINOUS	1 (1%)	
INFLAMMATION, ACUTE FOCAL		1 (0%)
INFLAMMATION, CHRONIC		1 (0%)
GRANULOMA, NOS	26 (30%)	49 (20%)
HEPATITIS, TOXIC	12 (14%)	37 (15%)
NECROSIS, FOCAL	4 (5%)	33 (14%)
INFARCT, NOS		1 (0%)
METAMORPHOSIS FATTY	30 (34%)	75 (31%)
PIGMENTATION, NOS	12 (14%)	56 (23%)
MITOTIC ALTERATION		2 (1%)
FOCAL CELLULAR CHANGE	42 (48%)	84 (34%)
HEPATOCYTOMEGALY		2 (1%)
ANGIECTASIS	6 (7%)	3 (1%)
#BILE DUCT	(87)	(244)
DILATATION, NOS		1 (0%)
CYST, NOS		1 (0%)
INFLAMMATION, CHRONIC	11 (13%)	28 (11%)
FIBROSIS	1 (1%)	2 (1%)
FIBROSIS, FOCAL		1 (0%)
HYPERPLASIA, NOS	3 (3%)	16 (7%)
HYPERPLASIA, FOCAL		1 (0%)
#PANCREAS	(86)	(245)
ECTOPIA	3 (3%)	5 (2%)
INFLAMMATION, CHRONIC DIFFUSE	1 (1%)	1 (0%)
ATROPHY, FOCAL	4 (5%)	8 (3%)
ATROPHY, DIFFUSE	2 (2%)	5 (2%)

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
DIGESTIVE SYSTEM (Continued)		
#PANCREATIC ACINUS	(86)	(245)
HYPERPLASIA, FOCAL	1 (1%)	3 (1%)
*PHARYNGEAL MUCOSA	(88)	(250)
HYPERKERATOSIS		1 (0%)
#ESOPHAGUS	(87)	(244)
HYPERKERATOSIS	4 (5%)	8 (3%)
#STOMACH	(87)	(245)
HEMORRHAGE		2 (1%)
INFLAMMATION, ACUTE FOCAL	2 (2%)	2 (1%)
INFLAMMATION, ACUTE DIFFUSE	1 (1%)	
INFLAMMATION, CHRONIC FOCAL	4 (5%)	9 (4%)
INFLAMMATION, CHRONIC DIFFUSE	9 (10%)	35 (14%)
ULCER, PERFORATED	7 (8%)	21 (9%)
ADHESION, NOS	2 (2%)	1 (0%)
NECROSIS, FOCAL	12 (14%)	33 (13%)
NECROSIS, DIFFUSE	2 (2%)	2 (1%)
HYPERKERATOSIS	21 (24%)	59 (24%)
ACANTHOSIS	19 (22%)	59 (24%)
#GASTRIC SUBMUCOSA	(87)	(245)
EDEMA, NOS		1 (0%)
#GASTRIC MUSCULARIS	(87)	(245)
DEGENERATION, NOS		1 (0%)
#GASTRIC FUNDUS	(87)	(245)
HYPERPLASIA, EPITHELIAL		1 (0%)
#SMALL INTESTINE	(87)	(244)
PARASITISM		1 (0%)
#DUODENUM	(87)	(244)
ULCER, PERFORATED		1 (0%)
#COLON	(87)	(244)
EDEMA, NOS		1 (0%)
INFLAMMATION, ACUTE FOCAL		1 (0%)
INFLAMMATION, CHRONIC FOCAL	2 (2%)	1 (0%)
PARASITISM	8 (9%)	13 (5%)
NECROSIS, FOCAL	1 (1%)	2 (1%)
#COLONIC SUBMUCOSA	(87)	(244)
FIBROSIS, FOCAL		1 (0%)
#CECUM	(87)	(244)
HEMORRHAGE	1 (1%)	
INFLAMMATION, ACUTE FOCAL	1 (1%)	
INFLAMMATION, ACUTE DIFFUSE		1 (0%)
INFLAMMATION, CHRONIC FOCAL	1 (1%)	3 (1%)
INFLAMMATION, CHRONIC DIFFUSE		1 (0%)
GRANULOMA, NOS		1 (0%)
FIBROSIS, FOCAL		1 (0%)
NECROSIS, FOCAL	2 (2%)	3 (1%)
HYPERPLASIA, EPITHELIAL	1 (1%)	
#DESCENDING COLON	(87)	(244)
PARASITISM		1 (0%)
URINARY SYSTEM		
#KIDNEY	(87)	(245)
MINERALIZATION	63 (72%)	208 (85%)
INFLAMMATION, ACUTE FOCAL		1 (0%)
INFLAMMATION, CHRONIC	84 (97%)	231 (94%)
NEPHROSIS, NOS		1 (0%)
METAMORPHOSIS FATTY		2 (1%)
PIGMENTATION, NOS		1 (0%)
HYPERPLASIA, TUBULAR CELL		1 (0%)

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
URINARY SYSTEM (Continued)		
#KIDNEY/TUBULE	(87)	(245)
DEGENERATION, NOS	1 (1%)	
NECROSIS, DIFFUSE		1 (0%)
PIGMENTATION, NOS	57 (66%)	198 (81%)
#URINARY BLADDER	(87)	(242)
HEMORRHAGE	1 (1%)	
INFLAMMATION, CHRONIC FOCAL	1 (1%)	
HYPERPLASIA, EPITHELIAL	1 (1%)	
HYPERPLASIA, DIFFUSE	1 (1%)	
HYPERPLASIA, PAPILLARY		1 (0%)
ENDOCRINE SYSTEM		
#PITUITARY	(87)	(244)
CYST, NOS	6 (7%)	21 (9%)
HEMORRHAGE	3 (3%)	4 (2%)
HEMORRHAGIC CYST		2 (1%)
GLIOSIS		1 (0%)
NECROSIS, FOCAL	1 (1%)	
PIGMENTATION, NOS		2 (1%)
HYPERPLASIA, FOCAL	6 (7%)	19 (8%)
HYPERPLASIA, DIFFUSE	1 (1%)	1 (0%)
ANGIECTASIS	15 (17%)	42 (17%)
METAPLASIA, OSSEOUS		1 (0%)
#ADRENAL	(87)	(245)
ATROPHY, NOS		1 (0%)
HYPERPLASIA, FOCAL		1 (0%)
ANGIECTASIS		1 (0%)
#ADRENAL CORTEX	(87)	(245)
DEGENERATION, NOS	2 (2%)	4 (2%)
NECROSIS, FOCAL	1 (1%)	1 (0%)
METAMORPHOSIS FATTY	32 (37%)	96 (39%)
HYPERPLASIA, FOCAL	8 (9%)	11 (4%)
ANGIECTASIS	1 (1%)	2 (1%)
#ADRENAL MEDULLA	(87)	(245)
HYPERPLASIA, NOS	1 (1%)	
HYPERPLASIA, FOCAL	16 (18%)	47 (19%)
#THYROID	(87)	(244)
CYSTIC FOLLICLES	1 (1%)	3 (1%)
FOLLICULAR CYST, NOS	4 (5%)	10 (4%)
HYPERPLASIA, C-CELL	20 (23%)	58 (24%)
ANGIECTASIS		1 (0%)
#PARATHYROID	(85)	(222)
HYPERPLASIA, NOS	1 (1%)	7 (3%)
#PANCREATIC ISLETS	(86)	(245)
HYPERPLASIA, FOCAL	1 (1%)	1 (0%)
REPRODUCTIVE SYSTEM		
*MAMMARY GLAND	(88)	(250)
GALACTOCELE	7 (8%)	39 (16%)
CYST, NOS		1 (0%)
CYSTIC DUCTS	46 (52%)	116 (46%)
INFLAMMATION, ACUTE DIFFUSE	1 (1%)	
ABSCESS, NOS		1 (0%)
HYPERPLASIA, NOS	8 (9%)	23 (9%)
HYPERPLASIA, FOCAL	1 (1%)	1 (0%)
HYPERPLASIA, DIFFUSE	2 (2%)	8 (3%)

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
REPRODUCTIVE SYSTEM (Continued)		
*PREPUTIAL GLAND	(88)	(250)
CYSTIC DUCTS	3 (3%)	5 (2%)
INFLAMMATION, ACUTE	1 (1%)	
ABSCCESS, NOS		4 (2%)
HYPERPLASIA, FOCAL		1 (0%)
HYPERKERATOSIS	1 (1%)	3 (1%)
*VAGINA	(88)	(250)
HYPERKERATOSIS	1 (1%)	
ACANTHOSIS	1 (1%)	
#UTERUS	(87)	(245)
HYDROMETRA	2 (2%)	9 (4%)
HEMORRHAGE	1 (1%)	1 (0%)
INFLAMMATION, ACUTE		1 (0%)
INFLAMMATION, ACUTE FOCAL	1 (1%)	
INFLAMMATION, CHRONIC FOCAL		1 (0%)
INFLAMMATION, CHRONIC DIFFUSE	1 (1%)	
NECROSIS, FOCAL		1 (0%)
NECROSIS, FAT	1 (1%)	
HYPERPLASIA, PAPILLARY	1 (1%)	
ANGIECTASIS		1 (0%)
#CERVIX UTERI	(87)	(245)
ABSCCESS, NOS		2 (1%)
INFLAMMATION, CHRONIC DIFFUSE		1 (0%)
FIBROSIS	1 (1%)	3 (1%)
HYPERKERATOSIS		2 (1%)
ACANTHOSIS		4 (2%)
#UTERUS/ENDOMETRIUM	(87)	(245)
CYST, NOS	3 (3%)	6 (2%)
HYPERPLASIA, FOCAL	1 (1%)	1 (0%)
HYPERPLASIA, PAPILLARY		2 (1%)
#FALLOPIAN TUBE	(87)	(245)
RETENTION FLUID	1 (1%)	
#OVARY	(87)	(245)
CYST, NOS	2 (2%)	16 (7%)
FOLLICULAR CYST, NOS	1 (1%)	3 (1%)
PAROVARIAN CYST		2 (1%)
HEMORRHAGE		1 (0%)
INFLAMMATION, ACUTE DIFFUSE		1 (0%)
ABSCCESS, NOS	1 (1%)	
NERVOUS SYSTEM		
#BRAIN/MENINGES	(87)	(245)
INFLAMMATION, ACUTE DIFFUSE		1 (0%)
#CEREBRUM	(87)	(245)
HEMORRHAGE	3 (3%)	3 (1%)
GLIOSIS	1 (1%)	2 (1%)
NECROSIS, FOCAL	1 (1%)	
#BRAIN	(87)	(245)
HEMORRHAGE		2 (1%)
#CEREBELLUM	(87)	(245)
HEMORRHAGE	1 (1%)	1 (0%)
NECROSIS, FOCAL		1 (0%)
SPECIAL SENSE ORGANS		
*EYE	(88)	(250)
HEMORRHAGE	4 (5%)	2 (1%)
EMPYEMA		1 (0%)
SYNECHIA, POSTERIOR	3 (3%)	4 (2%)
CATARACT	11 (13%)	21 (8%)
PHTHISIS BULBI		2 (1%)

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE
SPECIAL SENSE ORGANS (Continued)		
*EYE/CORNEA	(88)	(250)
INFLAMMATION, ACUTE FOCAL		1 (0%)
INFLAMMATION, CHRONIC FOCAL		2 (1%)
INFLAMMATION, CHRONIC DIFFUSE	1 (1%)	
*EYE/RETINA	(88)	(250)
DEGENERATION, NOS	26 (30%)	71 (28%)
*EYELID	(88)	(250)
ACANTHOSIS		1 (0%)
*HARDERIAN GLAND	(88)	(250)
INFLAMMATION, ACUTE DIFFUSE		2 (1%)
*ZYMBALE GLAND	(88)	(250)
CYSTIC DUCTS	2 (2%)	9 (4%)
ABSCESS, NOS		1 (0%)
MUSCULOSKELETAL SYSTEM		
*SKULL	(88)	(250)
OSTEOPETROSIS	3 (3%)	9 (4%)
FIBROUS OSTEODYSTROPHY		1 (0%)
*STERNUM	(88)	(250)
OSTEOPETROSIS	5 (6%)	13 (5%)
DEGENERATION, NOS		1 (0%)
*RIB	(88)	(250)
DEGENERATION, NOS	2 (2%)	
*FEMUR	(88)	(250)
OSTEOPETROSIS		1 (0%)
BODY CAVITIES		
*MEDIASTINUM	(88)	(250)
INFLAMMATION, FIBRINOUS	1 (1%)	
INFLAMMATION, ACUTE DIFFUSE		1 (0%)
*ABDOMINAL CAVITY	(88)	(250)
NECROSIS, FAT	2 (2%)	5 (2%)
*PERITONEUM	(88)	(250)
INFLAMMATION, NOS		1 (0%)
*PLEURA	(88)	(250)
INFLAMMATION, ACUTE FOCAL		1 (0%)
INFLAMMATION, CHRONIC FOCAL		1 (0%)
*MESENTERY	(88)	(250)
INFLAMMATION, ACUTE DIFFUSE		1 (0%)
INFLAMMATION, CHRONIC FOCAL	2 (2%)	2 (1%)
ALL OTHER SYSTEMS		
*MULTIPLE ORGANS	(88)	(250)
MINERALIZATION		2 (1%)
INFLAMMATION, CHRONIC	1 (1%)	1 (0%)
PIGMENTATION, NOS	2 (2%)	1 (0%)
DIAPHRAGM		
HERNIA, NOS	7	8
SPECIAL MORPHOLOGY SUMMARY		
NECROPSY PERF/NO HISTO PERFORMED		5
AUTO/NECROPSY/HISTO PERFORMED		1
AUTO/NECROPSY/NO HISTO	1	

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

APPENDIX D

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
ANIMALS INITIALLY IN STUDY	88	125	250	175	100
ANIMALS NECROPSIED	88	125	250	175	100
ANIMALS EXAMINED HISTOPATHOLOGICALLY	85	125	250	175	100
INTEGUMENTARY SYSTEM					
*SKIN	(88)	(125)	(250)	(175)	(100)
CYST, NOS			3 (1%)		
EPIDERMAL INCLUSION CYST	1 (1%)	3 (2%)	1 (0%)		
DERMAL INCLUSION CYST			1 (0%)	1 (1%)	
EDEMA, NOS			2 (1%)		
INFLAMMATION, ACUTE		1 (1%)			
INFLAMMATION, ACUTE/ CHRONIC		1 (1%)			
HYPERPLASIA, NOS			1 (0%)		
HYPERKERATOSIS		1 (1%)			
ACANTHOSIS		1 (1%)	2 (1%)		
*SUBCUT TISSUE	(88)	(125)	(250)	(175)	(100)
MINERALIZATION					1 (1%)
MULTILOCLULAR CYST	1 (1%)				
STEATITIS			1 (0%)		
INFLAMMATION, SUPPURATIVE		1 (1%)	3 (1%)		
INFLAMMATION, ACUTE					1 (1%)
ABSCESS, NOS				1 (1%)	
INFLAMMATION, ACUTE/ CHRONIC	1 (1%)				
INFLAMMATION, CHRONIC			1 (0%)		
NECROSIS, FAT	1 (1%)		1 (0%)		
HYPERPLASIA, FOCAL					1 (1%)
HYPERKERATOSIS			1 (0%)		
RESPIRATORY SYSTEM					
*NASAL CAVITY	(88)	(125)	(250)	(175)	(100)
HEMORRHAGE					1 (1%)
INFLAMMATION, SUPPURATIVE				1 (1%)	
INFLAMMATION, ACUTE					1 (1%)
*NASAL TURBINATE	(88)	(125)	(250)	(175)	(100)
CONGESTION, NOS			1 (0%)		
INFLAMMATION, SUPPURATIVE			1 (0%)		
#TRACHEA	(85)	(124)	(250)	(175)	(99)
CYST, NOS			1 (0%)		
#LUNG	(85)	(125)	(250)	(175)	(99)
BRONCHIECTASIS					2 (2%)
CONGESTION, NOS	11 (13%)	7 (6%)	8 (3%)	3 (2%)	7 (7%)
HEMORRHAGE	3 (4%)	1 (1%)	1 (0%)	2 (1%)	
INFLAMMATION, INTERSTITIAL	4 (5%)	2 (2%)	9 (4%)	4 (2%)	4 (4%)
PNEUMONIA, ASPIRATION	1 (1%)				
INFLAMMATION, SUPPURATIVE		1 (1%)	1 (0%)	1 (1%)	2 (2%)
BRONCHOPNEUMONIA, ACUTE	1 (1%)				
INFLAMMATION, ACUTE				1 (1%)	
INFLAMMATION, ACUTE/ CHRONIC			1 (0%)	1 (1%)	
INFLAMMATION, CHRONIC	45 (53%)	86 (69%)	98 (39%)	60 (34%)	51 (52%)
INFLAMMATION, CHRONIC FOCAL			1 (0%)		
ABSCESS, CHRONIC					3 (3%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
RESPIRATORY SYSTEM					
#LUNG (Continued)					
INFLAMMATION, GRANULOMATOUS			1 (0%)		
INFLAMMATION GRANULOMATOUS FOCAL			3 (1%)		1 (1%)
NECROSIS, FOCAL			1 (0%)		
HYPERPLASIA, ALVEOLAR EPITHELIUM	5 (6%)	3 (2%)	13 (5%)	5 (3%)	4 (4%)
METAPLASIA, OSSEOUS				1 (1%)	
#LUNG/ALVEOLI	(85)	(125)	(250)	(175)	(99)
EDEMA, NOS			1 (0%)		
HISTIOCYTOSIS			10 (4%)		
HEMATOPOIETIC SYSTEM					
*MULTIPLE ORGANS	(88)	(125)	(250)	(175)	(100)
HYPERPLASIA, LYMPHOID			1 (0%)		
#BONE MARROW	(84)	(122)	(248)	(175)	(98)
HYPERPLASIA, NOS				1 (1%)	
#SPLEEN	(85)	(125)	(250)	(175)	(99)
ECTOPIA			1 (0%)		
CONGESTION, NOS	1 (1%)		1 (0%)		1 (1%)
INFLAMMATION, CHRONIC			1 (0%)		
FIBROSIS	1 (1%)	2 (2%)	22 (9%)	5 (3%)	3 (3%)
FIBROSIS, FOCAL	2 (2%)		5 (2%)	1 (1%)	3 (3%)
NECROSIS, NOS		2 (2%)			
NECROSIS, FOCAL					1 (1%)
NECROSIS, ISCHEMIC					1 (1%)
INFARCT, NOS			6 (2%)	8 (5%)	
INFARCT, HEALED				1 (1%)	
PIGMENTATION, NOS	1 (1%)				
HEMOSIDEROSIS	13 (15%)	10 (8%)	46 (18%)	18 (10%)	16 (16%)
ATROPHY, NOS	7 (8%)	1 (1%)	1 (0%)		
HYPERPLASIA, STROMAL	1 (1%)				
ANGIECTASIS	1 (1%)		1 (0%)		
HYPERPLASIA, RETICULUM CELL	1 (1%)				
HEMATOPOIESIS	7 (8%)	9 (7%)	24 (10%)	13 (7%)	6 (6%)
#SPLENIC CAPSULE	(85)	(125)	(250)	(175)	(99)
INFLAMMATION, CHRONIC	1 (1%)				
FIBROSIS			1 (0%)		
#SPLENIC FOLLICLES	(85)	(125)	(250)	(175)	(99)
ATROPHY, NOS		2 (2%)			1 (1%)
#MANDIBULAR L. NODE	(85)	(125)	(250)	(175)	(100)
CONGESTION, NOS	1 (1%)	2 (2%)	3 (1%)		1 (1%)
HEMORRHAGE			2 (1%)	2 (1%)	2 (2%)
INFLAMMATION, SUPPURATIVE				1 (1%)	
INFLAMMATION, ACUTE			1 (0%)		
NECROSIS, NOS			1 (0%)		
PIGMENTATION, NOS	1 (1%)	1 (1%)	3 (1%)		2 (2%)
HYPERPLASIA, PLASMA CELL		13 (10%)	46 (18%)	40 (23%)	38 (38%)
HYPERPLASIA, RETICULUM CELL			1 (0%)	1 (1%)	
HYPERPLASIA, LYMPHOID	12 (14%)	12 (10%)	10 (4%)	2 (1%)	9 (9%)
#CERVICAL LYMPH NODE	(85)	(125)	(250)	(175)	(100)
CONGESTION, NOS	1 (1%)	1 (1%)			
HEMORRHAGE	1 (1%)				
PIGMENTATION, NOS			1 (0%)		
HYPERPLASIA, PLASMA CELL		3 (2%)	1 (0%)		3 (3%)
HYPERPLASIA, LYMPHOID	1 (1%)	2 (2%)	1 (0%)	1 (1%)	

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
HEMATOPOIETIC SYSTEM (Continued)					
#MEDIASTINAL L. NODE	(85)	(125)	(250)	(175)	(100)
CONGESTION, NOS	3 (4%)		4 (2%)	3 (2%)	1 (1%)
HEMORRHAGE	1 (1%)	9 (7%)	18 (7%)	12 (7%)	14 (14%)
INFLAMMATION, SUPPURATIVE				1 (1%)	1 (1%)
NECROSIS, NOS			1 (0%)		
PIGMENTATION, NOS	5 (6%)	15 (12%)	58 (23%)	41 (23%)	41 (41%)
HYPERPLASIA, PLASMA CELL			3 (1%)	11 (6%)	9 (9%)
HYPERPLASIA, RETICULUM					
CELL	1 (1%)	1 (1%)	3 (1%)	4 (2%)	1 (1%)
HYPERPLASIA, LYMPHOID	2 (2%)	1 (1%)	1 (0%)		
#CELIAC LYMPH NODE	(85)	(125)	(250)	(175)	(100)
HYPERPLASIA, RETICULUM					
CELL				1 (1%)	
#PANCREATIC L. NODE	(85)	(125)	(250)	(175)	(100)
HEMORRHAGE			3 (1%)		
INFLAMMATION, ACUTE			1 (0%)		
NECROSIS, NOS	1 (1%)				
PIGMENTATION, NOS		2 (2%)	14 (6%)	7 (4%)	6 (6%)
HEMOSIDEROSIS	1 (1%)				
HYPERPLASIA, PLASMA CELL					1 (1%)
HYPERPLASIA, RETICULUM CELL			1 (0%)	1 (1%)	1 (1%)
HYPERPLASIA, LYMPHOID	3 (4%)	1 (1%)		1 (1%)	2 (2%)
HEMATOPOIESIS				1 (1%)	
#MESENTERIC L. NODE	(85)	(125)	(250)	(175)	(100)
HEMORRHAGE	1 (1%)		2 (1%)	1 (1%)	2 (2%)
INFLAMMATION, SUPPURATIVE	1 (1%)				
PIGMENTATION, NOS		25 (20%)	28 (11%)	7 (4%)	28 (28%)
ANGIECTASIS	1 (1%)				
ERYTHROPHAGOCYTOSIS	1 (1%)				
HYPERPLASIA, PLASMA CELL		1 (1%)			1 (1%)
HYPERPLASIA, RETICULUM CELL	1 (1%)	4 (3%)	12 (5%)	2 (1%)	
HYPERPLASIA, LYMPHOID	6 (7%)	8 (6%)	7 (3%)		3 (3%)
#ILEOCOLIC LYMPH NODE	(85)	(125)	(250)	(175)	(100)
HYPERPLASIA, LYMPHOID		1 (1%)			
#RENAL LYMPH NODE	(85)	(125)	(250)	(175)	(100)
HEMORRHAGE	1 (1%)		2 (1%)		
INFLAMMATION, ACUTE			1 (0%)		
NECROSIS, NOS			1 (0%)		
PIGMENTATION, NOS		1 (1%)	5 (2%)		1 (1%)
HYPERPLASIA, LYMPHOID	1 (1%)		1 (0%)		
#ILIAC LYMPH NODE	(85)	(125)	(250)	(175)	(100)
HYPERPLASIA, PLASMA CELL			1 (0%)		
HYPERPLASIA, LYMPHOID	2 (2%)				
#AXILLARY LYMPH NODE	(85)	(125)	(250)	(175)	(100)
HEMORRHAGE			1 (0%)		
PIGMENTATION, NOS			1 (0%)		
#BRACHIAL LYMPH NODE	(85)	(125)	(250)	(175)	(100)
PIGMENTATION, NOS				1 (1%)	
#POPLITEAL LYMPH NODE	(85)	(125)	(250)	(175)	(100)
HYPERPLASIA, PLASMA CELL				1 (1%)	
*STERNUM	(88)	(125)	(250)	(175)	(100)
MYELOFIBROSIS			3 (1%)		
MYELOSCLEROSIS					2 (2%)
HEMATOPOIESIS	1 (1%)				
*FEMUR	(88)	(125)	(250)	(175)	(100)
MYELOSCLEROSIS					1 (1%)
#LUNG	(85)	(125)	(250)	(175)	(99)
LEUKOCYTOSIS, NOS	3 (4%)	2 (2%)	1 (0%)		

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
HEMATOPOIETIC SYSTEM (Continued)					
#LIVER	(85)	(125)	(250)	(175)	(100)
LEUKOCYTOSIS, NOS	2 (2%)	1 (1%)			
MEGAKARYOCYTOSIS			1 (0%)		
HEMATOPOIESIS		1 (1%)			
#HEPATIC SINUSOID	(85)	(125)	(250)	(175)	(100)
LEUKOCYTOSIS, NOS			3 (1%)		
#COLON	(85)	(125)	(250)	(175)	(100)
HYPERPLASIA, LYMPHOID					10 (10%)
#CECUM	(85)	(125)	(250)	(175)	(100)
HYPERPLASIA, LYMPHOID					1 (1%)
#ASCENDING COLON	(85)	(125)	(250)	(175)	(100)
HYPERPLASIA, LYMPHOID		1 (1%)			
#ADRENAL	(85)	(125)	(250)	(175)	(100)
HEMATOPOIESIS					1 (1%)
#THYMUS	(62)	(107)	(212)	(156)	(87)
ECTOPIA			1 (0%)		
THYROGLOSSAL DUCT CYST CONGESTION, NOS		1 (1%)	1 (0%)	1 (1%)	
CIRCULATORY SYSTEM					
#LYMPH NODE	(85)	(125)	(250)	(175)	(100)
LYMPHANGIECTASIS		1 (1%)	1 (0%)		
#MANDIBULAR L. NODE	(85)	(125)	(250)	(175)	(100)
LYMPHANGIECTASIS	9 (11%)	12 (10%)	23 (9%)	11 (6%)	13 (13%)
#CERVICAL LYMPH NODE	(85)	(125)	(250)	(175)	(100)
LYMPHANGIECTASIS		1 (1%)	1 (0%)		
#MEDIASTINAL L. NODE	(85)	(125)	(250)	(175)	(100)
LYMPHANGIECTASIS	1 (1%)	1 (1%)	5 (2%)	2 (1%)	1 (1%)
#CELIAC LYMPH NODE	(85)	(125)	(250)	(175)	(100)
LYMPHANGIECTASIS			1 (0%)	5 (3%)	2 (2%)
#PANCREATIC L. NODE	(85)	(125)	(250)	(175)	(100)
LYMPHANGIECTASIS			1 (0%)		
#MESENTERIC L. NODE	(85)	(125)	(250)	(175)	(100)
LYMPHANGIECTASIS	5 (6%)	6 (5%)	16 (6%)	6 (3%)	11 (11%)
#ILEOCOLIC LYMPH NODE	(85)	(125)	(250)	(175)	(100)
LYMPHANGIECTASIS	1 (1%)	6 (5%)	2 (1%)	1 (1%)	2 (2%)
#RENAL LYMPH NODE	(85)	(125)	(250)	(175)	(100)
LYMPHANGIECTASIS			1 (0%)		
#ILIAC LYMPH NODE	(85)	(125)	(250)	(175)	(100)
LYMPHANGIECTASIS	1 (1%)		1 (0%)		1 (1%)
#AXILLARY LYMPH NODE	(85)	(125)	(250)	(175)	(100)
LYMPHANGIECTASIS		1 (1%)			
*SKELETAL MUSCLE	(88)	(125)	(250)	(175)	(100)
THROMBOSIS, NOS			1 (0%)		
#LUNG/BRONCHIOLE	(85)	(125)	(250)	(175)	(99)
PERIARTERITIS					1 (1%)
#LUNG	(85)	(125)	(250)	(175)	(99)
THROMBUS, FIBRIN		2 (2%)	1 (0%)		
#HEART	(85)	(125)	(250)	(175)	(99)
THROMBUS, FIBRIN			1 (0%)		
INFLAMMATION, FIBRINOUS			1 (0%)		
INFLAMMATION, CHRONIC	1 (1%)	1 (1%)	1 (0%)		
FIBROSIS	1 (1%)		1 (0%)		
#HEART/ATRIUM	(85)	(125)	(250)	(175)	(99)
THROMBOSIS, NOS	1 (1%)				
THROMBUS, ORGANIZED			1 (0%)		
THROMBUS, FIBRIN			2 (1%)		

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
CIRCULATORY SYSTEM (Continued)					
#MYOCARDIUM	(85)	(125)	(250)	(175)	(99)
MINERALIZATION	2 (2%)	2 (2%)	2 (1%)		2 (2%)
THROMBUS, FIBRIN			1 (0%)		
INFLAMMATION, SUPPURATIVE	1 (1%)	1 (1%)			
INFLAMMATION, CHRONIC		6 (5%)	8 (3%)	15 (9%)	4 (4%)
FIBROSIS	53 (62%)	70 (56%)	170 (68%)	90 (51%)	72 (73%)
FIBROSIS, FOCAL	1 (1%)				
DEGENERATION, NOS	2 (2%)				
#CARDIAC VALVE	(85)	(125)	(250)	(175)	(99)
INFLAMMATION, CHRONIC		1 (1%)			
*AORTA	(88)	(125)	(250)	(175)	(100)
MINERALIZATION	9 (10%)		5 (2%)		2 (2%)
*CORONARY ARTERY	(88)	(125)	(250)	(175)	(100)
MINERALIZATION		1 (1%)			2 (2%)
*PULMONARY ARTERY	(88)	(125)	(250)	(175)	(100)
MINERALIZATION			1 (0%)		
*BRONCHIAL ARTERY	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, CHRONIC		1 (1%)			
*SUP. PANC-DUOD. ARTERY	(88)	(125)	(250)	(175)	(100)
MINERALIZATION			1 (0%)		
THROMBUS, ORGANIZED			1 (0%)		
PERIARTERITIS					1 (1%)
*MESENTERIC ARTERY	(88)	(125)	(250)	(175)	(100)
PERIARTERITIS					1 (1%)
#LIVER	(85)	(125)	(250)	(175)	(100)
THROMBOSIS, NOS	1 (1%)				
THROMBUS, FIBRIN			1 (0%)	1 (1%)	1 (1%)
#PANCREAS	(85)	(124)	(249)	(174)	(99)
THROMBUS, CANALIZED	1 (1%)				
PERIARTERITIS			1 (0%)	5 (3%)	
#COLONIC SEROSA	(85)	(125)	(250)	(175)	(100)
PERIARTERITIS			1 (0%)		
#TESTIS	(84)	(125)	(250)	(175)	(100)
PERIARTERITIS			1 (0%)		1 (1%)
#ADRENAL	(85)	(125)	(250)	(175)	(100)
THROMBOSIS, NOS	1 (1%)				
DIGESTIVE SYSTEM					
*MOUTH	(88)	(125)	(250)	(175)	(100)
ABSCESS, NOS			1 (0%)		
ACANTHOSIS			1 (0%)		
*MOUTH/ORAL CAVITY	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, CHRONIC				1 (1%)	
*TONGUE	(88)	(125)	(250)	(175)	(100)
ECTOPIA					1 (1%)
CYST, NOS				1 (1%)	
EDEMA, NOS					1 (1%)
INFLAMMATION, ACUTE					1 (1%)
ABSCESS, CHRONIC			1 (0%)		
HYPERKERATOSIS			2 (1%)		
ACANTHOSIS			1 (0%)		
#SALIVARY GLAND	(84)	(124)	(247)	(173)	(98)
CYST, NOS				1 (1%)	
INFLAMMATION, ACUTE/ CHRONIC			2 (1%)		
INFLAMMATION, CHRONIC		1 (1%)	3 (1%)	3 (2%)	
HYPERTROPHY, FOCAL			1 (0%)		
#SALIVARY SEROUS GLAND	(84)	(124)	(247)	(173)	(98)
ATROPHY, NOS		1 (1%)			

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
DIGESTIVE SYSTEM (Continued)					
#LIVER	(85)	(125)	(250)	(175)	(100)
CYST, NOS		1 (1%)	1 (0%)	1 (1%)	
MULTILOCLULAR CYST				3 (2%)	
CONGESTION, NOS	3 (4%)	1 (1%)	2 (1%)		4 (4%)
HEMORRHAGE			1 (0%)		1 (1%)
INFLAMMATION, SUPPURATIVE				1 (1%)	
INFLAMMATION, ACUTE		1 (1%)		2 (1%)	1 (1%)
INFLAMMATION, ACUTE FOCAL			1 (0%)		
INFLAMMATION, CHRONIC	4 (5%)	4 (3%)	5 (2%)	2 (1%)	
INFLAMMATION, CHRONIC FOCAL					1 (1%)
INFLAMMATION GRANULOMATOUS FOCAL			1 (0%)		
FIBROSIS	1 (1%)			1 (1%)	
HEPATITIS, TOXIC	12 (14%)	15 (12%)	33 (13%)	35 (20%)	16 (16%)
DEGENERATION, NOS		1 (1%)			
DEGENERATION, CYSTIC	4 (5%)	36 (29%)	44 (18%)	26 (15%)	21 (21%)
NECROSIS, NOS	4 (5%)	3 (2%)	3 (1%)	2 (1%)	
NECROSIS, FOCAL	1 (1%)		1 (0%)		
NECROSIS, COAGULATIVE			8 (3%)	4 (2%)	2 (2%)
METAMORPHOSIS, FATTY	13 (15%)	14 (11%)	21 (8%)	15 (9%)	11 (11%)
PIGMENTATION, NOS			6 (2%)	1 (1%)	2 (2%)
CYTOPLASMIC VACUOLIZATION			1 (0%)		
FOCAL CELLULAR CHANGE	20 (24%)	35 (28%)	65 (26%)	60 (34%)	25 (25%)
HYPERPLASIA, NOS		3 (2%)	7 (3%)	2 (1%)	2 (2%)
HYPERPLASIA, FOCAL	2 (2%)	6 (5%)	2 (1%)		3 (3%)
ANGIECTASIS	12 (14%)	11 (9%)	12 (5%)	10 (6%)	7 (7%)
#HEPATIC CAPSULE	(85)	(125)	(250)	(175)	(100)
INFLAMMATION, SUPPURATIVE	1 (1%)				
INFLAMMATION, ACUTE FIBRINOUS		1 (1%)			
INFLAMMATION, CHRONIC FOCAL	1 (1%)				
ADHESION, FIBROUS		1 (1%)			
#LIVER/PERIportal	(85)	(125)	(250)	(175)	(100)
FIBROSIS	26 (31%)	13 (10%)	14 (6%)	6 (3%)	27 (27%)
#BILE DUCT	(85)	(125)	(250)	(175)	(100)
CYST, NOS	2 (2%)				
MULTILOCLULAR CYST	1 (1%)				
CYSTIC DUCTS	1 (1%)	1 (1%)			
FIBROSIS	1 (1%)				
HYPERPLASIA, NOS	18 (21%)	7 (6%)	58 (23%)	11 (6%)	10 (10%)
HYPERPLASIA, CYSTIC				1 (1%)	
#PANCREAS	(85)	(124)	(249)	(174)	(99)
CYST, NOS		1 (1%)		1 (1%)	
EDEMA, INTERSTITIAL		1 (1%)			
INFLAMMATION, SUPPURATIVE		1 (1%)			
INFLAMMATION, CHRONIC				1 (1%)	
NECROSIS, FIBRINOID					1 (1%)
ATROPHY, NOS	18 (21%)	16 (13%)	50 (20%)	22 (13%)	7 (7%)
ATROPHY, FOCAL	2 (2%)				
#PANCREATIC DUCT	(85)	(124)	(249)	(174)	(99)
HYPERPLASIA, NOS				1 (1%)	
#PANCREATIC ACINUS	(85)	(124)	(249)	(174)	(99)
HYPERPLASIA, NOS			1 (0%)	1 (1%)	
HYPERPLASIA, FOCAL	1 (1%)		1 (0%)		
#ESOPHAGUS	(83)	(125)	(250)	(174)	(98)
INFLAMMATION, CHRONIC					1 (1%)
ABSCESS, CHRONIC					1 (1%)
HYPERKERATOSIS	1 (1%)	1 (1%)			2 (2%)
METAPLASIA, OSSEOUS					1 (1%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
DIGESTIVE SYSTEM (Continued)					
#STOMACH	(85)	(124)	(250)	(175)	(100)
MINERALIZATION	1 (1%)	1 (1%)	5 (2%)		
CYST, NOS	2 (2%)	1 (1%)	1 (0%)		
EDEMA, NOS	5 (6%)				
HEMORRHAGE	1 (1%)		1 (0%)		
ULCER, NOS	8 (9%)	5 (4%)	2 (1%)	1 (1%)	
INFLAMMATION, SUPPURATIVE			1 (0%)		
INFLAMMATION, ACUTE	6 (7%)	6 (5%)	14 (6%)		4 (4%)
ULCER, ACUTE	5 (6%)	2 (2%)	14 (6%)	2 (1%)	7 (7%)
INFLAMMATION, ACUTE FOCAL	2 (2%)		2 (1%)		1 (1%)
INFLAMMATION, ACUTE/ CHRONIC	8 (9%)	3 (2%)	12 (5%)	7 (4%)	3 (3%)
INFLAMMATION, CHRONIC	2 (2%)	1 (1%)		3 (2%)	1 (1%)
ULCER, CHRONIC			7 (3%)	3 (2%)	
ULCER, PERFORATED		1 (1%)	4 (2%)	2 (1%)	2 (2%)
ADHESION, FIBROUS		1 (1%)			
DEGENERATION, NOS		1 (1%)	2 (1%)		
NECROSIS, NOS		1 (1%)			
NECROSIS, FOCAL			4 (2%)		
HYPERPLASIA, EPITHELIAL					1 (1%)
HYPERPLASIA, BASAL CELL	1 (1%)		1 (0%)		
HYPERKERATOSIS	7 (8%)	3 (2%)		3 (2%)	
ACANTHOSIS	10 (12%)	13 (10%)	18 (7%)	12 (7%)	14 (14%)
METAPLASIA, SQUAMOUS			1 (0%)		
#GASTRIC MUCOSA	(85)	(124)	(250)	(175)	(100)
HYPERPLASIA, NOS			1 (0%)		
#GASTRIC SUBMUCOSA	(85)	(124)	(250)	(175)	(100)
EDEMA, NOS	1 (1%)	3 (2%)	23 (9%)	8 (5%)	10 (10%)
HEMORRHAGE				1 (1%)	
#GASTRIC MUSCULARIS	(85)	(124)	(250)	(175)	(100)
DEGENERATION, NOS			1 (0%)		1 (1%)
#GASTRIC SEROSA	(85)	(124)	(250)	(175)	(100)
ULCER, NOS		1 (1%)			
INFLAMMATION, SUPPURATIVE	1 (1%)				
INFLAMMATION, ACUTE					
FIBRINOUS		1 (1%)			
ACANTHOSIS		1 (1%)			
#SMALL INTESTINE/MUCOSA	(85)	(125)	(250)	(175)	(100)
HYPERPLASIA, NOS		1 (1%)			
#SMALL INTESTINAL SUB	(85)	(125)	(250)	(175)	(100)
EDEMA, NOS			1 (0%)		
#DUODENUM	(85)	(125)	(250)	(175)	(100)
INFLAMMATION, ACUTE			1 (0%)		
METAPLASIA, OSSEOUS				1 (1%)	
#DUODENAL MUCOSA	(85)	(125)	(250)	(175)	(100)
HYPERPLASIA, NOS				1 (1%)	
#DUODENAL SEROSA	(85)	(125)	(250)	(175)	(100)
INFLAMMATION, ACUTE/ CHRONIC				1 (1%)	
#JEJUNUM	(85)	(125)	(250)	(175)	(100)
DIVERTICULOSIS			1 (0%)		
INFLAMMATION, ACUTE/ CHRONIC				1 (1%)	
#LARGE INTESTINE	(85)	(125)	(250)	(175)	(100)
INFLAMMATION, ACUTE/ CHRONIC	1 (1%)				
INFLAMMATION, CHRONIC	1 (1%)				
FIBROSIS	1 (1%)				
PARASITISM	3 (4%)				

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
DIGESTIVE SYSTEM (Continued)					
#COLON	(85)	(125)	(250)	(175)	(100)
ULCER, NOS	1 (1%)				
INFLAMMATION, ACUTE	1 (1%)			1 (1%)	
INFLAMMATION, ACUTE/ CHRONIC					1 (1%)
INFLAMMATION, CHRONIC FOCAL			1 (0%)	1 (1%)	
PARASITISM		6 (5%)	11 (4%)	8 (5%)	
#COLONIC SUBMUCOSA	(85)	(125)	(250)	(175)	(100)
EDEMA, NOS			1 (0%)	1 (1%)	
#COLONIC MUSCULARIS	(85)	(125)	(250)	(175)	(100)
DEGENERATION, NOS			1 (0%)		
#COLONIC SEROSA	(85)	(125)	(250)	(175)	(100)
INFLAMMATION, FIBRINOUS			1 (0%)		
#CECUM	(85)	(125)	(250)	(175)	(100)
EDEMA, NOS		1 (1%)	5 (2%)		
HEMORRHAGE			1 (0%)		
INFLAMMATION, SUPPURATIVE			1 (0%)		
INFLAMMATION, ACUTE	2 (2%)				
ULCER, ACUTE				1 (1%)	
INFLAMMATION, ACUTE/ CHRONIC				1 (1%)	
ABSCESS, CHRONIC				1 (1%)	
PARASITISM	2 (2%)		2 (1%)	1 (1%)	1 (1%)
#ASCENDING COLON	(85)	(125)	(250)	(175)	(100)
INFLAMMATION, ACUTE/ CHRONIC	1 (1%)	1 (1%)		1 (1%)	
INFLAMMATION, CHRONIC		3 (2%)		1 (1%)	
ULCER, CHRONIC				1 (1%)	
INFLAMMATION, CHRONIC FOCAL		1 (1%)			
HYPERPLASIA, EPITHELIAL		2 (2%)		1 (1%)	
#TRANSVERSE COLON	(85)	(125)	(250)	(175)	(100)
PARASITISM		1 (1%)			
#DESCENDING COLON	(85)	(125)	(250)	(175)	(100)
PARASITISM		2 (2%)		3 (2%)	
URINARY SYSTEM					
#KIDNEY	(85)	(125)	(250)	(175)	(100)
MINERALIZATION	1 (1%)	1 (1%)	6 (2%)		1 (1%)
CAST, NOS	78 (92%)	97 (78%)	229 (92%)	125 (71%)	87 (87%)
HYDRONEPHROSIS			1 (0%)	1 (1%)	3 (3%)
CYST, NOS		2 (2%)	26 (10%)	8 (5%)	9 (9%)
CONGESTION, NOS	1 (1%)	1 (1%)	1 (0%)		1 (1%)
PYELONEPHRITIS, ACUTE					1 (1%)
INFLAMMATION, ACUTE	1 (1%)				
INFLAMMATION, ACUTE FOCAL	1 (1%)				
INFLAMMATION, CHRONIC	62 (73%)	77 (62%)	209 (84%)	117 (67%)	84 (84%)
GLOMERULOSCLEROSIS, NOS	1 (1%)				
PIGMENTATION, NOS	9 (11%)	19 (15%)	53 (21%)	7 (4%)	17 (17%)
HYPERPLASIA, TUBULAR CELL	1 (1%)				
HYPERPLASIA, EPITHELIAL	1 (1%)				
#RIGHT KIDNEY	(85)	(125)	(250)	(175)	(100)
CYST, NOS				1 (1%)	
INFLAMMATION, CHRONIC				1 (1%)	
#LEFT KIDNEY	(85)	(125)	(250)	(175)	(100)
CAST, NOS		1 (1%)		1 (1%)	
INFLAMMATION, CHRONIC		1 (1%)		1 (1%)	
#KIDNEY/CORTEX	(85)	(125)	(250)	(175)	(100)
CYST, NOS	3 (4%)				

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
URINARY SYSTEM (Continued)					
#KIDNEY/TUBULE	(85)	(125)	(250)	(175)	(100)
PIGMENTATION, NOS	1 (1%)				
HYPERPLASIA, EPITHELIAL	1 (1%)				
#URINARY BLADDER	(84)	(124)	(249)	(174)	(98)
EDEMA, NOS			1 (0%)		
HEMORRHAGE	4 (5%)	1 (1%)	7 (3%)		3 (3%)
INFLAMMATION, SUPPURATIVE	1 (1%)	1 (1%)	2 (1%)		1 (1%)
INFLAMMATION, ACUTE	1 (1%)	1 (1%)			4 (4%)
INFLAMMATION, ACUTE SUPPURATIVE		1 (1%)			
INFLAMMATION, ACUTE/CHRONIC			1 (0%)		1 (1%)
INFLAMMATION, CHRONIC FOCAL			1 (0%)		
INFLAMMATION, GRANULO- MATOUS			1 (0%)		
NECROSIS, FOCAL					1 (1%)
HYPERPLASIA, EPITHELIAL	2 (2%)		3 (1%)	1 (1%)	
HYPERPLASIA, PAPILLARY			3 (1%)		
POLYP, INFLAMMATORY			1 (0%)		
#U. BLADDER/SUBMUCOSA	(84)	(124)	(249)	(174)	(98)
HEMORRHAGE	1 (1%)				1 (1%)
*URETHRA	(88)	(125)	(250)	(175)	(100)
OBSTRUCTION, NOS			1 (0%)		
ENDOCRINE SYSTEM					
#PITUITARY	(85)	(124)	(246)	(175)	(100)
CYST, NOS	1 (1%)		3 (1%)	3 (2%)	
MULTILOCLAR CYST				2 (1%)	
HEMORRHAGE			1 (0%)		
FIBROSIS			1 (0%)		
FIBROSIS, FOCAL			1 (0%)		
NECROSIS, FOCAL			1 (0%)		
CHOLESTEROL DEPOSIT			1 (0%)		
PIGMENTATION, NOS			1 (0%)		
HEMOSIDEROSIS			1 (0%)		
HYPERTROPHY, FOCAL			4 (2%)	2 (1%)	
HYPERPLASIA, NOS	1 (1%)				
HYPERPLASIA, FOCAL			3 (1%)	1 (1%)	4 (4%)
ANGIECTASIS	8 (9%)	4 (3%)	6 (2%)	8 (5%)	4 (4%)
#ADRENAL	(85)	(125)	(250)	(175)	(100)
HEMORRHAGE	1 (1%)				
METAMORPHOSIS, FATTY		1 (1%)			
PIGMENTATION, NOS	2 (2%)				
ANGIECTASIS			2 (1%)		
#ADRENAL CORTEX	(85)	(125)	(250)	(175)	(100)
DEGENERATION, CYSTIC			2 (1%)	1 (1%)	
NECROSIS, NOS			1 (0%)		
METAMORPHOSIS, FATTY	22 (26%)	20 (16%)	27 (11%)	17 (10%)	16 (16%)
HYPERTROPHY, FOCAL		1 (1%)	2 (1%)	1 (1%)	1 (1%)
HYPERPLASIA, NOS				1 (1%)	
HYPERPLASIA, FOCAL	1 (1%)	3 (2%)	7 (3%)	1 (1%)	1 (1%)
#ADRENAL MEDULLA	(85)	(125)	(250)	(175)	(100)
MINERALIZATION			1 (0%)		
NECROSIS, NOS		1 (1%)			
HYPERPLASIA, NOS			1 (0%)		
HYPERPLASIA, FOCAL	8 (9%)	7 (6%)	29 (12%)	6 (3%)	8 (8%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
ENDOCRINE SYSTEM (Continued)					
#THYROID	(84)	(124)	(250)	(175)	(99)
CYST, NOS			1 (0%)		
CYSTIC FOLLICLES	10 (12%)	7 (6%)	17 (7%)	6 (3%)	12 (12%)
FOLLICULAR CYST, NOS	1 (1%)		1 (0%)		
INFLAMMATION, ACUTE	1 (1%)				
INFLAMMATION, CHRONIC			1 (0%)		
HYPERPLASIA, NOS				1 (1%)	
HYPERPLASIA, C-CELL	9 (11%)	21 (17%)	51 (20%)	36 (21%)	13 (13%)
HYPERPLASIA, FOLLICULAR-CELL		1 (1%)	1 (0%)		
METAPLASIA, SQUAMOUS			1 (0%)		
#PARATHYROID	(78)	(119)	(243)	(166)	(93)
HYPERPLASIA, NOS	12 (15%)	13 (11%)	30 (12%)	2 (1%)	16 (17%)
#PANCREATIC ISLETS	(85)	(124)	(249)	(174)	(99)
HYPERPLASIA, NOS			1 (0%)	1 (1%)	
HYPERPLASIA, FOCAL	1 (1%)		2 (1%)		
REPRODUCTIVE SYSTEM					
*MAMMARY GLAND	(88)	(125)	(250)	(175)	(100)
DILATATION/DUCTS			2 (1%)		1 (1%)
GALACTOCELE	5 (6%)	5 (4%)	11 (4%)	6 (3%)	3 (3%)
CYSTIC DUCTS	1 (1%)	1 (1%)			
HEMORRHAGE		1 (1%)	1 (0%)		
INFLAMMATION, CHRONIC		1 (1%)	1 (0%)		
INFLAMMATION GRANULO- MATOUS FOCAL					1 (1%)
HYPERPLASIA, NOS	13 (15%)	2 (2%)	7 (3%)	1 (1%)	
HYPERPLASIA, EPITHELIAL	1 (1%)				
*PREPUTIAL GLAND	(88)	(125)	(250)	(175)	(100)
DILATATION/DUCTS			3 (1%)		
CYST, NOS					1 (1%)
CYSTIC DUCTS	1 (1%)	3 (2%)			2 (2%)
INFLAMMATION, SUPPURATIVE			1 (0%)		
ABCESS, NOS			2 (1%)		1 (1%)
INFLAMMATION, ACUTE/ CHRONIC			1 (0%)		1 (1%)
ABCESS, CHRONIC			1 (0%)		
HYPERPLASIA, EPITHELIAL			1 (0%)		
ANGIECTASIS			1 (0%)		
#PROSTATE	(85)	(125)	(249)	(174)	(99)
EDEMA, INTERSTITIAL		1 (1%)			
INFLAMMATION, SUPPURATIVE		1 (1%)	31 (12%)	1 (1%)	2 (2%)
INFLAMMATION, ACUTE	1 (1%)	2 (2%)	1 (0%)		
INFLAMMATION, ACUTE FOCAL			1 (0%)		
ABCESS, NOS	2 (2%)	1 (1%)	2 (1%)		1 (1%)
INFLAMMATION, ACUTE/ CHRONIC	10 (12%)	14 (11%)	52 (21%)	41 (24%)	41 (41%)
INFLAMMATION, CHRONIC	4 (5%)	4 (3%)	1 (0%)		1 (1%)
ABCESS, CHRONIC					2 (2%)
INFLAMMATION, GRANULO- MATOUS		1 (1%)			
INFLAMMATION GRANULO- MATOUS FOCAL			1 (0%)		
HYPERPLASIA, NOS			2 (1%)	4 (2%)	
HYPERPLASIA, EPITHELIAL	1 (1%)		21 (8%)		
HYPERPLASIA, FOCAL	1 (1%)		8 (3%)	6 (3%)	3 (3%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
REPRODUCTIVE SYSTEM (Continued)					
*SEMINAL VESICLE	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, SUPPURATIVE		1 (1%)	3 (1%)		1 (1%)
INFLAMMATION, ACUTE	1 (1%)				1 (1%)
INFLAMMATION, ACUTE/ CHRONIC	2 (2%)				1 (1%)
HYPERPLASIA, NOS		1 (1%)			
HYPERPLASIA, EPITHELIAL	5 (6%)		1 (0%)		1 (1%)
HYPERPLASIA, FOCAL		1 (1%)	2 (1%)		
*COAGULATING GLAND	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, ACUTE/ CHRONIC	1 (1%)		1 (0%)		
INFLAMMATION, CHRONIC	1 (1%)				
HYPERPLASIA, EPITHELIAL	2 (2%)				
#TESTIS	(84)	(125)	(250)	(175)	(100)
MINERALIZATION	4 (5%)		13 (5%)	3 (2%)	
STEATITIS				1 (1%)	
GRANULOMA, SPERMATIC DEGENERATION, NOS	9 (11%)	1 (1%) 11 (9%)	15 (6%)	3 (2%)	1 (1%) 5 (5%)
HYPERPLASIA, INTERSTITIAL CELL		8 (6%)	6 (2%)	12 (7%)	4 (4%)
#TESTIS/TUBULE	(84)	(125)	(250)	(175)	(100)
DEGENERATION, NOS	2 (2%)		3 (1%)		
*EPIDIDYMIS	(88)	(125)	(250)	(175)	(100)
STEATITIS	4 (5%)	2 (2%)	6 (2%)	5 (3%)	3 (3%)
INFLAMMATION, ACUTE/ CHRONIC					1 (1%)
INFLAMMATION, CHRONIC					1 (1%)
GRANULOMA, SPERMATIC		1 (1%)			
FIBROSIS	1 (1%)				
NECROSIS, FAT	3 (3%)		8 (3%)	3 (2%)	2 (2%)
NERVOUS SYSTEM					
#BRAIN/MENINGES	(85)	(125)	(250)	(175)	(100)
INFLAMMATION, SUPPURATIVE				1 (1%)	
#CEREBRAL VENTRICLE	(85)	(125)	(250)	(175)	(100)
DILATATION, NOS			2 (1%)		1 (1%)
#BRAIN	(85)	(125)	(250)	(175)	(100)
HEMORRHAGE			1 (0%)	1 (1%)	
INFLAMMATION, SUPPURATIVE				1 (1%)	
GLIOSIS			1 (0%)		1 (1%)
#MEDULLA OBLONGATA	(85)	(125)	(250)	(175)	(100)
ABSCESS, NOS				1 (1%)	
SPECIAL SENSE ORGANS					
*EYE	(88)	(125)	(250)	(175)	(100)
HEMORRHAGE	2 (2%)	2 (2%)	4 (2%)	1 (1%)	1 (1%)
INFLAMMATION, SUPPURATIVE			5 (2%)	1 (1%)	
INFLAMMATION, ACUTE					1 (1%)
INFLAMMATION, ACUTE SUPPURATIVE	1 (1%)				
INFLAMMATION, CHRONIC		1 (1%)	2 (1%)		3 (3%)
CATARACT	19 (22%)	27 (22%)	71 (28%)	20 (11%)	24 (24%)
*EYE/CORNEA	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, ACUTE					2 (2%)
INFLAMMATION, ACUTE SUPPURATIVE	1 (1%)				

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
SPECIAL SENSE ORGANS (Continued)					
*EYE/RETINA	(88)	(125)	(250)	(175)	(100)
DEGENERATION, NOS	19 (22%)	28 (22%)	68 (27%)	21 (12%)	24 (24%)
*HARDERIAN GLAND	(88)	(125)	(250)	(175)	(100)
INFLAMMATION GRANULO- MATOUS FOCAL			1 (0%)		
*EAR	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, ACUTE/ CHRONIC					1 (1%)
HYPERPLASIA, EPITHELIAL		1 (1%)	1 (0%)		
*ZYMBAL GLAND	(88)	(125)	(250)	(175)	(100)
DILATATION/DUCTS			1 (0%)	3 (2%)	
CYSTIC DUCTS	2 (2%)			1 (1%)	
INFLAMMATION, ACUTE				1 (1%)	
ABSCESS, NOS		1 (1%)	2 (1%)	1 (1%)	
INFLAMMATION, ACUTE/CHRONIC		1 (1%)			
ABSCESS, CHRONIC		1 (1%)			
INFLAMMATION, GRANULOMATOUS			1 (0%)		
HYPERPLASIA, EPITHELIAL			1 (0%)	1 (1%)	
HYPERKERATOSIS		1 (1%)	1 (0%)		
MUSCULOSKELETAL SYSTEM					
*SKULL	(88)	(125)	(250)	(175)	(100)
HYPEROSTOSIS		1 (1%)	5 (2%)	1 (1%)	2 (2%)
*MANDIBLE	(88)	(125)	(250)	(175)	(100)
ABSCESS, CHRONIC			1 (0%)		
PERIODONTAL CYST				1 (1%)	
*STERNUM	(88)	(125)	(250)	(175)	(100)
HYPEROSTOSIS			1 (0%)		
HYPERPLASIA, NOS					1 (1%)
BODY CAVITIES					
*THORACIC CAVITY	(88)	(125)	(250)	(175)	(100)
ABSCESS, CHRONIC					1 (1%)
*MEDIASTINUM	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, SUPPURATIVE	2 (2%)	1 (1%)			
INFLAMMATION, ACUTE	1 (1%)				
*ABDOMINAL CAVITY	(88)	(125)	(250)	(175)	(100)
STEATITIS			2 (1%)		1 (1%)
NECROSIS, FAT			2 (1%)		1 (1%)
*ABDOMINAL WALL	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, CHRONIC			1 (0%)		
*PLEURA	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, SUPPURATIVE	2 (2%)				
FIBROSIS					1 (1%)
*EPICARDIUM	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, FIBRINOUS		1 (1%)			
INFLAMMATION, ACUTE					2 (2%)
*MESENTERY	(88)	(125)	(250)	(175)	(100)
HEMORRHAGE					1 (1%)
INFLAMMATION, CHRONIC		2 (2%)			1 (1%)
INFLAMMATION, CHRONIC FOCAL					1 (1%)
NECROSIS, FAT				1 (1%)	1 (1%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
ALL OTHER SYSTEMS					
*MULTIPLE ORGANS	(88)	(125)	(250)	(175)	(100)
MINERALIZATION			2 (1%)	1 (1%)	3 (3%)
CONGESTION, NOS			2 (1%)	1 (1%)	
HEMORRHAGE			1 (0%)		
INFLAMMATION, SUPPURATIVE		1 (1%)	3 (1%)		1 (1%)
INFLAMMATION, ACUTE/ CHRONIC			1 (0%)		
INFLAMMATION, CHRONIC	1 (1%)	4 (3%)	1 (0%)		
FIBROSIS	1 (1%)				
PIGMENTATION, NOS	1 (1%)		1 (0%)		1 (1%)
HYPERPLASIA, NOS	1 (1%)				
DIAPHRAGM					
HERNIA, NOS		2		5	4
INFLAMMATION, CHRONIC	1				1
ADHESION, NOS					1
FOOT					
INFLAMMATION, CHRONIC					1
ADIPOSE TISSUE					
CONGESTION, NOS	1				
HEMORRHAGE		1	1		
INFLAMMATION, CHRONIC	1		1	2	
INFLAMMATION, GRANULO- MATOUS			1		
FIBROSIS	1				
SPECIAL MORPHOLOGY SUMMARY					
NECROPSY PERF/NO HISTO PERFORMED	3				

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

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
ANIMALS INITIALLY IN STUDY	88	125	250	175	100
ANIMALS NECROPSIED	88	125	250	175	100
ANIMALS EXAMINED HISTOPATHOLOGICALLY	87	125	250	175	100
INTEGUMENTARY SYSTEM					
*SKIN	(88)	(125)	(250)	(175)	(100)
CYST, NOS				1 (1%)	
INFLAMMATION, CHRONIC			1 (0%)		
HYPERKERATOSIS					2 (2%)
*SUBCUT TISSUE	(88)	(125)	(250)	(175)	(100)
ABSCESS, CHRONIC			1 (0%)	1 (1%)	
RESPIRATORY SYSTEM					
#LUNG/BRONCHUS	(87)	(125)	(250)	(175)	(99)
BRONCHIECTASIS					1 (1%)
EDEMA, NOS			1 (0%)		
#LUNG	(87)	(125)	(250)	(175)	(99)
MINERALIZATION					1 (1%)
BRONCHIECTASIS					1 (1%)
CYST, NOS					1 (1%)
CONGESTION, NOS	4 (5%)	6 (5%)	3 (1%)	1 (1%)	
HEMORRHAGE	1 (1%)				1 (1%)
INFLAMMATION, INTERSTITIAL	3 (3%)	3 (2%)	5 (2%)	2 (1%)	1 (1%)
PNEUMONIA, ASPIRATION					3 (3%)
INFLAMMATION, SUPPURATIVE					4 (4%)
INFLAMMATION, ACUTE FOCAL	1 (1%)				
ABSCESS, NOS					1 (1%)
INFLAMMATION, ACUTE/CHRONIC	1 (1%)	5 (4%)			
INFLAMMATION, CHRONIC	16 (18%)	33 (26%)	29 (12%)	17 (10%)	14 (14%)
INFLAMMATION, GRANULOMATOUS				1 (1%)	1 (1%)
FIBROSIS				1 (1%)	
HYPERPLASIA, EPITHELIAL		1 (1%)			
HYPERPLASIA, ALVEOLAR					
EPITHELIUM	1 (1%)	2 (2%)	6 (2%)	3 (2%)	2 (2%)
#LUNG/ALVEOLI	(87)	(125)	(250)	(175)	(99)
HISTIOCYTOSIS		1 (1%)	3 (1%)	1 (1%)	1 (1%)
HEMATOPOIETIC SYSTEM					
*MULTIPLE ORGANS	(88)	(125)	(250)	(175)	(100)
HYPERPLASIA, PLASMA CELL			1 (0%)		
HYPERPLASIA, LYMPHOID			1 (0%)		
#BONE MARROW	(87)	(125)	(248)	(174)	(98)
ATROPHY, NOS				1 (1%)	
#SPLEEN	(87)	(125)	(249)	(175)	(99)
HEMORRHAGE		1 (1%)			
FIBROSIS	2 (2%)	6 (5%)	4 (2%)	4 (2%)	2 (2%)
FIBROSIS, FOCAL	1 (1%)	2 (2%)		1 (1%)	
INFARCT, NOS		3 (2%)	3 (1%)		2 (2%)
INFARCT, ACUTE			1 (0%)		
PIGMENTATION, NOS			1 (0%)		
HEMOSIDEROSIS	34 (39%)	19 (15%)	121 (49%)	17 (10%)	35 (35%)
HEMATOPOIESIS	4 (5%)	5 (4%)	24 (10%)	20 (11%)	13 (13%)
MYELOPOIESIS		1 (1%)			
#SPLENIC CAPSULE	(87)	(125)	(249)	(175)	(99)
INFLAMMATION, CHRONIC			1 (0%)		
FIBROSIS					2 (2%)

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
HEMATOPOIETIC SYSTEM (Continued)					
#MANDIBULAR L. NODE	(87)	(125)	(250)	(175)	(99)
CONGESTION, NOS	1 (1%)	1 (1%)	1 (0%)	2 (1%)	1 (1%)
HEMORRHAGE		3 (2%)	2 (1%)	5 (3%)	1 (1%)
INFLAMMATION, SUPPURATIVE			2 (1%)		
INFLAMMATION, CHRONIC					1 (1%)
PIGMENTATION, NOS	3 (3%)	1 (1%)	7 (3%)	2 (1%)	2 (2%)
HYPERPLASIA, PLASMA CELL	16 (18%)	20 (16%)	73 (29%)	14 (8%)	27 (27%)
HYPERPLASIA, RETICULUM CELL			2 (1%)		
HYPERPLASIA, LYMPHOID		1 (1%)	3 (1%)		1 (1%)
#CERVICAL LYMPH NODE	(87)	(125)	(250)	(175)	(99)
CONGESTION, NOS			1 (0%)		
HEMORRHAGE		1 (1%)	1 (0%)		
INFLAMMATION, SUPPURATIVE			1 (0%)		
PIGMENTATION, NOS			1 (0%)	1 (1%)	1 (1%)
HYPERPLASIA, PLASMA CELL	1 (1%)	1 (1%)	5 (2%)	1 (1%)	
#THORACIC LYMPH NODE	(87)	(125)	(250)	(175)	(99)
CONGESTION, NOS			1 (0%)		
#MEDIASTINAL L. NODE	(87)	(125)	(250)	(175)	(99)
MINERALIZATION				1 (1%)	
CONGESTION, NOS		2 (2%)	2 (1%)	4 (2%)	4 (4%)
HEMORRHAGE	10 (11%)	5 (4%)	17 (7%)	14 (8%)	18 (18%)
INFLAMMATION, SUPPURATIVE				1 (1%)	
PIGMENTATION, NOS	22 (25%)	27 (22%)	91 (36%)	47 (27%)	39 (39%)
HYPERPLASIA, PLASMA CELL	2 (2%)	3 (2%)	1 (0%)		4 (4%)
HYPERPLASIA, RETICULUM CELL			1 (0%)	3 (2%)	
HYPERPLASIA, LYMPHOID	1 (1%)		1 (0%)		2 (2%)
#CELIAC LYMPH NODE	(87)	(125)	(250)	(175)	(99)
INFLAMMATION, SUPPURATIVE				1 (1%)	
FIBROSIS			1 (0%)		
PIGMENTATION, NOS			1 (0%)		
#PANCREATIC LYMPH NODE	(87)	(125)	(250)	(175)	(99)
HEMORRHAGE			2 (1%)	1 (1%)	
PIGMENTATION, NOS		1 (1%)	19 (8%)	10 (6%)	5 (5%)
HYPERPLASIA, PLASMA CELL		1 (1%)			1 (1%)
HYPERPLASIA, RETICULUM CELL			4 (2%)		1 (1%)
HYPERPLASIA, LYMPHOID					1 (1%)
#MESENTERIC LYMPH NODE	(87)	(125)	(250)	(175)	(99)
HEMORRHAGE			4 (2%)	1 (1%)	3 (3%)
INFLAMMATION, SUPPURATIVE			1 (0%)		
NECROSIS, NOS					1 (1%)
PIGMENTATION, NOS	10 (11%)	1 (1%)	40 (16%)	5 (3%)	4 (4%)
HYPERPLASIA, PLASMA CELL		1 (1%)	2 (1%)		
HYPERPLASIA, RETICULUM CELL	1 (1%)		6 (2%)	1 (1%)	2 (2%)
HYPERPLASIA, LYMPHOID					1 (1%)
#ILEOCOLIC LYMPH NODE	(87)	(125)	(250)	(175)	(99)
HEMORRHAGE					1 (1%)
INFLAMMATION, SUPPURATIVE		1 (1%)	1 (0%)		
HYPERPLASIA, LYMPHOID			1 (0%)		
#RENAL LYMPH NODE	(87)	(125)	(250)	(175)	(99)
PIGMENTATION, NOS			1 (0%)		1 (1%)
HYPERPLASIA, RETICULUM CELL		1 (1%)	1 (0%)		
#ILIAC LYMPH NODE	(87)	(125)	(250)	(175)	(99)
HYPERPLASIA, PLASMA CELL		1 (1%)			
#AXILLARY LYMPH NODE	(87)	(125)	(250)	(175)	(99)
HYPERPLASIA, PLASMA CELL			1 (0%)		
*STERNUM	(88)	(125)	(250)	(175)	(100)
MYELOFIBROSIS		1 (1%)	4 (2%)	1 (1%)	
HYPERPLASIA, HEMATOPOIETIC		1 (1%)			
#LUNG	(87)	(125)	(250)	(175)	(99)
LEUKOCYTOSIS, NOS		2 (2%)			
LEUKOCYTOSIS, NEUTROPHILIC					1 (1%)

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
HEMATOPOIETIC SYSTEM (Continued)					
#ALVEOLAR WALL	(87)	(125)	(250)	(175)	(99)
LEUKOCYTOSIS, NOS			2 (1%)		
#LIVER	(87)	(125)	(250)	(175)	(99)
LEUKOCYTOSIS, NOS			1 (0%)		
LEUKOCYTOSIS, NEUTROPHILIC					1 (1%)
HEMATOPOIESIS	1 (1%)		2 (1%)	1 (1%)	1 (1%)
#HEPATIC SINUSOID	(87)	(125)	(250)	(175)	(99)
LEUKOCYTOSIS, NOS			3 (1%)	1 (1%)	1 (1%)
#PEYERS PATCH	(87)	(125)	(249)	(175)	(99)
HYPERPLASIA, LYMPHOID			1 (0%)		1 (1%)
#ADRENAL	(87)	(124)	(249)	(175)	(99)
HEMATOPOIESIS					1 (1%)
#THYMUS	(70)	(106)	(199)	(146)	(95)
CYST, NOS			1 (1%)		
CONGESTION, NOS					1 (1%)
EDEMA, NOS				1 (1%)	
NECROSIS, NOS			1 (1%)		
CIRCULATORY SYSTEM					
#SPLEEN	(87)	(125)	(249)	(175)	(99)
THROMBUS, FIBRIN				1 (1%)	
#MANDIBULAR LYMPH NODE	(87)	(125)	(250)	(175)	(99)
LYMPHANGIECTASIS	2 (2%)	3 (2%)	5 (2%)	5 (3%)	3 (3%)
#CERVICAL LYMPH NODE	(87)	(125)	(250)	(175)	(99)
LYMPHANGIECTASIS		1 (1%)	1 (0%)		
#MEDIASTINAL LYMPH NODE	(87)	(125)	(250)	(175)	(99)
LYMPHANGIECTASIS	1 (1%)	1 (1%)		1 (1%)	
#CELIAC LYMPH NODE	(87)	(125)	(250)	(175)	(99)
LYMPHANGIECTASIS			2 (1%)		
#MESENTERIC LYMPH NODE	(87)	(125)	(250)	(175)	(99)
LYMPHANGIECTASIS	1 (1%)		4 (2%)	1 (1%)	
#ILEOCOLIC LYMPH NODE	(87)	(125)	(250)	(175)	(99)
LYMPHANGIECTASIS	1 (1%)	1 (1%)	4 (2%)	4 (2%)	5 (5%)
#LUNG	(87)	(125)	(250)	(175)	(99)
THROMBUS, FIBRIN			1 (0%)		
#HEART	(87)	(125)	(250)	(175)	(99)
INFLAMMATION, CHRONIC	1 (1%)		1 (0%)		
#HEART/ATRIUM	(87)	(125)	(250)	(175)	(99)
THROMBUS, ORGANIZED					1 (1%)
#HEART/VENTRICLE	(87)	(125)	(250)	(175)	(99)
FIBROSIS					1 (1%)
#MYOCARDIUM	(87)	(125)	(250)	(175)	(99)
INFLAMMATION, CHRONIC	3 (3%)	1 (1%)	10 (4%)	2 (1%)	2 (2%)
FIBROSIS	34 (39%)	15 (12%)	84 (34%)	9 (5%)	32 (32%)
*CORONARY ARTERY	(88)	(125)	(250)	(175)	(100)
MINERALIZATION					2 (2%)
#LIVER	(87)	(125)	(250)	(175)	(99)
THROMBUS, ORGANIZED			1 (0%)		1 (1%)
THROMBUS, FIBRIN					1 (1%)
PERIARTERITIS		1 (1%)			
#KIDNEY	(87)	(125)	(250)	(175)	(99)
THROMBUS, FIBRIN			1 (0%)		
#UTERUS	(87)	(125)	(249)	(175)	(99)
THROMBUS, FIBRIN			1 (0%)		
#ADRENAL	(87)	(124)	(249)	(175)	(99)
THROMBUS, ORGANIZED			1 (0%)		

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
DIGESTIVE SYSTEM					
*MOUTH	(88)	(125)	(250)	(175)	(100)
ABSCESS, NOS		1 (1%)	1 (0%)		
*MOUTH/ORAL CAVITY	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, SUPPURATIVE			1 (0%)		
#SALIVARY GLAND	(87)	(122)	(248)	(173)	(99)
MINERALIZATION				1 (1%)	
INFLAMMATION, SUPPURATIVE			1 (0%)		
INFLAMMATION, ACUTE				1 (1%)	
INFLAMMATION, CHRONIC			2 (1%)		2 (2%)
ABSCESS, CHRONIC			1 (0%)	1 (1%)	
HYPERPLASIA, EPITHELIAL					1 (1%)
#LIVER	(87)	(125)	(250)	(175)	(99)
HERNIA, NOS					1 (1%)
CYST, NOS	1 (1%)	1 (1%)	1 (0%)	14 (8%)	
HEMORRHAGE	1 (1%)			1 (1%)	
INFLAMMATION, SUPPURATIVE			2 (1%)		
INFLAMMATION, ACUTE	1 (1%)		1 (0%)		2 (2%)
INFLAMMATION, ACUTE/CHRONIC	1 (1%)		1 (0%)		
INFLAMMATION, CHRONIC	3 (3%)	4 (3%)	1 (0%)	10 (6%)	4 (4%)
INFLAMMATION, GRANULOMATOUS	5 (6%)	14 (11%)	31 (12%)	8 (5%)	12 (12%)
FIBROSIS, FOCAL		1 (1%)			
HEPATITIS, TOXIC	15 (17%)	47 (38%)	38 (15%)	58 (33%)	15 (15%)
DEGENERATION, CYSTIC		2 (2%)		5 (3%)	2 (2%)
NECROSIS, NOS			1 (0%)	1 (1%)	
NECROSIS, COAGULATIVE	2 (2%)	8 (6%)	14 (6%)	5 (3%)	5 (5%)
METAMORPHOSIS, FATTY	18 (21%)	13 (10%)	48 (19%)	15 (9%)	22 (22%)
PIGMENTATION, NOS		1 (1%)	12 (5%)	5 (3%)	3 (3%)
FOCAL CELLULAR CHANGE	42 (48%)	57 (46%)	106 (42%)	79 (45%)	59 (60%)
HEPATOCTOMEALY				1 (1%)	
HYPERPLASIA, NOS		7 (6%)	6 (2%)	14 (8%)	
HYPERPLASIA, FOCAL		11 (9%)			
ANGIECTASIS	4 (5%)	4 (3%)	6 (2%)	12 (7%)	5 (5%)
#HEPATIC CAPSULE	(87)	(125)	(250)	(175)	(99)
INFLAMMATION, SUPPURATIVE			1 (0%)		
#LIVER/PERIportal	(87)	(125)	(250)	(175)	(99)
FIBROSIS			4 (2%)	1 (1%)	2 (2%)
#BILE DUCT	(87)	(125)	(250)	(175)	(99)
CYST, NOS				1 (1%)	
HYPERPLASIA, NOS			19 (8%)	12 (7%)	4 (4%)
#PANCREAS	(87)	(124)	(249)	(175)	(99)
INFLAMMATION, CHRONIC				2 (1%)	
ATROPHY, NOS	6 (7%)		15 (6%)	3 (2%)	6 (6%)
#ESOPHAGUS	(86)	(121)	(250)	(173)	(99)
HYPERKERATOSIS					2 (2%)
#STOMACH	(87)	(124)	(250)	(174)	(99)
CYST, NOS	1 (1%)	1 (1%)	1 (0%)		1 (1%)
ULCER, NOS			1 (0%)		
INFLAMMATION, SUPPURATIVE			4 (2%)		
INFLAMMATION, ACUTE		1 (1%)	4 (2%)	2 (1%)	1 (1%)
ULCER, ACUTE	4 (5%)	3 (2%)	12 (5%)	7 (4%)	4 (4%)
INFLAMMATION, ACUTE/CHRONIC	5 (6%)	2 (2%)	23 (9%)	6 (3%)	9 (9%)
INFLAMMATION, CHRONIC	4 (5%)		1 (0%)	4 (2%)	
ULCER, CHRONIC		1 (1%)	6 (2%)	3 (2%)	2 (2%)
INFLAMMATION, CHRONIC FOCAL			1 (0%)		
ULCER, PERFORATED	3 (3%)		7 (3%)		1 (1%)
NECROSIS, NOS				1 (1%)	
NECROSIS, FOCAL			2 (1%)	1 (1%)	1 (1%)
HYPERPLASIA, EPITHELIAL			1 (0%)		
HYPERPLASIA, ADENOMATOUS			1 (0%)		
HYPERKERATOSIS	2 (2%)	3 (2%)	4 (2%)	2 (1%)	5 (5%)
ACANTHOSIS	7 (8%)	2 (2%)	20 (8%)	7 (4%)	10 (10%)

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
DIGESTIVE SYSTEM (Continued)					
#GASTRIC MUCOSA	(87)	(124)	(250)	(174)	(99)
DILATATION, NOS			1 (0%)		
NECROSIS, NOS			1 (0%)		
#GASTRIC SUBMUCOSA	(87)	(124)	(250)	(174)	(99)
EDEMA, NOS	2 (2%)	2 (2%)	13 (5%)	5 (3%)	2 (2%)
EDEMA, INTERSTITIAL			1 (0%)		
#SMALL INTESTINE	(87)	(125)	(249)	(175)	(99)
INFLAMMATION, ACUTE			1 (0%)		
ULCER, ACUTE			1 (0%)		
#SMALL INTESTINAL SUBMUCOSA	(87)	(125)	(249)	(175)	(99)
EDEMA, NOS			1 (0%)		
#PEYER'S PATCH	(87)	(125)	(249)	(175)	(99)
ULCER, ACUTE					1 (1%)
INFLAMMATION, ACUTE/CHRONIC					1 (1%)
HYPERPLASIA, NOS					1 (1%)
HYPERPLASIA, EPITHELIAL					1 (1%)
#COLON	(87)	(125)	(250)	(175)	(99)
INFLAMMATION, ACUTE/CHRONIC				1 (1%)	
INFLAMMATION, CHRONIC		1 (1%)		1 (1%)	
ULCER, CHRONIC				1 (1%)	
PARASITISM		9 (7%)	6 (2%)	5 (3%)	1 (1%)
#COLONIC SUBMUCOSA	(87)	(125)	(250)	(175)	(99)
FIBROSIS, FOCAL			1 (0%)		
#COLONIC SEROSA	(87)	(125)	(250)	(175)	(99)
INFLAMMATION, CHRONIC			1 (0%)		
#CECUM	(87)	(125)	(250)	(175)	(99)
ULCER, NOS		1 (1%)			1 (1%)
INFLAMMATION, SUPPURATIVE			1 (0%)		
INFLAMMATION, ACUTE		1 (1%)			
ULCER, ACUTE			2 (1%)		
INFLAMMATION, ACUTE FOCAL			1 (0%)		
INFLAMMATION, ACUTE/CHRONIC		1 (1%)	1 (0%)		1 (1%)
INFLAMMATION, CHRONIC					2 (2%)
PARASITISM			1 (0%)	1 (1%)	
#ASCENDING COLON	(87)	(125)	(250)	(175)	(99)
PARASITISM				1 (1%)	
#TRANSVERSE COLON	(87)	(125)	(250)	(175)	(99)
DIVERTICULUM				1 (1%)	
INFLAMMATION, CHRONIC				1 (1%)	
PARASITISM		1 (1%)			
ANGIECTASIS			1 (0%)		
#DESCENDING COLON	(87)	(125)	(250)	(175)	(99)
DIVERTICULUM			1 (0%)		
PARASITISM		2 (2%)		1 (1%)	
*ANUS	(88)	(125)	(250)	(175)	(100)
EPIDERMAL INCLUSION CYST	1 (1%)				
URINARY SYSTEM					
#KIDNEY	(87)	(125)	(250)	(175)	(99)
MINERALIZATION	61 (70%)	97 (78%)	194 (78%)	114 (65%)	77 (78%)
CAST, NOS	57 (66%)	51 (41%)	161 (64%)	83 (47%)	65 (66%)
HYDRONEPHROSIS		2 (2%)			2 (2%)
CYST, NOS	1 (1%)	1 (1%)	4 (2%)	1 (1%)	2 (2%)
INFLAMMATION, SUPPURATIVE		1 (1%)			
PYELONEPHRITIS, ACUTE				1 (1%)	
INFLAMMATION, CHRONIC	52 (60%)	25 (20%)	111 (44%)	17 (10%)	36 (36%)
INFLAMMATION, CHRONIC FOCAL				2 (1%)	
NEPHROSIS, NOS				1 (1%)	

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
URINARY SYSTEM					
#KIDNEY (Continued)	(87)	(125)	(250)	(175)	(99)
INFARCT, NOS			1 (0%)		
INFARCT, ACUTE	1 (1%)				
PIGMENTATION, NOS	30 (34%)	13 (10%)	104 (42%)	18 (10%)	11 (11%)
CYTOMEGALY				1 (1%)	
HYPERPLASIA, TUBULAR CELL				2 (1%)	
ANGIECTASIS			1 (0%)		
#URINARY BLADDER	(85)	(125)	(247)	(175)	(98)
HEMORRHAGE			1 (0%)		1 (1%)
INFLAMMATION, ACUTE/CHRONIC				1 (1%)	
INFLAMMATION, GRANULOMATOUS			4 (2%)	1 (1%)	
CRYSTALS, NOS			1 (0%)		
HYPERPLASIA, EPITHELIAL			5 (2%)	1 (1%)	1 (1%)
ENDOCRINE SYSTEM					
#PITUITARY	(87)	(124)	(249)	(173)	(100)
CYST, NOS		6 (5%)	5 (2%)	6 (3%)	3 (3%)
CONGESTION, NOS				1 (1%)	
EDEMA, NOS		1 (1%)			
INFLAMMATION, ACUTE/CHRONIC			1 (0%)		
INFLAMMATION, CHRONIC			1 (0%)		
PIGMENTATION, NOS		1 (1%)	8 (3%)	3 (2%)	
HYPERTROPHY, NOS					1 (1%)
HYPERTROPHY, FOCAL	3 (3%)	2 (2%)	5 (2%)	1 (1%)	2 (2%)
HYPERPLASIA, FOCAL	1 (1%)	2 (2%)	9 (4%)	3 (2%)	2 (2%)
ANGIECTASIS	7 (8%)	9 (7%)	29 (12%)	22 (13%)	8 (8%)
#ADRENAL	(87)	(124)	(249)	(175)	(99)
CONGESTION, NOS	1 (1%)		2 (1%)	3 (2%)	1 (1%)
HEMORRHAGE					1 (1%)
DEGENERATION, NOS	1 (1%)				
DEGENERATION, CYSTIC			1 (0%)		3 (3%)
DEGENERATION, LIPOID		1 (1%)			
PIGMENTATION, NOS				2 (1%)	
ATROPHY, NOS			1 (0%)	1 (1%)	
HYPERTROPHY, FOCAL				1 (1%)	
ANGIECTASIS			5 (2%)		3 (3%)
#ADRENAL/CAPSULE	(87)	(124)	(249)	(175)	(99)
INFLAMMATION, CHRONIC				1 (1%)	
#ADRENAL CORTEX	(87)	(124)	(249)	(175)	(99)
DEGENERATION, NOS				1 (1%)	
DEGENERATION, CYSTIC			4 (2%)		
NECROSIS, NOS			2 (1%)		
METAMORPHOSIS, FATTY	25 (29%)	18 (15%)	79 (32%)	25 (14%)	25 (25%)
HYPERTROPHY, NOS					1 (1%)
HYPERTROPHY, FOCAL	6 (7%)	4 (3%)	4 (2%)	2 (1%)	
HYPERPLASIA, FOCAL		2 (2%)	7 (3%)	2 (1%)	2 (2%)
ANGIECTASIS	1 (1%)	2 (2%)	4 (2%)		
#ADRENAL MEDULLA	(87)	(124)	(249)	(175)	(99)
METAMORPHOSIS, FATTY		2 (2%)			
HYPERPLASIA, NOS	1 (1%)		1 (0%)		1 (1%)
HYPERPLASIA, FOCAL	3 (3%)	5 (4%)	11 (4%)	3 (2%)	7 (7%)
#THYROID	(87)	(124)	(248)	(174)	(100)
CYST, NOS				1 (1%)	
CYSTIC FOLLICLES	2 (2%)	5 (4%)	13 (5%)	6 (3%)	1 (1%)
INFLAMMATION, CHRONIC FOCAL			1 (0%)		
HYPERPLASIA, NOS		1 (1%)			
HYPERPLASIA, C-CELL	24 (28%)	42 (34%)	53 (21%)	31 (18%)	24 (24%)
HYPERPLASIA, FOLLICULAR-CELL					1 (1%)

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
ENDOCRINE SYSTEM (Continued)					
#PARATHYROID	(73)	(119)	(235)	(164)	(97)
HYPERPLASIA, NOS	4 (5%)		10 (4%)	1 (1%)	8 (8%)
#PANCREATIC ISLETS	(87)	(124)	(249)	(175)	(99)
HYPERPLASIA, NOS	1 (1%)		1 (0%)	1 (1%)	
REPRODUCTIVE SYSTEM					
*MAMMARY GLAND	(88)	(125)	(250)	(175)	(100)
DILATATION/DUCTS	9 (10%)	1 (1%)			5 (5%)
GALACTOCELE	22 (25%)	19 (15%)	91 (36%)	20 (11%)	36 (36%)
CYST, NOS			1 (0%)		
CYSTIC DUCTS	1 (1%)				
HYPERPLASIA, NOS	1 (1%)	4 (3%)	5 (2%)	7 (4%)	1 (1%)
*PREPUTIAL GLAND	(88)	(125)	(250)	(175)	(100)
DILATATION/DUCTS			1 (0%)		
*CLITORAL GLAND	(88)	(125)	(250)	(175)	(100)
DILATATION/DUCTS	1 (1%)		2 (1%)	1 (1%)	2 (2%)
INFLAMMATION, SUPPURATIVE		1 (1%)	1 (0%)		
ABCESS, NOS			2 (1%)		1 (1%)
INFLAMMATION, ACUTE/CHRONIC		1 (1%)			
HYPERPLASIA, EPITHELIAL			1 (0%)		
HYPERKERATOSIS					1 (1%)
*VAGINA	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, ACUTE				1 (1%)	
INFLAMMATION, ACUTE/CHRONIC					1 (1%)
HYPERPLASIA, STROMAL				1 (1%)	
#UTERUS	(87)	(125)	(249)	(175)	(99)
HYDROMETRA		2 (2%)	8 (3%)	7 (4%)	4 (4%)
CYST, NOS	1 (1%)				
STEATITIS		1 (1%)			
INFLAMMATION, SUPPURATIVE			1 (0%)	1 (1%)	1 (1%)
PYOMETRA			1 (0%)		
INFLAMMATION, ACUTE	3 (3%)			1 (1%)	
INFLAMMATION, ACUTE/CHRONIC		1 (1%)			1 (1%)
NECROSIS, FAT		1 (1%)			
HEMOSIDEROSIS			1 (0%)		
#CERVIX UTERI	(87)	(125)	(249)	(175)	(99)
CYST, NOS			1 (0%)	1 (1%)	
INFLAMMATION, SUPPURATIVE			1 (0%)		
INFLAMMATION, ACUTE/CHRONIC					1 (1%)
INFLAMMATION, GRANULO-					
MATOUS		1 (1%)			
HYPERPLASIA, EPITHELIAL			1 (0%)		
HYPERPLASIA, STROMAL		3 (2%)	3 (1%)	3 (2%)	
#UTERUS/ENDOMETRIUM	(87)	(125)	(249)	(175)	(99)
CYST, NOS		5 (4%)	5 (2%)	7 (4%)	
HYPERPLASIA, NOS	1 (1%)	2 (2%)	2 (1%)	4 (2%)	
HYPERPLASIA, CYSTIC	4 (5%)	4 (3%)	4 (2%)	2 (1%)	
#OVARY/PAROVARIAN	(87)	(125)	(249)	(174)	(99)
STEATITIS		1 (1%)			
#OVARY	(87)	(125)	(249)	(174)	(99)
MINERALIZATION			1 (0%)		
CYST, NOS		1 (1%)	10 (4%)	2 (1%)	4 (4%)
PAROVARIAN CYST	4 (5%)	2 (2%)	11 (4%)	10 (6%)	4 (4%)
INFLAMMATION, SUPPURATIVE			1 (0%)	1 (1%)	

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
NERVOUS SYSTEM					
#BRAIN/MENINGES	(87)	(125)	(250)	(175)	(100)
INFLAMMATION, ACUTE/CHRONIC			1 (0%)		
#CEREBRAL VENTRICLE	(87)	(125)	(250)	(175)	(100)
DILATATION, NOS	4 (5%)	1 (1%)	9 (4%)	2 (1%)	10 (10%)
#BRAIN	(87)	(125)	(250)	(175)	(100)
HEMORRHAGE		1 (1%)	1 (0%)		1 (1%)
SPECIAL SENSE ORGANS					
*EYE	(88)	(125)	(250)	(175)	(100)
HEMORRHAGE	1 (1%)	1 (1%)	1 (0%)		
INFLAMMATION, SUPPURATIVE		1 (1%)	1 (0%)		
INFLAMMATION, CHRONIC	1 (1%)		4 (2%)		
CATARACT	30 (34%)	3 (2%)	73 (29%)	28 (16%)	26 (26%)
*EYE/RETINA	(88)	(125)	(250)	(175)	(100)
DEGENERATION, NOS	30 (34%)	4 (3%)	72 (29%)	30 (17%)	27 (27%)
*HARDERIAN GLAND	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, GRANULOMATOUS				1 (1%)	
ATROPHY, NOS			1 (0%)		
*EAR	(88)	(125)	(250)	(175)	(100)
CYST, NOS			1 (0%)		
*ZYMBALE GLAND	(88)	(125)	(250)	(175)	(100)
DILATATION/DUCTS	1 (1%)	2 (2%)		1 (1%)	2 (2%)
INFLAMMATION, ACUTE		1 (1%)			
ABSCESS, CHRONIC				2 (1%)	
HYPERKERATOSIS		5 (4%)		2 (1%)	2 (2%)
MUSCULOSKELETAL SYSTEM					
*SKULL	(88)	(125)	(250)	(175)	(100)
HYPEROSTOSIS	2 (2%)	1 (1%)	5 (2%)	2 (1%)	6 (6%)
*STERNUM	(88)	(125)	(250)	(175)	(100)
CHONDRODYSSTROPHY			1 (0%)		
OSTEOCHONDRODYSSTROPHY				1 (1%)	
HYPEROSTOSIS	2 (2%)	8 (6%)	20 (8%)	12 (7%)	6 (6%)
*RIB	(88)	(125)	(250)	(175)	(100)
CHONDRODYSSTROPHY			1 (0%)		
*SKELETAL MUSCLE	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, CHRONIC FOCAL	1 (1%)				
BODY CAVITIES					
*MEDIASTINUM	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, CHRONIC			1 (0%)		
*ABDOMINAL CAVITY	(88)	(125)	(250)	(175)	(100)
STEATITIS	1 (1%)	1 (1%)	4 (2%)	2 (1%)	
NECROSIS, FAT	1 (1%)		1 (0%)	1 (1%)	
*PLEURA	(88)	(125)	(250)	(175)	(100)
FIBROSIS, FOCAL					1 (1%)
*PERICARDIUM	(88)	(125)	(250)	(175)	(100)
INFLAMMATION, SUPPURATIVE			1 (0%)		
INFLAMMATION, FIBRINOUS			1 (0%)		
*MESENTERY	(88)	(125)	(250)	(175)	(100)
CONGESTION, NOS				1 (1%)	
INFLAMMATION, ACUTE/CHRONIC		1 (1%)			
INFLAMMATION, CHRONIC		1 (1%)			2 (2%)
NECROSIS, FAT		2 (2%)		2 (1%)	1 (1%)

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR/PW
ALL OTHER SYSTEMS					
*MULTIPLE ORGANS	(88)	(125)	(250)	(175)	(100)
CONGESTION, NOS		1 (1%)			
INFLAMMATION, SUPPURATIVE			1 (0%)		
INFLAMMATION, CHRONIC			1 (0%)		
PIGMENTATION, NOS			1 (0%)		
DIAPHRAGM					
HERNIA, NOS	3	3	6	3	
ADIPOSE TISSUE					
INFLAMMATION, CHRONIC			1	3	
NECROSIS, FAT		1		1	
BROAD LIGAMENT					
FIBROSIS	1				
SPECIAL MORPHOLOGY SUMMARY					
NECROPSY PERF/NO HISTO PERFORMED		1			
AUTO/NECROPSY/HISTO PERF			1		1

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

* NUMBER OF ANIMALS NECROPSIED

APPENDIX E

ANALYSES OF PRIMARY TUMORS IN RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE AND INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS AND INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS

	CONTROL (UNTR)	SHORT RANGE (a)
Skin: Keratoacanthoma		
Overall Rates (b)	5/88 (6%)	14/250 (6%)
Adjusted Rates (c)	23.1%	16.8%
Terminal Rates (d)	3/15 (20%)	0/38 (0%)
Life Table Test (e)		P=0.592N
Incidental Tumor Test (e)		P=0.602
Fisher Exact Test (e)		P=0.580N
Subcutaneous Tissue: Fibroma		
Overall Rates (b)	13/88 (15%)	25/250 (10%)
Adjusted Rates (c)	37.9%	26.8%
Terminal Rates (d)	2/15 (13%)	4/38 (11%)
Life Table Test (e)		P=0.185N
Incidental Tumor Test (e)		P=0.133N
Fisher Exact Test (e)		P=0.154N
Subcutaneous Tissue: Fibroma or Fibrosarcoma		
Overall Rates (b)	16/88 (18%)	30/250 (12%)
Adjusted Rates (c)	43.3%	30.0%
Terminal Rates (d)	2/15 (13%)	4/38 (11%)
Life Table Test (e)		P=0.138N
Incidental Tumor Test (e)		P=0.081N
Fisher Exact Test (e)		P=0.104N
Integumentary System: Basal Cell Tumor or Carcinoma		
Overall Rates (b)	3/88 (3%)	16/250 (6%)
Adjusted Rates (c)	7.0%	22.3%
Terminal Rates (d)	0/15 (0%)	4/38 (11%)
Life Table Test (e)		P=0.227
Incidental Tumor Test (e)		P=0.232
Fisher Exact Test (e)		P=0.223
Hematopoietic System: Leukemia		
Overall Rates (b)	37/88 (42%)	109/250 (44%)
Adjusted Rates (c)	71.8%	78.7%
Terminal Rates (d)	6/15 (40%)	19/38 (50%)
Life Table Test (e)		P=0.401
Incidental Tumor Test (e)		P=0.544N
Fisher Exact Test (e)		P=0.450
Liver: Neoplastic Nodule		
Overall Rates (b)	12/88 (14%)	17/248 (7%)
Adjusted Rates (c)	39.7%	21.1%
Terminal Rates (d)	4/15 (27%)	3/38 (8%)
Life Table Test (e)		P=0.056N
Incidental Tumor Test (e)		P=0.031N
Fisher Exact Test (e)		P=0.046N
Liver: Neoplastic Nodule or Hepatocellular Carcinoma		
Overall Rates (b)	15/88 (17%)	19/248 (8%)
Adjusted Rates (c)	47.9%	23.8%
Terminal Rates (d)	4/15 (27%)	4/38 (11%)
Life Table Test (e)		P=0.018N
Incidental Tumor Test (e)		P=0.007N
Fisher Exact Test (e)		P=0.013N
Pancreas: Acinar Cell Adenoma		
Overall Rates (b)	7/86 (8%)	14/247 (6%)
Adjusted Rates (c)	22.7%	19.6%
Terminal Rates (d)	1/15 (7%)	4/38 (11%)
Life Table Test (e)		P=0.362N
Incidental Tumor Test (e)		P=0.258N
Fisher Exact Test (e)		P=0.282N

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE (a)
Pituitary: Adenoma		
Overall Rates (b)	20/87 (23%)	42/247 (17%)
Adjusted Rates (c)	54.3%	40.8%
Terminal Rates (d)	4/15 (27%)	5/38 (13%)
Life Table Test (e)		P=0.182N
Incidental Tumor Test (e)		P=0.118N
Fisher Exact Test (e)		P=0.142N
Pituitary: Adenoma or Carcinoma		
Overall Rates (b)	21/87 (24%)	45/247 (18%)
Adjusted Rates (c)	58.4%	42.3%
Terminal Rates (d)	5/15 (33%)	5/38 (13%)
Life Table Test (e)		P=0.196N
Incidental Tumor Test (e)		P=0.124N
Fisher Exact Test (e)		P=0.151N
Adrenal: Pheochromocytoma		
Overall Rates (b)	25/88 (28%)	73/248 (29%)
Adjusted Rates (c)	67.1%	70.0%
Terminal Rates (d)	6/15 (40%)	17/38 (45%)
Life Table Test (e)		P=0.437
Incidental Tumor Test (e)		P=0.500
Fisher Exact Test (e)		P=0.485
Adrenal: Pheochromocytoma or Pheochromocytoma, Malignant		
Overall Rates (b)	26/88 (30%)	78/248 (31%)
Adjusted Rates (c)	67.8%	74.7%
Terminal Rates (d)	6/15 (40%)	20/38 (53%)
Life Table Test (e)		P=0.376
Incidental Tumor Test (e)		P=0.443
Fisher Exact Test (e)		P=0.425
Thyroid: Follicular Cell Adenoma		
Overall Rates (b)	4/86 (5%)	13/246 (5%)
Adjusted Rates (c)	13.5%	14.4%
Terminal Rates (d)	1/15 (7%)	3/38 (8%)
Life Table Test (e)		P=0.505
Incidental Tumor Test (e)		P=0.458
Fisher Exact Test (e)		P=0.538
Thyroid: Follicular Cell Adenoma or Carcinoma		
Overall Rates (b)	6/86 (7%)	25/246 (10%)
Adjusted Rates (c)	16.6%	24.3%
Terminal Rates (d)	1/15 (7%)	4/38 (11%)
Life Table Test (e)		P=0.237
Incidental Tumor Test (e)		P=0.234
Fisher Exact Test (e)		P=0.261
Thyroid: C-Cell Adenoma		
Overall Rates (b)	13/86 (15%)	28/246 (11%)
Adjusted Rates (c)	35.8%	32.1%
Terminal Rates (d)	2/15 (13%)	6/38 (16%)
Life Table Test (e)		P=0.274N
Incidental Tumor Test (e)		P=0.198N
Fisher Exact Test (e)		P=0.234N
Thyroid: C-Cell Carcinoma		
Overall Rates (b)	11/86 (13%)	24/246 (10%)
Adjusted Rates (c)	36.2%	26.2%
Terminal Rates (d)	3/15 (20%)	5/38 (13%)
Life Table Test (e)		P=0.321N
Incidental Tumor Test (e)		P=0.251N
Fisher Exact Test (e)		P=0.274N

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE (a)
Thyroid: C-Cell Adenoma or Carcinoma		
Overall Rates (b)	24/86 (28%)	52/246 (21%)
Adjusted Rates (c)	60.8%	51.4%
Terminal Rates (d)	5/15 (33%)	11/38 (29%)
Life Table Test (e)		P=0.182N
Incidental Tumor Test (e)		P=0.094N
Fisher Exact Test (e)		P=0.129N
Parathyroid: Adenoma		
Overall Rates (b)	6/83 (7%)	4/229 (2%)
Adjusted Rates (c)	22.8%	7.8%
Terminal Rates (d)	1/15 (7%)	2/36 (6%)
Life Table Test (e)		P=0.024N
Incidental Tumor Test (e)		P=0.023N
Fisher Exact Test (e)		P=0.025N
Pancreatic Islets: Islet Cell Adenoma		
Overall Rates (b)	6/86 (7%)	18/247 (7%)
Adjusted Rates (c)	19.5%	21.5%
Terminal Rates (d)	1/15 (7%)	3/38 (8%)
Life Table Test (e)		P=0.525
Incidental Tumor Test (e)		P=0.583
Fisher Exact Test (e)		P=0.571
Pancreatic Islets: Islet Cell Carcinoma		
Overall Rates (b)	3/86 (3%)	14/247 (6%)
Adjusted Rates (c)	16.1%	18.7%
Terminal Rates (d)	2/15 (13%)	3/38 (8%)
Life Table Test (e)		P=0.298
Incidental Tumor Test (e)		P=0.277
Fisher Exact Test (e)		P=0.318
Pancreatic Islets: Islet Cell Adenoma or Carcinoma		
Overall Rates (b)	9/86 (10%)	30/247 (12%)
Adjusted Rates (c)	33.3%	35.4%
Terminal Rates (d)	3/15 (20%)	6/38 (16%)
Life Table Test (e)		P=0.376
Incidental Tumor Test (e)		P=0.403
Fisher Exact Test (e)		P=0.421
Mammary Gland: Fibroadenoma		
Overall Rates (b)	11/88 (13%)	27/250 (11%)
Adjusted Rates (c)	46.2%	37.5%
Terminal Rates (d)	5/15 (33%)	7/38 (18%)
Life Table Test (e)		P=0.468N
Incidental Tumor Test (e)		P=0.401N
Fisher Exact Test (e)		P=0.397N
Preputial Gland: Carcinoma		
Overall Rates (b)	6/88 (7%)	13/250 (5%)
Adjusted Rates (c)	20.3%	12.8%
Terminal Rates (d)	2/15 (13%)	2/38 (5%)
Life Table Test (e)		P=0.421N
Incidental Tumor Test (e)		P=0.373N
Fisher Exact Test (e)		P=0.370N
Preputial Gland: Adenoma or Carcinoma		
Overall Rates (b)	6/88 (7%)	14/250 (6%)
Adjusted Rates (c)	20.3%	14.2%
Terminal Rates (d)	2/15 (13%)	2/38 (5%)
Life Table Test (e)		P=0.467N
Incidental Tumor Test (e)		P=0.432N
Fisher Exact Test (e)		P=0.425N

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE (a)
Testis: Interstitial Cell Tumor		
Overall Rates (b)	81/87 (93%)	238/246 (97%)
Adjusted Rates (c)	100.0%	100.0%
Terminal Rates (d)	15/15 (100%)	38/38 (100%)
Life Table Test (e)		P=0.336
Incidental Tumor Test (e)		P=0.590
Fisher Exact Test (e)		P=0.128
Testis: Interstitial Cell Tumor or Interstitial Cell Tumor, Malignant		
Overall Rates (b)	81/87 (93%)	239/246 (97%)
Adjusted Rates (c)	100.0%	100.0%
Terminal Rates (d)	15/15 (100%)	38/38 (100%)
Life Table Test (e)		P=0.324
Incidental Tumor Test (e)		P=0.512
Fisher Exact Test (e)		P=0.092
Zymbal Gland: Squamous Cell Papilloma or Carcinoma		
Overall Rates (b)	5/88 (6%)	5/250 (2%)
Adjusted Rates (c)	13.6%	5.8%
Terminal Rates (d)	1/15 (7%)	1/38 (3%)
Life Table Test (e)		P=0.101N
Incidental Tumor Test (e)		P=0.085N
Fisher Exact Test (e)		P=0.088N
Tunica Vaginalis: Mesothelioma, Malignant		
Overall Rates (b)	2/88 (2%)	14/250 (6%)
Adjusted Rates (c)	3.4%	9.6%
Terminal Rates (d)	0/15 (0%)	0/38 (0%)
Life Table Test (e)		P=0.172
Incidental Tumor Test (e)		P=0.191
Fisher Exact Test (e)		P=0.166
All Sites: Mesothelioma, Malignant		
Overall Rates (b)	2/88 (2%)	15/250 (6%)
Adjusted Rates (c)	3.4%	10.1%
Terminal Rates (d)	0/15 (0%)	0/38 (0%)
Life Table Test (e)		P=0.145
Incidental Tumor Test (e)		P=0.161
Fisher Exact Test (e)		P=0.135

(a) Administered 1% short-range chrysotile asbestos in the diet

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

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

(d) Observed tumor incidence at terminal kill

(e) Beneath the dosed group incidence is the P value corresponding to the pairwise comparison between the dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in the dosed group is indicated by (N).

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS

	CONTROL (UNTR)	SHORT RANGE (a)
Hematopoietic System: Leukemia		
Overall Rates (b)	28/88 (32%)	101/250 (40%)
Adjusted Rates (c)	68.3%	74.7%
Terminal Rates (d)	3/9 (33%)	10/26 (38%)
Life Table Test (e)		P=0.155
Incidental Tumor Test (e)		P=0.069
Fisher Exact Test (e)		P=0.097
Pituitary: Adenoma		
Overall Rates (b)	39/87 (45%)	101/244 (41%)
Adjusted Rates (c)	89.5%	80.1%
Terminal Rates (d)	6/9 (67%)	13/26 (50%)
Life Table Test (e)		P=0.368N
Incidental Tumor Test (e)		P=0.335N
Fisher Exact Test (e)		P=0.333N
Pituitary: Carcinoma		
Overall Rates (b)	6/87 (7%)	13/244 (5%)
Adjusted Rates (c)	22.6%	10.3%
Terminal Rates (d)	1/9 (11%)	0/26 (0%)
Life Table Test (e)		P=0.362N
Incidental Tumor Test (e)		P=0.439N
Fisher Exact Test (e)		P=0.380N
Pituitary: Adenoma or Carcinoma		
Overall Rates (b)	45/87 (52%)	114/244 (47%)
Adjusted Rates (c)	93.9%	82.2%
Terminal Rates (d)	7/9 (78%)	13/26 (50%)
Life Table Test (e)		P=0.295N
Incidental Tumor Test (e)		P=0.268N
Fisher Exact Test (e)		P=0.249N
Adrenal: Pheochromocytoma		
Overall Rates (b)	9/87 (10%)	38/245 (16%)
Adjusted Rates (c)	38.2%	51.8%
Terminal Rates (d)	2/9 (22%)	7/26 (27%)
Life Table Test (e)		P=0.170
Incidental Tumor Test (e)		P=0.206
Fisher Exact Test (e)		P=0.156
Adrenal: Pheochromocytoma or Pheochromocytoma, Malignant		
Overall Rates (b)	9/87 (10%)	39/245 (16%)
Adjusted Rates (c)	38.2%	52.2%
Terminal Rates (d)	2/9 (22%)	7/26 (27%)
Life Table Test (e)		P=0.153
Incidental Tumor Test (e)		P=0.175
Fisher Exact Test (e)		P=0.136
Thyroid: Follicular Cell Adenoma or Carcinoma		
Overall Rates (b)	5/87 (6%)	12/244 (5%)
Adjusted Rates (c)	38.1%	18.5%
Terminal Rates (d)	3/9 (33%)	2/26 (8%)
Life Table Test (e)		P=0.494N
Incidental Tumor Test (e)		P=0.465N
Fisher Exact Test (e)		P=0.476N
Thyroid: C-Cell Adenoma		
Overall Rates (b)	11/87 (13%)	20/244 (8%)
Adjusted Rates (c)	41.0%	23.9%
Terminal Rates (d)	1/9 (11%)	2/26 (8%)
Life Table Test (e)		P=0.170N
Incidental Tumor Test (e)		P=0.154N
Fisher Exact Test (e)		P=0.157N

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	SHORT RANGE (a)
Thyroid: C-Cell Carcinoma		
Overall Rates (b)	7/87 (8%)	21/244 (9%)
Adjusted Rates (c)	33.3%	30.1%
Terminal Rates (d)	1/9 (11%)	4/26 (15%)
Life Table Test (e)		P=0.522
Incidental Tumor Test (e)		P=0.555
Fisher Exact Test (e)		P=0.537
Thyroid: C-Cell Adenoma or Carcinoma		
Overall Rates (b)	17/87 (20%)	40/244 (16%)
Adjusted Rates (c)	57.7%	47.4%
Terminal Rates (d)	2/9 (22%)	6/26 (23%)
Life Table Test (e)		P=0.319N
Incidental Tumor Test (e)		P=0.289N
Fisher Exact Test (e)		P=0.304N
Mammary Gland: Adenoma		
Overall Rates (b)	2/88 (2%)	14/250 (6%)
Adjusted Rates (c)	10.0%	21.9%
Terminal Rates (d)	0/9 (0%)	2/26 (8%)
Life Table Test (e)		P=0.175
Incidental Tumor Test (e)		P=0.161
Fisher Exact Test (e)		P=0.166
Mammary Gland: Fibroadenoma		
Overall Rates (b)	49/88 (56%)	146/250 (58%)
Adjusted Rates (c)	97.1%	96.4%
Terminal Rates (d)	8/9 (89%)	22/26 (85%)
Life Table Test (e)		P=0.399
Incidental Tumor Test (e)		P=0.353
Fisher Exact Test (e)		P=0.374
Mammary Gland: Adenocarcinoma		
Overall Rates (b)	6/88 (7%)	19/250 (8%)
Adjusted Rates (c)	40.8%	27.4%
Terminal Rates (d)	2/9 (22%)	3/26 (12%)
Life Table Test (e)		P=0.488
Incidental Tumor Test (e)		P=0.562
Fisher Exact Test (e)		P=0.511
Clitoral Gland: Carcinoma		
Overall Rates (b)	2/88 (2%)	17/250 (7%)
Adjusted Rates (c)	8.2%	22.2%
Terminal Rates (d)	0/9 (0%)	3/26 (12%)
Life Table Test (e)		P=0.101
Incidental Tumor Test (e)		P=0.085
Fisher Exact Test (e)		P=0.087
Clitoral Gland: Papilloma, Adenoma or Carcinoma		
Overall Rates (b)	3/88 (3%)	19/250 (8%)
Adjusted Rates (c)	10.5%	23.2%
Terminal Rates (d)	0/9 (0%)	3/26 (12%)
Life Table Test (e)		P=0.144
Incidental Tumor Test (e)		P=0.102
Fisher Exact Test (e)		P=0.129
Uterus: Endometrial Stromal Polyp		
Overall Rates (b)	15/87 (17%)	34/245 (14%)
Adjusted Rates (c)	49.1%	43.8%
Terminal Rates (d)	2/9 (22%)	4/26 (15%)
Life Table Test (e)		P=0.321N
Incidental Tumor Test (e)		P=0.256N
Fisher Exact Test (e)		P=0.276N

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS (Continued)

- (a) Administered 1% short-range chrysotile asbestos in the diet
- (b) Number of tumor-bearing animals/number of animals examined at the site
- (c) Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality
- (d) Observed tumor incidence at terminal kill
- (e) Beneath the dosed group incidence is the P value corresponding to the pairwise comparison between the dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in the dosed group is indicated by (N).

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

	CONTROL (UNTR)	IR (a)	IR/PW	IR vs IR/PW
Skin: Papilloma or Squamous Cell Papilloma				
Overall Rates (b)	5/88 (6%)	8/250 (3%)	3/100 (3%)	
Adjusted Rates (c)	46.1%	12.2%	14.0%	
Terminal Rates (d)	3/7 (43%)	0/29 (0%)	1/11 (9%)	
Life Table Test (e)		P=0.159N	P=0.224N	P=0.617
Incidental Tumor Test (e)		P=0.225N	P=0.326N	P=0.622N
Fisher Exact Test (e)		P=0.230N	P=0.292N	P=0.612N
Integumentary System: Keratoacanthoma				
Overall Rates (b)	1/88 (1%)	19/250 (8%)	8/100 (8%)	
Adjusted Rates (c)	3.2%	23.9%	32.7%	
Terminal Rates (d)	0/7 (0%)	3/29 (10%)	3/11 (27%)	
Life Table Test (e)		P=0.039	P=0.048	P=0.506
Incidental Tumor Test (e)		P=0.027	P=0.026	P=0.512
Fisher Exact Test (e)		P=0.017	P=0.027	P=0.527
Integumentary System: Fibroma				
Overall Rates (b)	17/88 (19%)	51/250 (20%)	12/100 (12%)	
Adjusted Rates (c)	45.2%	61.4%	49.2%	
Terminal Rates (d)	1/7 (14%)	10/29 (34%)	3/11 (27%)	
Life Table Test (e)		P=0.485N	P=0.103N	P=0.083N
Incidental Tumor Test (e)		P=0.465	P=0.156N	P=0.057N
Fisher Exact Test (e)		P=0.480	P=0.119N	P=0.042N
Integumentary System: Fibrosarcoma				
Overall Rates (b)	7/88 (8%)	6/250 (2%)	1/100 (1%)	
Adjusted Rates (c)	21.5%	5.2%	3.8%	
Terminal Rates (d)	0/7 (0%)	0/29 (0%)	0/11 (0%)	
Life Table Test (e)		P=0.021N	P=0.024N	P=0.373N
Incidental Tumor Test (e)		P=0.024N	P=0.017N	P=0.411N
Fisher Exact Test (e)		P=0.028N	P=0.021N	P=0.358N
Subcutaneous Tissue: Sarcoma				
Overall Rates (b)	1/88 (1%)	3/250 (1%)	5/100 (5%)	
Adjusted Rates (c)	1.3%	5.4%	21.3%	
Terminal Rates (d)	0/7 (0%)	1/29 (3%)	1/11 (9%)	
Life Table Test (e)		P=0.706N	P=0.164	P=0.034
Incidental Tumor Test (e)		P=0.688	P=0.117	P=0.032
Fisher Exact Test (e)		P=0.721	P=0.138	P=0.046
Integumentary System: Fibroma, Fibrosarcoma, or Sarcoma				
Overall Rates (b)	24/88 (27%)	59/250 (24%)	17/100 (17%)	
Adjusted Rates (c)	56.6%	65.9%	61.7%	
Terminal Rates (d)	1/7 (14%)	11/29 (38%)	4/11 (36%)	
Life Table Test (e)		P=0.186N	P=0.058N	P=0.191N
Incidental Tumor Test (e)		P=0.302N	P=0.086N	P=0.157N
Fisher Exact Test (e)		P=0.291N	P=0.064N	P=0.113N
Hematopoietic System: Leukemia				
Overall Rates (b)	31/88 (35%)	96/250 (38%)	37/100 (37%)	
Adjusted Rates (c)	67.8%	72.9%	72.9%	
Terminal Rates (d)	1/7 (14%)	11/29 (38%)	4/11 (36%)	
Life Table Test (e)		P=0.506	P=0.520	P=0.529N
Incidental Tumor Test (e)		P=0.309	P=0.356	P=0.508N
Fisher Exact Test (e)		P=0.346	P=0.460	P=0.453N
Liver: Neoplastic Nodule				
Overall Rates (b)	6/85 (7%)	13/250 (5%)	5/100 (5%)	
Adjusted Rates (c)	23.1%	17.9%	10.4%	
Terminal Rates (d)	0/7 (0%)	2/29 (7%)	0/11 (0%)	
Life Table Test (e)		P=0.321N	P=0.407N	P=0.592N
Incidental Tumor Test (e)		P=0.362N	P=0.377N	P=0.571N
Fisher Exact Test (e)		P=0.344N	P=0.389N	P=0.589N

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	IR (a)	IR/PW	IR vs IR/PW
Liver: Neoplastic Nodule or Hepatocellular Carcinoma				
Overall Rates (b)	8/85 (9%)	19/250 (8%)	6/100 (6%)	
Adjusted Rates (c)	27.9%	28.9%	11.5%	
Terminal Rates (d)	0/7 (0%)	5/29 (17%)	0/11 (0%)	
Life Table Test (e)		P=0.321N	P=0.300N	P=0.408N
Incidental Tumor Test (e)		P=0.391N	P=0.277N	P=0.387N
Fisher Exact Test (e)		P=0.372N	P=0.275N	P=0.395N
Pancreas: Acinar Cell Adenoma				
Overall Rates (b)	3/85 (4%)	23/249 (9%)	9/99 (9%)	
Adjusted Rates (c)	19.5%	38.5%	26.8%	
Terminal Rates (d)	0/7 (0%)	7/29 (24%)	1/11 (9%)	
Life Table Test (e)		P=0.113	P=0.108	P=0.564
Incidental Tumor Test (e)		P=0.066	P=0.102	P=0.578
Fisher Exact Test (e)		P=0.065	P=0.109	P=0.574N
Large Intestine: Adenomatous Polyp				
Overall Rates (b)	0/85 (0%)	9/250 (4%)	2/100 (2%)	
Adjusted Rates (c)	0.0%	10.2%	7.4%	
Terminal Rates (d)	0/7 (0%)	1/29 (3%)	0/11 (0%)	
Life Table Test (e)		P=0.088	P=0.315	P=0.343N
Incidental Tumor Test (e)		P=0.084	P=0.235	P=0.385N
Fisher Exact Test (e)		P=0.069	P=0.291	P=0.348N
Pituitary: Adenoma				
Overall Rates (b)	14/85 (16%)	49/246 (20%)	18/100 (18%)	
Adjusted Rates (c)	39.1%	50.3%	47.8%	
Terminal Rates (d)	0/7 (0%)	5/29 (17%)	3/11 (27%)	
Life Table Test (e)		P=0.398	P=0.435	P=0.531N
Incidental Tumor Test (e)		P=0.284	P=0.415	P=0.458N
Fisher Exact Test (e)		P=0.299	P=0.470	P=0.403N
Pituitary: Adenoma or Carcinoma				
Overall Rates (b)	18/85 (21%)	52/246 (21%)	19/100 (19%)	
Adjusted Rates (c)	43.7%	52.0%	48.8%	
Terminal Rates (d)	0/7 (0%)	5/29 (17%)	3/11 (27%)	
Life Table Test (e)		P=0.461N	P=0.470N	P=0.523N
Incidental Tumor Test (e)		P=0.552	P=0.479N	P=0.438N
Fisher Exact Test (e)		P=0.553N	P=0.426N	P=0.387N
Adrenal: Pheochromocytoma				
Overall Rates (b)	16/85 (19%)	59/250 (24%)	32/100 (32%)	
Adjusted Rates (c)	61.5%	60.6%	87.2%	
Terminal Rates (d)	2/7 (29%)	8/29 (28%)	8/11 (73%)	
Life Table Test (e)		P=0.322	P=0.058	P=0.051
Incidental Tumor Test (e)		P=0.189	P=0.014	P=0.045
Fisher Exact Test (e)		P=0.225	P=0.030	P=0.070
Adrenal: Pheochromocytoma or Pheochromocytoma, Malignant				
Overall Rates (b)	17/85 (20%)	63/250 (25%)	32/100 (32%)	
Adjusted Rates (c)	62.7%	64.7%	87.2%	
Terminal Rates (d)	2/7 (29%)	10/29 (28%)	8/11 (73%)	
Life Table Test (e)		P=0.310	P=0.082	P=0.089
Incidental Tumor Test (e)		P=0.170	P=0.023	P=0.083
Fisher Exact Test (e)		P=0.206	P=0.046	P=0.124
Thyroid: Follicular Cell Carcinoma				
Overall Rates (b)	5/84 (6%)	13/250 (5%)	2/99 (2%)	
Adjusted Rates (c)	19.8%	17.8%	12.6%	
Terminal Rates (d)	0/7 (0%)	2/29 (7%)	1/11 (9%)	
Life Table Test (e)		P=0.468N	P=0.161N	P=0.201N
Incidental Tumor Test (e)		P=0.532N	P=0.191N	P=0.155N
Fisher Exact Test (e)		P=0.489N	P=0.160N	P=0.151N

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	IR (a)	IR/PW	IR vs IR/PW
Thyroid: Follicular Cell Adenoma or Carcinoma				
Overall Rates (b)	6/84 (7%)	25/250 (10%)	5/99 (5%)	
Adjusted Rates (c)	21.5%	31.6%	21.8%	
Terminal Rates (d)	0/7 (0%)	3/29 (10%)	1/11 (9%)	
Life Table Test (e)		P=0.329	P=0.365N	P=0.150N
Incidental Tumor Test (e)		P=0.270	P=0.429N	P=0.108N
Fisher Exact Test (e)		P=0.294	P=0.387N	P=0.098N
Thyroid: C-Cell Adenoma				
Overall Rates (b)	13/84 (15%)	29/250 (12%)	9/99 (9%)	
Adjusted Rates (c)	44.6%	38.6%	34.5%	
Terminal Rates (d)	1/7 (14%)	6/29 (21%)	3/11 (27%)	
Life Table Test (e)		P=0.196N	P=0.144N	P=0.364N
Incidental Tumor Test (e)		P=0.260N	P=0.153N	P=0.300N
Fisher Exact Test (e)		P=0.228N	P=0.137N	P=0.320N
Thyroid: C-Cell Carcinoma				
Overall Rates (b)	19/84 (23%)	38/250 (15%)	23/99 (23%)	
Adjusted Rates (c)	59.9%	47.2%	57.6%	
Terminal Rates (d)	2/7 (29%)	5/29 (17%)	3/11 (27%)	
Life Table Test (e)		P=0.068N	P=0.526	P=0.046
Incidental Tumor Test (e)		P=0.095N	P=0.436	P=0.040
Fisher Exact Test (e)		P=0.084N	P=0.532	P=0.054
Thyroid: C-Cell Adenoma or Carcinoma				
Overall Rates (b)	30/84 (36%)	65/250 (26%)	32/99 (32%)	
Adjusted Rates (c)	76.9%	69.1%	76.1%	
Terminal Rates (d)	3/7 (43%)	11/29 (38%)	6/11 (55%)	
Life Table Test (e)		P=0.051N	P=0.381N	P=0.121
Incidental Tumor Test (e)		P=0.071N	P=0.470N	P=0.124
Fisher Exact Test (e)		P=0.061N	P=0.372N	P=0.146
Pancreatic Islet: Islet Cell Adenoma				
Overall Rates (b)	5/85 (6%)	6/249 (2%)	5/99 (5%)	
Adjusted Rates (c)	29.1%	9.6%	18.4%	
Terminal Rates (d)	1/7 (14%)	1/29 (3%)	0/11 (0%)	
Life Table Test (e)		P=0.088N	P=0.483N	P=0.141
Incidental Tumor Test (e)		P=0.114N	P=0.542N	P=0.176
Fisher Exact Test (e)		P=0.119N	P=0.528N	P=0.174
Pancreatic Islets: Islet Cell Carcinoma				
Overall Rates (b)	3/85 (4%)	17/249 (7%)	6/99 (6%)	
Adjusted Rates (c)	6.9%	36.3%	19.6%	
Terminal Rates (d)	0/7 (0%)	8/29 (28%)	1/11 (9%)	
Life Table Test (e)		P=0.278	P=0.337	P=0.526N
Incidental Tumor Test (e)		P=0.188	P=0.304	P=0.519N
Fisher Exact Test (e)		P=0.204	P=0.330	P=0.504N
Pancreatic Islets: Islet Cell Adenoma or Carcinoma				
Overall Rates (b)	8/85 (9%)	23/249 (9%)	11/99 (11%)	
Adjusted Rates (c)	34.0%	43.2%	34.4%	
Terminal Rates (d)	1/7 (14%)	9/29 (31%)	1/11 (9%)	
Life Table Test (e)		P=0.440N	P=0.489	P=0.315
Incidental Tumor Test (e)		P=0.577N	P=0.420	P=0.345
Fisher Exact Test (e)		P=0.556N	P=0.449	P=0.363
Mammary Gland: Fibroadenoma				
Overall Rates (b)	3/88 (3%)	16/250 (6%)	7/100 (7%)	
Adjusted Rates (c)	10.5%	28.5%	27.9%	
Terminal Rates (d)	0/7 (0%)	5/29 (17%)	1/11 (9%)	
Life Table Test (e)		P=0.301	P=0.238	P=0.459
Incidental Tumor Test (e)		P=0.219	P=0.223	P=0.488
Fisher Exact Test (e)		P=0.223	P=0.223	P=0.501

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	IR (a)	IR/PW	IR vs IR/PW
Preputial Gland: Carcinoma				
Overall Rates (b)	3/88 (3%)	11/250 (4%)	3/100 (3%)	
Adjusted Rates (c)	7.1%	9.5%	9.5%	
Terminal Rates (d)	0/7 (0%)	0/29 (0%)	0/11 (0%)	
Life Table Test (e)		P=0.489	P=0.611N	P=0.403N
Incidental Tumor Test (e)		P=0.446	P=0.579N	P=0.390N
Fisher Exact Test (e)		P=0.483	P=0.597N	P=0.397N
Preputial Gland: Adenoma or Carcinoma				
Overall Rates (b)	4/88 (5%)	11/250 (4%)	3/100 (3%)	
Adjusted Rates (c)	11.1%	9.5%	9.5%	
Terminal Rates (d)	0/7 (0%)	0/29 (0%)	0/11 (0%)	
Life Table Test (e)		P=0.567N	P=0.453N	P=0.403N
Incidental Tumor Test (e)		P=0.612N	P=0.414N	P=0.390N
Fisher Exact Test (e)		P=0.579N	P=0.429N	P=0.397N
Testis: Interstitial Cell Tumor				
Overall Rates (b)	79/84 (94%)	237/250 (95%)	89/100 (89%)	
Adjusted Rates (c)	100.0%	100.0%	100.0%	
Terminal Rates (d)	7/7 (100%)	29/29 (100%)	11/11 (100%)	
Life Table Test (e)		P=0.471N	P=0.404N	P=0.439N
Incidental Tumor Test (e)		P=0.306	P=0.572	P=0.330N
Fisher Exact Test (e)		P=0.489	P=0.172N	P=0.048N
Testis: Interstitial Cell Tumor or Interstitial Cell Tumor, Malignant				
Overall Rates (b)	79/84 (94%)	238/250 (95%)	89/100 (89%)	
Adjusted Rates (c)	100.0%	100.0%	100.0%	
Terminal Rates (d)	7/7 (100%)	29/29 (100%)	11/11 (100%)	
Life Table Test (e)		P=0.484N	P=0.404N	P=0.428N
Incidental Tumor Test (e)		P=0.242	P=0.572	P=0.257N
Fisher Exact Test (e)		P=0.432	P=0.172N	P=0.035N
Tunica Vaginalis: Mesothelioma, Malignant				
Overall Rates (b)	2/88 (2%)	13/250 (5%)	5/100 (5%)	
Adjusted Rates (c)	2.4%	9.8%	18.0%	
Terminal Rates (d)	0/7 (0%)	0/29 (0%)	1/11 (9%)	
Life Table Test (e)		P=0.208	P=0.315	P=0.570N
Incidental Tumor Test (e)		P=0.189	P=0.199	P=0.583N
Fisher Exact Test (e)		P=0.203	P=0.278	P=0.589N
All Sites: Mesothelioma, Malignant				
Overall Rates (b)	2/88 (2%)	14/250 (6%)	5/100 (5%)	
Adjusted Rates (c)	2.4%	10.2%	18.0%	
Terminal Rates (d)	0/7 (0%)	0/29 (0%)	1/11 (9%)	
Life Table Test (e)		P=0.173	P=0.315	P=0.512N
Incidental Tumor Test (e)		P=0.153	P=0.199	P=0.531N
Fisher Exact Test (e)		P=0.166	P=0.278	P=0.529N
All Sites: Mesothelioma				
Overall Rates (b)	5/88 (6%)	16/250 (6%)	6/100 (6%)	
Adjusted Rates (c)	13.4%	15.0%	19.3%	
Terminal Rates (d)	0/7 (0%)	0/29 (0%)	1/11 (9%)	
Life Table Test (e)		P=0.521	P=0.610	P=0.538N
Incidental Tumor Test (e)		P=0.490	P=0.519	P=0.557N
Fisher Exact Test (e)		P=0.521	P=0.588	P=0.554N

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS (Continued)

- (a) Administered 1% intermediate-range (IR) chrysotile asbestos in the diet
- (b) Number of tumor-bearing animals/number of animals examined at the site
- (c) Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality
- (d) Observed tumor incidence at terminal kill
- (e) Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The pairwise comparison between the dosed groups is in the final column. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in a dosed group than in the controls or in the IR plus preweaning gavage than the IR group is indicated by (N).

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS (a)

	CONTROL (UNTR)	IR (a)	IR/PW	IR vs IR/PW
Subcutaneous Tissue: Fibroma				
Overall Rates (b)	5/88 (6%)	9/250 (4%)	3/100 (3%)	
Adjusted Rates (c)	27.2%	10.5%	10.1%	
Terminal Rates (d)	1/10 (10%)	1/29 (3%)	0/11 (0%)	
Life Table Test (e)		P=0.262N	P=0.289N	P=0.569N
Incidental Tumor Test (e)		P=0.308N	P=0.302N	P=0.496N
Fisher Exact Test (e)		P=0.287N	P=0.292N	P=0.537N
Subcutaneous Tissue: Fibroma or Fibrosarcoma				
Overall Rates (b)	6/88 (7%)	13/250 (5%)	3/100 (3%)	
Adjusted Rates (c)	31.8%	13.9%	10.1%	
Terminal Rates (d)	1/10 (10%)	1/29 (3%)	0/11 (0%)	
Life Table Test (e)		P=0.322N	P=0.185N	P=0.323N
Incidental Tumor Test (e)		P=0.403N	P=0.195N	P=0.252N
Fisher Exact Test (e)		P=0.370N	P=0.190N	P=0.281N
Hematopoietic System: Leukemia				
Overall Rates (b)	34/88 (39%)	82/250 (33%)	29/100 (29%)	
Adjusted Rates (c)	75.1%	59.5%	58.2%	
Terminal Rates (d)	3/10 (30%)	6/29 (21%)	3/11 (27%)	
Life Table Test (e)		P=0.184N	P=0.155N	P=0.389N
Incidental Tumor Test (e)		P=0.227N	P=0.150N	P=0.294N
Fisher Exact Test (e)		P=0.195N	P=0.108N	P=0.289N
Liver: Neoplastic Nodule or Hepatocellular Carcinoma				
Overall Rates (b)	4/87 (5%)	6/250 (2%)	1/99 (1%)	
Adjusted Rates (c)	16.0%	6.5%	1.8%	
Terminal Rates (d)	0/10 (0%)	0/29 (0%)	0/11 (0%)	
Life Table Test (e)		P=0.215N	P=0.152N	P=0.359N
Incidental Tumor Test (e)		P=0.256N	P=0.156N	P=0.346N
Fisher Exact Test (e)		P=0.241N	P=0.147N	P=0.363N
Pituitary: Adenoma				
Overall Rates (b)	49/87 (56%)	103/249 (41%)	50/100 (50%)	
Adjusted Rates (c)	93.4%	88.2%	90.2%	
Terminal Rates (d)	8/10 (80%)	20/29 (69%)	7/11 (64%)	
Life Table Test (e)		P=0.017N	P=0.332N	P=0.064
Incidental Tumor Test (e)		P=0.014N	P=0.314N	P=0.056
Fisher Exact Test (e)		P=0.012N	P=0.237N	P=0.089
Pituitary: Carcinoma				
Overall Rates (b)	4/87 (5%)	14/249 (6%)	1/100 (1%)	
Adjusted Rates (c)	13.1%	11.1%	3.2%	
Terminal Rates (d)	0/10 (0%)	0/29 (0%)	0/11 (0%)	
Life Table Test (e)		P=0.475	P=0.150N	P=0.056N
Incidental Tumor Test (e)		P=0.382	P=0.156N	P=0.044N
Fisher Exact Test (e)		P=0.481	P=0.144N	P=0.041N
Pituitary: Adenoma or Carcinoma				
Overall Rates (b)	53/87 (61%)	117/249 (47%)	51/100 (51%)	
Adjusted Rates (c)	94.2%	89.5%	90.5%	
Terminal Rates (d)	8/10 (80%)	20/29 (69%)	7/11 (64%)	
Life Table Test (e)		P=0.031N	P=0.220N	P=0.202
Incidental Tumor Test (e)		P=0.027N	P=0.160N	P=0.236
Fisher Exact Test (e)		P=0.018N	P=0.112N	P=0.288
Adrenal: Cortical Adenoma				
Overall Rates (b)	4/87 (5%)	10/249 (4%)	5/99 (5%)	
Adjusted Rates (c)	15.5%	11.1%	17.8%	
Terminal Rates (d)	1/10 (10%)	0/29 (0%)	0/11 (0%)	
Life Table Test (e)		P=0.477N	P=0.592	P=0.409
Incidental Tumor Test (e)		P=0.563N	P=0.548	P=0.439
Fisher Exact Test (e)		P=0.512N	P=0.581	P=0.431

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	IR (a)	IR/PW	IR vs IR/PW
Adrenal: Pheochromocytoma				
Overall Rates (b)	8/87 (9%)	25/249 (10%)	11/99 (11%)	
Adjusted Rates (c)	45.3%	39.6%	44.6%	
Terminal Rates (d)	3/10 (30%)	6/29 (17%)	3/11 (27%)	
Life Table Test (e)		P=0.573N	P=0.440	P=0.370
Incidental Tumor Test (e)		P=0.495	P=0.404	P=0.412
Fisher Exact Test (e)		P=0.503	P=0.427	P=0.451
Adrenal: Pheochromocytoma or Pheochromocytoma, Malignant				
Overall Rates (b)	10/87 (11%)	25/249 (10%)	13/99 (13%)	
Adjusted Rates (c)	47.9%	39.6%	50.1%	
Terminal Rates (d)	3/10 (30%)	6/29 (17%)	3/11 (27%)	
Life Table Test (e)		P=0.336N	P=0.472	P=0.189
Incidental Tumor Test (e)		P=0.430N	P=0.430	P=0.213
Fisher Exact Test (e)		P=0.420N	P=0.456	P=0.256
Thyroid: Follicular Cell Adenoma				
Overall Rates (b)	6/87 (7%)	13/248 (5%)	6/100 (6%)	
Adjusted Rates (c)	37.5%	19.1%	9.7%	
Terminal Rates (d)	3/10 (30%)	2/29 (7%)	0/11 (0%)	
Life Table Test (e)		P=0.341N	P=0.530N	P=0.449
Incidental Tumor Test (e)		P=0.364N	P=0.563N	P=0.512
Fisher Exact Test (e)		P=0.367N	P=0.517N	P=0.478
Thyroid: Follicular Cell Carcinoma				
Overall Rates (b)	1/87 (1%)	14/248 (6%)	7/100 (7%)	
Adjusted Rates (c)	6.2%	23.3%	26.1%	
Terminal Rates (d)	0/10 (0%)	4/29 (14%)	0/11 (0%)	
Life Table Test (e)		P=0.097	P=0.069	P=0.345
Incidental Tumor Test (e)		P=0.079	P=0.048	P=0.354
Fisher Exact Test (e)		P=0.065	P=0.050	P=0.397
Thyroid: Follicular Cell Adenoma or Carcinoma				
Overall Rates (b)	7/87 (8%)	27/248 (11%)	13/100 (13%)	
Adjusted Rates (c)	41.4%	38.7%	33.3%	
Terminal Rates (d)	3/10 (30%)	6/29 (21%)	0/11 (0%)	
Life Table Test (e)		P=0.362	P=0.219	P=0.288
Incidental Tumor Test (e)		P=0.311	P=0.167	P=0.330
Fisher Exact Test (e)		P=0.299	P=0.197	P=0.348
Thyroid: C-Cell Adenoma				
Overall Rates (b)	11/87 (13%)	26/248 (10%)	20/100 (20%)	
Adjusted Rates (c)	58.3%	40.1%	52.0%	
Terminal Rates (d)	5/10 (50%)	8/29 (28%)	2/11 (18%)	
Life Table Test (e)		P=0.281N	P=0.130	P=0.009
Incidental Tumor Test (e)		P=0.341N	P=0.093	P=0.012
Fisher Exact Test (e)		P=0.354N	P=0.124	P=0.016
Thyroid: C-Cell Carcinoma				
Overall Rates (b)	11/87 (13%)	41/248 (17%)	12/100 (12%)	
Adjusted Rates (c)	34.6%	47.4%	52.7%	
Terminal Rates (d)	2/10 (20%)	6/29 (21%)	4/11 (36%)	
Life Table Test (e)		P=0.320	P=0.547N	P=0.272N
Incidental Tumor Test (e)		P=0.219	P=0.554N	P=0.191N
Fisher Exact Test (e)		P=0.249	P=0.534N	P=0.185N
Thyroid: C-Cell Adenoma or Carcinoma				
Overall Rates (b)	21/87 (24%)	65/248 (26%)	30/100 (30%)	
Adjusted Rates (c)	72.7%	71.0%	79.5%	
Terminal Rates (d)	6/10 (60%)	14/29 (48%)	6/11 (55%)	
Life Table Test (e)		P=0.518	P=0.236	P=0.186
Incidental Tumor Test (e)		P=0.386	P=0.184	P=0.246
Fisher Exact Test (e)		P=0.410	P=0.232	P=0.277

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	IR (a)	IR/PW	IR vs IR/PW
Pancreatic Islets: Islet Cell Adenoma or Carcinoma				
Overall Rates (b)	6/87 (7%)	13/249 (5%)	7/99 (7%)	
Adjusted Rates (c)	13.9%	22.7%	23.6%	
Terminal Rates (d)	0/10 (0%)	3/29 (10%)	0/11 (0%)	
Life Table Test (e)		P=0.315N	P=0.604	P=0.279
Incidental Tumor Test (e)		P=0.382N	P=0.565	P=0.304
Fisher Exact Test (e)		P=0.366N	P=0.597	P=0.330
Mammary Gland: Adenoma				
Overall Rates (b)	6/88 (7%)	21/250 (8%)	11/100 (11%)	
Adjusted Rates (c)	22.4%	31.3%	32.0%	
Terminal Rates (d)	0/10 (0%)	6/29 (21%)	1/11 (9%)	
Life Table Test (e)		P=0.465	P=0.248	P=0.244
Incidental Tumor Test (e)		P=0.377	P=0.203	P=0.279
Fisher Exact Test (e)		P=0.416	P=0.230	P=0.283
Mammary Gland: Fibroadenoma				
Overall Rates (b)	49/88 (56%)	128/250 (51%)	58/100 (58%)	
Adjusted Rates (c)	100.0%	92.0%	93.9%	
Terminal Rates (d)	10/10 (100%)	21/29 (72%)	8/11 (73%)	
Life Table Test (e)		P=0.209N	P=0.445	P=0.123
Incidental Tumor Test (e)		P=0.318N	P=0.322	P=0.110
Fisher Exact Test (e)		P=0.275N	P=0.431	P=0.151
Mammary Gland: Adenocarcinoma				
Overall Rates (b)	5/88 (6%)	9/250 (4%)	4/100 (4%)	
Adjusted Rates (c)	15.7%	21.2%	12.7%	
Terminal Rates (d)	0/10 (0%)	4/29 (14%)	1/11 (9%)	
Life Table Test (e)		P=0.248N	P=0.435N	P=0.504
Incidental Tumor Test (e)		P=0.286N	P=0.421N	P=0.532
Fisher Exact Test (e)		P=0.287N	P=0.420N	P=0.536
Clitoral Gland: Carcinoma or Squamous Cell Carcinoma				
Overall Rates (b)	1/88 (1%)	18/250 (7%)	4/100 (4%)	
Adjusted Rates (c)	3.2%	26.1%	12.6%	
Terminal Rates (d)	0/10 (0%)	5/29 (17%)	0/11 (0%)	
Life Table Test (e)		P=0.037	P=0.214	P=0.218N
Incidental Tumor Test (e)		P=0.031	P=0.247	P=0.186N
Fisher Exact Test (e)		P=0.022	P=0.227	P=0.195N
Uterus: Endometrial Stromal Polyp				
Overall Rates (b)	13/87 (15%)	22/249 (9%)	10/99 (10%)	
Adjusted Rates (c)	37.4%	31.4%	30.2%	
Terminal Rates (d)	1/10 (10%)	6/29 (21%)	0/11 (0%)	
Life Table Test (e)		P=0.070N	P=0.231N	P=0.375
Incidental Tumor Test (e)		P=0.078N	P=0.227N	P=0.385
Fisher Exact Test (e)		P=0.084N	P=0.219N	P=0.426

(a) Administered 1% intermediate-range (IR) chrysotile asbestos in the diet

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

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

(d) Observed tumor incidence at terminal kill

(e) Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The pairwise comparison between the dosed groups is in the final column. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in a dosed group than in the controls or in the IR plus preweaning gavage than the IR group is indicated by (N).

TABLE E5. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE

	CONTROL (UNTR)	DMH (a)	IR + DMH (b)	DMH vs IR + DMH
Skin: Papilloma or Squamous Cell Papilloma				
Overall Rates (c)	5/88 (6%)	2/125 (2%)	4/175 (2%)	
Adjusted Rates (d)	16.8%	11.1%	13.9%	
Terminal Rates (e)	4/26 (15%)	2/18 (11%)	2/18 (11%)	
Life Table Test (f)		P=0.373N	P=0.621N	P=0.378
Incidental Tumor Test (f)		P=0.358N	P=0.499N	P=0.396
Fisher Exact Test (f)		P=0.106N	P=0.143N	P=0.509
Skin: Keratoacanthoma				
Overall Rates (c)	1/88 (1%)	6/125 (5%)	11/175 (6%)	
Adjusted Rates (d)	3.2%	24.2%	30.0%	
Terminal Rates (e)	0/26 (0%)	4/18 (22%)	1/18 (6%)	
Life Table Test (f)		P=0.028	P=0.002	P=0.240
Incidental Tumor Test (f)		P=0.070	P=0.018	P=0.356
Fisher Exact Test (f)		P=0.138	P=0.049	P=0.389
Subcutaneous Tissue: Fibroma				
Overall Rates (c)	17/88 (19%)	13/125 (10%)	15/175 (9%)	
Adjusted Rates (d)	33.8%	38.7%	43.7%	
Terminal Rates (e)	3/26 (12%)	5/18 (28%)	5/18 (28%)	
Life Table Test (f)		P=0.502N	P=0.508N	P=0.573
Incidental Tumor Test (f)		P=0.134N	P=0.094N	P=0.455N
Fisher Exact Test (f)		P=0.052N	P=0.012N	P=0.366N
Subcutaneous Tissue: Fibrosarcoma				
Overall Rates (c)	7/88 (8%)	3/125 (2%)	2/175 (1%)	
Adjusted Rates (d)	17.0%	5.2%	6.3%	
Terminal Rates (e)	1/26 (4%)	0/18 (0%)	1/18 (6%)	
Life Table Test (f)		P=0.258N	P=0.113N	P=0.416N
Incidental Tumor Test (f)		P=0.096N	P=0.023N	P=0.379N
Fisher Exact Test (f)		P=0.061N	P=0.008N	P=0.346N
Subcutaneous Tissue: Fibroma or Fibrosarcoma				
Overall Rates (c)	23/88 (26%)	16/125 (13%)	17/175 (10%)	
Adjusted Rates (d)	44.1%	41.9%	48.4%	
Terminal Rates (e)	4/26 (15%)	5/18 (28%)	6/18 (33%)	
Life Table Test (f)		P=0.363N	P=0.286N	P=0.471N
Incidental Tumor Test (f)		P=0.042N	P=0.014N	P=0.335N
Fisher Exact Test (f)		P=0.012N	P=0.001N	P=0.255N
Hematopoietic System: Leukemia				
Overall Rates (c)	31/88 (35%)	42/125 (34%)	71/175 (41%)	
Adjusted Rates (d)	60.4%	68.9%	76.6%	
Terminal Rates (e)	10/26 (38%)	6/18 (33%)	5/18 (28%)	
Life Table Test (f)		P=0.016	P<0.001	P=0.076
Incidental Tumor Test (f)		P=0.181	P=0.065	P=0.172
Fisher Exact Test (f)		P=0.460N	P=0.241	P=0.134
Liver: Neoplastic Nodule				
Overall Rates (c)	6/85 (7%)	12/125 (10%)	10/175 (6%)	
Adjusted Rates (d)	17.5%	33.4%	20.3%	
Terminal Rates (e)	3/26 (12%)	3/18 (17%)	2/18 (11%)	
Life Table Test (f)		P=0.039	P=0.211	P=0.249N
Incidental Tumor Test (f)		P=0.105	P=0.500	P=0.155N
Fisher Exact Test (f)		P=0.351	P=0.431N	P=0.148N
Liver: Hepatocellular Carcinoma				
Overall Rates (c)	2/85 (2%)	17/125 (14%)	20/175 (11%)	
Adjusted Rates (d)	5.8%	38.3%	41.1%	
Terminal Rates (e)	1/26 (4%)	3/18 (17%)	3/18 (17%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.528N
Incidental Tumor Test (f)		P<0.001	P<0.003	P=0.336N
Fisher Exact Test (f)		P=0.003	P=0.009	P=0.348N

TABLE E5. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

	CONTROL (UNTR)	DMH (a)	IR + DMH (b)	DMH vs IR + DMH
Liver: Neoplastic Nodule or Hepatocellular Carcinoma				
Overall Rates (c)	8/85 (9%)	27/125 (22%)	29/175 (17%)	
Adjusted Rates (d)	22.8%	59.5%	50.7%	
Terminal Rates (e)	4/26 (15%)	6/18 (33%)	4/18 (22%)	
Life Table Test (f)		P < 0.001	P < 0.001	P = 0.372N
Incidental Tumor Test (f)		P < 0.001	P < 0.016	P = 0.159N
Fisher Exact Test (f)		P = 0.014	P = 0.084	P = 0.171N
Pancreas: Acinar Cell Adenoma				
Overall Rates (c)	3/85 (4%)	7/124 (6%)	14/174 (8%)	
Adjusted Rates (d)	11.5%	28.9%	35.1%	
Terminal Rates (e)	3/26 (12%)	4/18 (22%)	3/18 (17%)	
Life Table Test (f)		P = 0.059	P = 0.003	P = 0.148
Incidental Tumor Test (f)		P = 0.073	P = 0.026	P = 0.237
Fisher Exact Test (f)		P = 0.362	P = 0.131	P = 0.288
Large Intestine: Adenomatous Polyp				
Overall Rates (c)	0/85 (0%)	31/125 (25%)	45/175 (26%)	
Adjusted Rates (d)	0.0%	45.0%	45.7%	
Terminal Rates (e)	0/26 (0%)	2/18 (11%)	1/18 (6%)	
Life Table Test (f)		P < 0.001	P < 0.001	P = 0.376
Incidental Tumor Test (f)		P < 0.001	P < 0.001	P = 0.479
Fisher Exact Test (f)		P < 0.001	P < 0.001	P = 0.483
Large Intestine: Mucinous Cystadenocarcinoma				
Overall Rates (c)	0/85 (0%)	7/125 (6%)	19/175 (11%)	
Adjusted Rates (d)	0.0%	9.5%	19.9%	
Terminal Rates (e)	0/26 (0%)	0/18 (0%)	0/18 (0%)	
Life Table Test (f)		P = 0.016	P < 0.001	P = 0.077
Incidental Tumor Test (f)		P = 0.125	P = 0.019	P = 0.085
Fisher Exact Test (f)		P = 0.025	P < 0.001	P = 0.081
Large Intestine: Adenocarcinoma or Mucinous Cystadenocarcinoma				
Overall Rates (c)	0/85 (0%)	9/125 (7%)	20/175 (11%)	
Adjusted Rates (d)	0.0%	11.7%	20.5%	
Terminal Rates (e)	0/26 (0%)	0/18 (0%)	0/18 (0%)	
Life Table Test (f)		P = 0.006	P < 0.001	P = 0.142
Incidental Tumor Test (f)		P = 0.090	P = 0.017	P = 0.156
Fisher Exact Test (f)		P = 0.008	P < 0.001	P = 0.153
Large Intestine: Adenomatous Polyp, Adenocarcinoma, or Mucinous Cystadenocarcinoma				
Overall Rates (c)	0/85 (0%)	40/125 (32%)	62/175 (35%)	
Adjusted Rates (d)	0.0%	51.5%	54.4%	
Terminal Rates (e)	0/26 (0%)	2/18 (11%)	1/18 (6%)	
Life Table Test (f)		P < 0.001	P < 0.001	P = 0.248
Incidental Tumor Test (f)		P < 0.001	P < 0.001	P = 0.326
Fisher Exact Test (f)		P < 0.001	P < 0.001	P = 0.311
Pituitary: Adenoma				
Overall Rates (c)	14/85 (16%)	12/124 (10%)	16/175 (9%)	
Adjusted Rates (d)	35.3%	39.8%	48.0%	
Terminal Rates (e)	6/26 (23%)	5/18 (28%)	6/18 (33%)	
Life Table Test (f)		P = 0.463	P = 0.266	P = 0.402
Incidental Tumor Test (f)		P = 0.487N	P = 0.564N	P = 0.566
Fisher Exact Test (f)		P = 0.107N	P = 0.066N	P = 0.514N
Pituitary: Adenoma or Carcinoma				
Overall Rates (c)	18/85 (21%)	15/124 (12%)	17/175 (10%)	
Adjusted Rates (d)	40.2%	44.5%	50.1%	
Terminal Rates (e)	6/26 (23%)	5/18 (28%)	6/18 (33%)	
Life Table Test (f)		P = 0.492	P = 0.477	P = 0.564N
Incidental Tumor Test (f)		P = 0.365N	P = 0.260N	P = 0.374N
Fisher Exact Test (f)		P = 0.059N	P = 0.012N	P = 0.318N

TABLE E5. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

	CONTROL (UNTR)	DMH (a)	IR + DMH (b)	DMH vs IR + DMH
Adrenal: Pheochromocytoma				
Overall Rates (c)	16/85 (19%)	20/125 (16%)	34/175 (19%)	
Adjusted Rates (d)	41.6%	59.9%	68.5%	
Terminal Rates (e)	8/26 (31%)	9/18 (50%)	8/18 (44%)	
Life Table Test (f)		P=0.085	P=0.002	P=0.102
Incidental Tumor Test (f)		P=0.239	P=0.050	P=0.204
Fisher Exact Test (f)		P=0.362N	P=0.525	P=0.272
Adrenal: Pheochromocytoma or Pheochromocytoma, Malignant				
Overall Rates (c)	17/85 (20%)	20/125 (16%)	34/175 (19%)	
Adjusted Rates (d)	43.4%	59.9%	68.5%	
Terminal Rates (e)	8/26 (31%)	9/18 (50%)	8/18 (44%)	
Life Table Test (f)		P=0.115	P=0.003	P=0.102
Incidental Tumor Test (f)		P=0.306	P=0.078	P=0.204
Fisher Exact Test (f)		P=0.286N	P=0.519N	P=0.272
Thyroid: Follicular Cell Adenoma				
Overall Rates (c)	1/84 (1%)	1/124 (1%)	14/175 (8%)	
Adjusted Rates (d)	2.1%	2.8%	28.5%	
Terminal Rates (e)	0/26 (0%)	0/18 (0%)	2/18 (11%)	
Life Table Test (f)		P=0.720	P=0.001	P=0.003
Incidental Tumor Test (f)		P=0.752	P=0.011	P=0.006
Fisher Exact Test (f)		P=0.646N	P=0.020	P=0.003
Thyroid: Follicular Cell Carcinoma				
Overall Rates (c)	5/84 (6%)	8/124 (6%)	14/175 (8%)	
Adjusted Rates (d)	13.1%	29.9%	19.7%	
Terminal Rates (e)	2/26 (8%)	4/18 (22%)	0/18 (0%)	
Life Table Test (f)		P=0.130	P=0.045	P=0.299
Incidental Tumor Test (f)		P=0.171	P=0.246	P=0.403
Fisher Exact Test (f)		P=0.564	P=0.377	P=0.394
Thyroid: Follicular Cell Adenoma or Carcinoma				
Overall Rates (c)	6/84 (7%)	9/124 (7%)	28/175 (16%)	
Adjusted Rates (d)	14.9%	31.8%	42.7%	
Terminal Rates (e)	2/26 (8%)	4/18 (22%)	2/18 (11%)	
Life Table Test (f)		P=0.138	P<0.001	P=0.010
Incidental Tumor Test (f)		P=0.184	P=0.009	P=0.020
Fisher Exact Test (f)		P=0.600	P=0.034	P=0.017
Thyroid: C-Cell Adenoma				
Overall Rates (c)	13/84 (15%)	11/124 (9%)	18/175 (10%)	
Adjusted Rates (d)	33.6%	22.4%	31.9%	
Terminal Rates (e)	6/26 (23%)	2/18 (11%)	1/18 (6%)	
Life Table Test (f)		P=0.576	P=0.225	P=0.291
Incidental Tumor Test (f)		P=0.184N	P=0.461N	P=0.431
Fisher Exact Test (f)		P=0.108N	P=0.159N	P=0.421
Thyroid: C-Cell Carcinoma				
Overall Rates (c)	19/84 (23%)	15/124 (12%)	21/175 (12%)	
Adjusted Rates (d)	42.4%	38.3%	44.6%	
Terminal Rates (e)	6/26 (23%)	3/18 (17%)	3/18 (17%)	
Life Table Test (f)		P=0.559N	P=0.361	P=0.385
Incidental Tumor Test (f)		P=0.184N	P=0.124N	P=0.538N
Fisher Exact Test (f)		P=0.035N	P=0.024N	P=0.559N
Thyroid: C-Cell Adenoma or Carcinoma				
Overall Rates (c)	30/84 (36%)	25/124 (20%)	37/175 (21%)	
Adjusted Rates (d)	60.3%	52.4%	61.5%	
Terminal Rates (e)	10/26 (38%)	5/18 (28%)	4/18 (22%)	
Life Table Test (f)		P=0.529	P=0.183	P=0.258
Incidental Tumor Test (f)		P=0.069N	P=0.134N	P=0.499
Fisher Exact Test (f)		P=0.011N	P=0.011N	P=0.477

TABLE E5. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

	CONTROL (UNTR)	DMH (a)	IR + DMH (b)	DMH vs IR + DMH
Pancreatic Islets: Islet Cell Adenoma				
Overall Rates (c)	5/85 (6%)	1/124 (1%)	5/174 (3%)	
Adjusted Rates (d)	12.7%	5.6%	18.2%	
Terminal Rates (e)	2/26 (8%)	1/18 (6%)	2/18 (11%)	
Life Table Test (f)		P=0.166N	P=0.532	P=0.123
Incidental Tumor Test (f)		P=0.091N	P=0.489N	P=0.164
Fisher Exact Test (f)		P=0.042N	P=0.199N	P=0.206
Pancreatic Islets: Islet Cell Adenoma or Carcinoma				
Overall Rates (c)	8/85 (9%)	7/124 (6%)	9/174 (5%)	
Adjusted Rates (d)	18.9%	28.7%	30.8%	
Terminal Rates (e)	3/26 (12%)	4/18 (22%)	3/18 (17%)	
Life Table Test (f)		P=0.509	P=0.381	P=0.468
Incidental Tumor Test (f)		P=0.577N	P=0.521N	P=0.602N
Fisher Exact Test (f)		P=0.221N	P=0.153N	P=0.527N
Preputial Gland: Carcinoma				
Overall Rates (c)	3/88 (3%)	7/125 (6%)	10/175 (6%)	
Adjusted Rates (d)	7.1%	13.6%	15.6%	
Terminal Rates (e)	0/26 (0%)	0/18 (0%)	0/18 (0%)	
Life Table Test (f)		P=0.114	P=0.066	P=0.506
Incidental Tumor Test (f)		P=0.320	P=0.330	P=0.569N
Fisher Exact Test (f)		P=0.346	P=0.313	P=0.588
Preputial Gland: Adenoma or Carcinoma				
Overall Rates (c)	4/88 (5%)	7/125 (6%)	10/175 (6%)	
Adjusted Rates (d)	10.6%	13.6%	15.6%	
Terminal Rates (e)	1/26 (4%)	0/18 (0%)	0/18 (0%)	
Life Table Test (f)		P=0.183	P=0.110	P=0.506
Incidental Tumor Test (f)		P=0.429	P=0.431	P=0.569N
Fisher Exact Test (f)		P=0.496	P=0.469	P=0.588
Testis: Interstitial Cell Tumor				
Overall Rates (c)	79/84 (94%)	112/125 (90%)	160/175 (91%)	
Adjusted Rates (d)	100.0%	100.0%	100.0%	
Terminal Rates (e)	26/26 (100%)	18/18 (100%)	18/18 (100%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.149
Incidental Tumor Test (f)		P=0.284	P=0.055	P=0.344
Fisher Exact Test (f)		P=0.193N	P=0.320N	P=0.366
Testis: Interstitial Cell Tumor or Interstitial Cell Tumor, Malignant				
Overall Rates (c)	79/84 (94%)	113/125 (90%)	160/175 (91%)	
Adjusted Rates (d)	100.0%	100.0%	100.0%	
Terminal Rates (e)	26/26 (100%)	18/18 (100%)	18/18 (100%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.168
Incidental Tumor Test (f)		P=0.236	P=0.055	P=0.463
Fisher Exact Test (f)		P=0.249N	P=0.320N	P=0.455
Zymbal Gland: Squamous Cell Carcinoma				
Overall Rates (c)	1/88 (1%)	15/125 (12%)	22/175 (13%)	
Adjusted Rates (d)	2.5%	25.3%	28.6%	
Terminal Rates (e)	0/26 (0%)	1/18 (6%)	1/18 (6%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.433
Incidental Tumor Test (f)		P=0.011	P=0.007	P=0.555
Fisher Exact Test (f)		P=0.002	P<0.001	P=0.515
Zymbal Gland: Squamous Cell Papilloma or Carcinoma				
Overall Rates (c)	1/88 (1%)	16/125 (13%)	25/175 (14%)	
Adjusted Rates (d)	2.5%	25.9%	33.9%	
Terminal Rates (e)	0/26 (0%)	1/18 (6%)	2/18 (11%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.344
Incidental Tumor Test (f)		P=0.010	P=0.003	P=0.458
Fisher Exact Test (f)		P=0.001	P<0.001	P=0.424

TABLE E5. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

	CONTROL (UNTR)	DMH (a)	IR + DMH (b)	DMH vs IR + DMH
Zymbal Gland: Carcinoma				
Overall Rates (c)	2/88 (2%)	18/125 (14%)	24/175 (14%)	
Adjusted Rates (d)	4.5%	27.9%	30.0%	
Terminal Rates (e)	0/26 (0%)	1/18 (6%)	1/18 (6%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.547
Incidental Tumor Test (f)		P=0.016	P=0.013	P=0.454N
Fisher Exact Test (f)		P=0.002	P=0.002	P=0.497N
Zymbal Gland: Papilloma or Carcinoma				
Overall Rates (c)	2/88 (2%)	19/125 (15%)	27/175 (15%)	
Adjusted Rates (d)	4.5%	28.5%	35.1%	
Terminal Rates (e)	0/26 (0%)	1/18 (6%)	2/18 (11%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.454
Incidental Tumor Test (f)		P=0.014	P=0.005	P=0.547N
Fisher Exact Test (f)		P=0.001	P<0.001	P=0.545
All Sites: Mesothelioma				
Overall Rates (c)	4/88 (5%)	6/125 (5%)	7/175 (4%)	
Adjusted Rates (d)	7.6%	17.1%	8.2%	
Terminal Rates (e)	0/26 (0%)	1/18 (6%)	0/18 (0%)	
Life Table Test (f)		P=0.274	P=0.408	P=0.552N
Incidental Tumor Test (f)		P=0.562	P=0.289N	P=0.470N
Fisher Exact Test (f)		P=0.601	P=0.533N	P=0.475N

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

(b) Administered 1% intermediate-range (IR) chrysotile asbestos in the diet and DMH by gavage

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

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

(e) Observed tumor incidence at terminal kill

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

TABLE E6. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE

	CONTROL (UNTR)	DMH (a)	IR + DMH (b)	DMH vs IR + DMH
Subcutaneous Tissue: Fibroma				
Overall Rates (c)	5/88 (6%)	2/125 (2%)	1/175 (1%)	
Adjusted Rates (d)	9.1%	8.3%	0.8%	
Terminal Rates (e)	5/55 (9%)	0/16 (0%)	0/27 (0%)	
Life Table Test (f)		P=0.567	P=0.258N	P=0.347N
Incidental Tumor Test (f)		P=0.619N	P=0.182N	P=0.340N
Fisher Exact Test (f)		P=0.106N	P=0.018N	P=0.376N
Subcutaneous Tissue: Fibroma or Fibrosarcoma				
Overall Rates (c)	6/88 (7%)	3/125 (2%)	2/175 (1%)	
Adjusted Rates (d)	10.9%	10.6%	1.8%	
Terminal Rates (e)	6/55 (11%)	0/16 (0%)	0/27 (0%)	
Life Table Test (f)		P=0.428	P=0.315N	P=0.308N
Incidental Tumor Test (f)		P=0.593N	P=0.172N	P=0.353N
Fisher Exact Test (f)		P=0.110N	P=0.019N	P=0.346N
Hematopoietic System: Leukemia				
Overall Rates (c)	34/88 (39%)	70/125 (56%)	93/175 (53%)	
Adjusted Rates (d)	51.5%	86.1%	85.8%	
Terminal Rates (e)	24/55 (44%)	8/16 (50%)	15/27 (56%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.175N
Incidental Tumor Test (f)		P=0.002	P<0.001	P=0.347N
Fisher Exact Test (f)		P=0.009	P=0.018	P=0.355N
Liver: Neoplastic Nodule				
Overall Rates (c)	3/87 (3%)	12/125 (10%)	21/175 (12%)	
Adjusted Rates (d)	5.2%	33.5%	32.4%	
Terminal Rates (e)	2/55 (4%)	3/16 (19%)	3/27 (11%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.446
Incidental Tumor Test (f)		P=0.027	P=0.017	P=0.319
Fisher Exact Test (f)		P=0.071	P=0.016	P=0.322
Liver: Hepatocellular Carcinoma				
Overall Rates (c)	1/87 (1%)	12/125 (10%)	19/175 (11%)	
Adjusted Rates (d)	1.8%	36.2%	38.3%	
Terminal Rates (e)	1/55 (2%)	3/16 (19%)	7/27 (26%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.572
Incidental Tumor Test (f)		P=0.002	P<0.001	P=0.505
Fisher Exact Test (f)		P=0.009	P=0.003	P=0.439
Liver: Neoplastic Nodule or Hepatocellular Carcinoma				
Overall Rates (c)	4/87 (5%)	22/125 (18%)	38/175 (22%)	
Adjusted Rates (d)	7.0%	54.2%	57.4%	
Terminal Rates (e)	3/55 (5%)	5/16 (31%)	9/27 (33%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.406
Incidental Tumor Test (f)		P<0.001	P<0.001	P=0.258
Fisher Exact Test (f)		P=0.003	P<0.001	P=0.233
Large Intestine: Adenomatous Polyp				
Overall Rates (c)	0/87 (0%)	33/125 (26%)	46/175 (26%)	
Adjusted Rates (d)	0.0%	71.0%	53.3%	
Terminal Rates (e)	0/55 (0%)	8/16 (50%)	6/27 (22%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.390N
Incidental Tumor Test (f)		P<0.001	P<0.001	P=0.531
Fisher Exact Test (f)		P<0.001	P<0.001	P=0.543N
Large Intestine: Mucinous Cystadenocarcinoma				
Overall Rates (c)	0/87 (0%)	14/125 (11%)	16/175 (9%)	
Adjusted Rates (d)	0.0%	20.9%	19.3%	
Terminal Rates (e)	0/55 (0%)	1/16 (6%)	2/27 (7%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.327N
Incidental Tumor Test (f)		P=0.055	P=0.036	P=0.305N
Fisher Exact Test (f)		P<0.001	P=0.001	P=0.346N

TABLE E6. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

	CONTROL (UNTR)	DMH (a)	IR + DMH (b)	DMH vs IR + DMH
Large Intestine: Adenocarcinoma or Mucinous Cystadenocarcinoma				
Overall Rates (c)	0/87 (0%)	15/125 (12%)	19/175 (11%)	
Adjusted Rates (d)	0.0%	21.6%	24.5%	
Terminal Rates (e)	0/55 (0%)	1/16 (6%)	3/27 (11%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.410N
Incidental Tumor Test (f)		P=0.055	P=0.009	P=0.396N
Fisher Exact Test (f)		P<0.001	P<0.001	P=0.448N
Large Intestine: Adenomatous Polyp, Adenocarcinoma, or Mucinous Cystadenocarcinoma				
Overall Rates (c)	0/87 (0%)	46/125 (37%)	61/175 (35%)	
Adjusted Rates (d)	0.0%	74.8%	62.7%	
Terminal Rates (e)	0/55 (0%)	8/16 (50%)	8/27 (30%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.291N
Incidental Tumor Test (f)		P<0.001	P<0.001	P=0.435N
Fisher Exact Test (f)		P<0.001	P<0.001	P=0.411N
Kidney: Mixed Tumor, Malignant				
Overall Rates (c)	0/87 (0%)	13/125 (10%)	34/175 (19%)	
Adjusted Rates (d)	0.0%	21.8%	30.0%	
Terminal Rates (e)	0/55 (0%)	1/16 (6%)	0/27 (0%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.043
Incidental Tumor Test (f)		P=0.073	P=0.022	P=0.021
Fisher Exact Test (f)		P<0.001	P<0.001	P=0.023
Pituitary: Adenoma				
Overall Rates (c)	49/87 (56%)	31/124 (25%)	51/173 (29%)	
Adjusted Rates (d)	68.5%	60.6%	80.5%	
Terminal Rates (e)	33/55 (60%)	4/16 (25%)	18/27 (67%)	
Life Table Test (f)		P=0.054	P=0.005	P=0.472
Incidental Tumor Test (f)		P=0.009N	P=0.225N	P=0.337
Fisher Exact Test (f)		P<0.001N	P<0.001N	P=0.236
Pituitary: Carcinoma				
Overall Rates (c)	4/87 (5%)	1/124 (1%)	1/173 (1%)	
Adjusted Rates (d)	6.7%	6.2%	1.3%	
Terminal Rates (e)	3/55 (5%)	1/16 (6%)	0/27 (0%)	
Life Table Test (f)		P=0.601N	P=0.336N	P=0.642N
Incidental Tumor Test (f)		P=0.398N	P=0.104N	P=0.685N
Fisher Exact Test (f)		P=0.094N	P=0.045N	P=0.662N
Pituitary: Adenoma or Carcinoma				
Overall Rates (c)	53/87 (61%)	32/124 (26%)	52/173 (30%)	
Adjusted Rates (d)	73.2%	63.9%	80.8%	
Terminal Rates (e)	36/55 (65%)	5/16 (31%)	18/27 (67%)	
Life Table Test (f)		P=0.064	P=0.011	P=0.497
Incidental Tumor Test (f)		P=0.004N	P=0.095N	P=0.355
Fisher Exact Test (f)		P<0.001N	P<0.001N	P=0.251
Adrenal: Pheochromocytoma				
Overall Rates (c)	8/87 (9%)	6/124 (5%)	8/175 (5%)	
Adjusted Rates (d)	14.2%	19.2%	18.0%	
Terminal Rates (e)	7/55 (13%)	1/16 (6%)	2/27 (7%)	
Life Table Test (f)		P=0.149	P=0.215	P=0.449N
Incidental Tumor Test (f)		P=0.588	P=0.612	P=0.505N
Fisher Exact Test (f)		P=0.166N	P=0.117N	P=0.562N
Adrenal: Pheochromocytoma or Pheochromocytoma, Malignant				
Overall Rates (c)	10/87 (11%)	7/124 (6%)	9/175 (5%)	
Adjusted Rates (d)	17.8%	20.5%	21.2%	
Terminal Rates (e)	9/55 (16%)	1/16 (6%)	3/27 (11%)	
Life Table Test (f)		P=0.156	P=0.228	P=0.407N
Incidental Tumor Test (f)		P=0.589N	P=0.602	P=0.471N
Fisher Exact Test (f)		P=0.101N	P=0.057N	P=0.523N

TABLE E6. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

	CONTROL (UNTR)	DMH (a)	IR + DMH (b)	DMH vs IR + DMH
Thyroid: Follicular Cell Adenoma				
Overall Rates (c)	6/87 (7%)	7/124 (6%)	9/174 (5%)	
Adjusted Rates (d)	10.9%	24.4%	18.6%	
Terminal Rates (e)	6/55 (11%)	3/16 (19%)	3/27 (11%)	
Life Table Test (f)		P=0.036	P=0.086	P=0.424N
Incidental Tumor Test (f)		P=0.206	P=0.314	P=0.533N
Fisher Exact Test (f)		P=0.462N	P=0.379N	P=0.527N
Thyroid: Follicular Cell Carcinoma				
Overall Rates (c)	1/87 (1%)	5/124 (4%)	7/174 (4%)	
Adjusted Rates (d)	1.8%	14.4%	14.0%	
Terminal Rates (e)	1/55 (2%)	1/16 (6%)	2/27 (7%)	
Life Table Test (f)		P=0.015	P=0.014	P=0.541N
Incidental Tumor Test (f)		P=0.150	P=0.081	P=0.558N
Fisher Exact Test (f)		P=0.211	P=0.191	P=0.610N
Thyroid: Follicular Cell Adenoma or Carcinoma				
Overall Rates (c)	7/87 (8%)	12/124 (10%)	16/174 (9%)	
Adjusted Rates (d)	12.7%	36.3%	30.7%	
Terminal Rates (e)	7/55 (13%)	4/16 (25%)	5/27 (19%)	
Life Table Test (f)		P=0.001	P=0.004	P=0.391N
Incidental Tumor Test (f)		P=0.055	P=0.068	P=0.483N
Fisher Exact Test (f)		P=0.440	P=0.478	P=0.521N
Thyroid: C-Cell Adenoma				
Overall Rates (c)	11/87 (13%)	9/124 (7%)	18/174 (10%)	
Adjusted Rates (d)	18.5%	28.7%	32.1%	
Terminal Rates (e)	9/55 (16%)	2/16 (13%)	4/27 (15%)	
Life Table Test (f)		P=0.072	P=0.019	P=0.348
Incidental Tumor Test (f)		P=0.474	P=0.398	P=0.287
Fisher Exact Test (f)		P=0.141N	P=0.358N	P=0.241
Thyroid: C-Cell Carcinoma				
Overall Rates (c)	11/87 (13%)	9/124 (7%)	12/174 (7%)	
Adjusted Rates (d)	17.0%	35.5%	21.5%	
Terminal Rates (e)	6/55 (11%)	4/16 (25%)	1/27 (4%)	
Life Table Test (f)		P=0.093	P=0.225	P=0.410N
Incidental Tumor Test (f)		P=0.537	P=0.188N	P=0.450N
Fisher Exact Test (f)		P=0.141N	P=0.097N	P=0.539N
Thyroid: C-Cell Adenoma or Carcinoma				
Overall Rates (c)	21/87 (24%)	17/124 (14%)	29/174 (17%)	
Adjusted Rates (d)	32.3%	55.1%	45.2%	
Terminal Rates (e)	14/55 (25%)	6/16 (38%)	5/27 (19%)	
Life Table Test (f)		P=0.017	P=0.015	P=0.472
Incidental Tumor Test (f)		P=0.467	P=0.397N	P=0.381
Fisher Exact Test (f)		P=0.040N	P=0.102N	P=0.298
Mammary Gland: Adenoma				
Overall Rates (c)	6/88 (7%)	2/125 (2%)	5/175 (3%)	
Adjusted Rates (d)	10.9%	5.3%	9.2%	
Terminal Rates (e)	6/55 (11%)	0/16 (0%)	1/27 (4%)	
Life Table Test (f)		P=0.627N	P=0.441	P=0.443
Incidental Tumor Test (f)		P=0.436N	P=0.548N	P=0.404
Fisher Exact Test (f)		P=0.055N	P=0.120N	P=0.382
Mammary Gland: Fibroadenoma				
Overall Rates (c)	49/88 (56%)	36/125 (29%)	41/175 (23%)	
Adjusted Rates (d)	76.1%	82.1%	70.7%	
Terminal Rates (e)	40/55 (73%)	10/16 (63%)	13/27 (48%)	
Life Table Test (f)		P<0.001	P=0.036	P=0.059N
Incidental Tumor Test (f)		P=0.269	P=0.206N	P=0.030N
Fisher Exact Test (f)		P<0.001N	P<0.001N	P=0.180N

TABLE E6. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS PLUS 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE (Continued)

	CONTROL (UNTR)	DMH (a)	IR + DMH (b)	DMH vs IR + DMH
Mammary Gland: Adenocarcinoma				
Overall Rates (c)	5/88 (6%)	0/125 (0%)	1/175 (1%)	
Adjusted Rates (d)	8.4%	0.0%	1.3%	
Terminal Rates (e)	4/55 (7%)	0/16 (0%)	0/27 (0%)	
Life Table Test (f)		P=0.170N	P=0.216N	(g)
Incidental Tumor Test (f)		P=0.087N	P=0.077N	(g)
Fisher Exact Test (f)		P=0.012N	P=0.018N	(g)
Uterus: Endometrial Stromal Polyp				
Overall Rates (c)	13/87 (15%)	7/125 (6%)	15/175 (9%)	
Adjusted Rates (d)	21.2%	19.6%	25.1%	
Terminal Rates (e)	9/55 (16%)	2/16 (13%)	3/27 (11%)	
Life Table Test (f)		P=0.433	P=0.158	P=0.310
Incidental Tumor Test (f)		P=0.195N	P=0.306N	P=0.230
Fisher Exact Test (f)		P=0.021N	P=0.089N	P=0.229
Zymbal Gland: Squamous Cell Carcinoma				
Overall Rates (c)	1/88 (1%)	14/125 (11%)	26/175 (15%)	
Adjusted Rates (d)	1.4%	27.9%	40.2%	
Terminal Rates (e)	0/55 (0%)	0/16 (0%)	5/27 (19%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.338
Incidental Tumor Test (f)		P=0.041	P<0.001	P=0.235
Fisher Exact Test (f)		P=0.003	P<0.001	P=0.229
Zymbal Gland: Squamous Cell Papilloma or Carcinoma				
Overall Rates (c)	1/88 (1%)	15/125 (12%)	28/175 (16%)	
Adjusted Rates (d)	1.4%	30.1%	41.9%	
Terminal Rates (e)	0/55 (0%)	0/16 (0%)	5/27 (19%)	
Life Table Test (f)		P<0.001	P<0.001	P=0.328
Incidental Tumor Test (f)		P=0.024	P<0.001	P=0.224
Fisher Exact Test (f)		P=0.002	P<0.001	P=0.210

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

(b) Administered 1% intermediate-range (IR) chrysotile asbestos in the diet and DMH by gavage

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

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

(e) Observed tumor incidence at terminal kill

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

(g) P value not calculated because of low incidence in both dose groups

APPENDIX F

**INCIDENCES OF TUMORS IN F344/N RATS
RECEIVING NO TREATMENT IN
CONTEMPORARY LIFETIME ASBESTOS STUDIES**

TABLE F1. INCIDENCE OF EPITHELIAL TUMORS OF THE LARGE INTESTINE IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Incidence	Diagnosis
SR Chrysotile	0/87 (0.0%)	
IR Chrysotile	0/85 (0.0%)	
Tremolite	1/118 (0.8%)	Adenomatous polyp, NOS
Crocidolite	1/117 (0.8%)	Adenomatous polyp, NOS
Amosite	0/117 (0.0%)	Carcinoma, NOS
TOTAL	3/524 (0.6%)	
SD (a)	0.8%	

(a) Standard deviation

TABLE F2. INCIDENCE OF INTEGUMENTARY SYSTEM KERATOACANTHOMAS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Incidence
SR Chrysotile	5/88 (6%)
IR Chrysotile	1/88 (1%)
Tremolite	6/118 (5%)
Crocidolite	4/118 (3%)
Amosite	4/117 (3%)
TOTAL	20/529 (3.8%)
SD (a)	1.8%

(a) Standard deviation

TABLE F3. INCIDENCE OF CLITORAL GLAND TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	All Adenoma	All Carcinoma	Adenoma or Carcinoma
SR Chrysotile	1/88 (1%)	2/88 (2%)	3/88 (3%)
IR Chrysotile	0/88 (0%)	1/88 (1%)	1/88 (1%)
Tremolite	0/118 (0%)	6/118 (5%)	6/118 (5%)
Crocidolite	1/118 (1%)	5/118 (4%)	6/118 (5%)
Amosite	0/117 (0%)	6/117 (5%)	6/117 (5%)
TOTAL	2/529 (0.4%)	20/529 (3.8%)	22/529 (4.2%)
SD (a)	0.6%	1.8%	1.7%

(a) Standard deviation

TABLE F4. INCIDENCE OF ADRENAL GLAND TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	Pheochromocytoma	Malignant Pheochromocytoma	All Pheochromocytoma
SR Chrysotile	25/88 (28%)	2/88 (1%)	26/88 (30%)
IR Chrysotile	16/85 (19%)	1/85 (1%)	17/85 (20%)
Tremolite	38/118 (32%)	3/118 (3%)	41/118 (35%)
Crocidolite	33/117 (28%)	2/117 (2%)	35/117 (30%)
Amosite	39/117 (33%)	3/117 (3%)	39/117 (33%)
TOTAL	151/525 (28.8%)	10/525 (1.9%)	158/525 (30.1%)
SD (a)	5.7%	0.7%	5.8%

(a) Standard deviation

TABLE F5. INCIDENCE OF MESOTHELIOMAS IN MALE F344/N RATS RECEIVING NO TREATMENT IN LIFETIME STUDIES

Asbestos Studies	NOS	Malignant	Malignant or NOS
SR Chrysotile	0/88 (0%)	2/88 (2%)	2/88 (2%)
IR Chrysotile	3/88 (3%)	2/88 (2%)	5/88 (6%)
Tremolite	0/118 (0%)	10/118 (8%)	10/118 (8%)
Crocidolite	1/118 (1%)	4/118 (3%)	5/118 (4%)
Amosite	0/117 (0%)	2/117 (2%)	2/117 (2%)
TOTAL	4/529 (1%)	20/529 (4%)	24/529 (5%)
SD (a)	1.5%	2.8%	2.7%

(a) Standard deviation

APPENDIX G

**ANALYSIS OF FORMULATED DIETS AND
DOSE MIXTURES**

APPENDIX G. ANALYSIS OF DIETS AND DOSE MIXTURES

I. Analysis of Formulated Diets (Illinois Institute of Technology Research Institute)

A. Ashing Procedure

Five pellets were taken from each formulated diet and seven pellets from the untreated control diet. Each pellet was individually crushed and transferred to a tared crucible. The sample size was 350-500 mg of asbestos-containing diet and 1,000-1,500 mg of control diet in each crucible. The sample size was selected on the basis of the linear range of atomic absorption and the average background concentration of magnesium in the diet.

The crucibles containing the diet were placed in a muffle furnace. The temperature was raised slowly to 550° C to prevent loss of material by flashing and maintained overnight. The ashed samples were cooled to room temperature before being chemically digested.

B. Chemical Digestion

The chemical resistance of chrysotile asbestos to acids is poor; therefore, magnesium, a major constituent of chrysotile, can be extracted by hydrochloric acid.

The ashed samples were quantitatively transferred to 100-ml beakers through the use of distilled water. Twenty milliliters of a 1:1:2 solution of nitric and hydrochloric acid in distilled water were added to each beaker. The samples were placed on a hot plate and gently boiled for 8 hours; hydrochloric acid and distilled water were added to maintain the 20-ml volume. Any sample evaporated to dryness was discarded. The samples were cooled and diluted.

C. Dilution of Samples for Atomic Absorption

The sample dilution procedure included the addition of potassium (K^+), lanthanum (La^{3+}), and hydrochloric acid from a stock solution to the volumetric flask. The potassium ion conditions the flame; the lanthanum complexes with potentially interfering phosphates; and the hydrochloric acid assures a pH less than 3 in each sample. The final dilution contained 100 mg/liter of K^+ and 30 mg/liter of La^{3+} . The sample was quantitatively transferred to the volumetric flask and dilution was completed. If digestion or silica removal was incomplete, the dilution would be cloudy and the sample discarded.

D. Atomic Absorption Analysis

Atomic absorption spectroscopy provides sensitive, precise analysis for magnesium at low concentrations. Standards, treated as the samples, were used to determine calibration curves. A linear calibration curve from 0 to 2 mg/liter for magnesium is typical. Calibration data were taken immediately before the sample data and at the conclusion of the sample run; spot checks were made throughout each sample set. The instrument response was converted to concentration by a calibration curve. Samples greater than 110% of the highest standard were diluted and reanalyzed.

E. Results

Results are presented in Tables G1 and G2.

TABLE G1. ANALYSIS OF FORMULATED DIETS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS

Date Mixed	Determined Concentration in Feed for Target Concentration of 10,000 ppm (1%)
11/21/77	8,500 ± 400
12/07/77	11,100 ± 600
12/07/77	10,000 ± 600
02/01/78	9,100 ± 900
03/22/78	10,900 ± 4,500
05/22/78	9,300 ± 600
07/11/78	8,600 ± 500
09/14/78	8,900 ± 1,200
10/30/78	8,000 ± 400
12/11/78	9,300 ± 1,700
02/15/79	10,600 ± 400
04/06/79	10,700 ± 600
05/19/79	10,600 ± 500
06/26/79	8,700 ± 100
08/28/79	9,700 ± 600
10/16/79	9,100 ± 400
12/03/79	9,300 ± 900
01/10/80	8,600 ± 200
02/27/80	11,700 ± 1,600
04/18/80	9,000 ± 1,200
05/29/80	11,900 ± 900
07/18/80	10,000 ± 1,100
	Mean = 9,700 ± 2,100

TABLE G2. ANALYSIS OF FORMULATED DIETS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Date Mixed	Determined Concentration in Feed for Target Concentration of 10,000 ppm (1%)
11/21/77	8,900 ± 1,000
12/07/77	10,200 ± 500
12/07/77	10,800 ± 800
12/07/77	10,400 ± 1,000
02/10/78	10,200 ± 1,100
02/01/78	10,400 ± 1,400
03/22/78	10,900 ± 700
03/22/78	11,000 ± 1,000
05/22/78	10,200 ± 700
05/22/78	9,900 ± 2,300
07/11/78	9,300 ± 300
07/11/78	9,100 ± 700
09/14/78	9,000 ± 400
09/14/78	9,100 ± 1,200
10/30/78	9,100 ± 200
10/30/78	8,500 ± 900
12/15/78	10,400 ± 1,200
12/15/78	10,900 ± 800
02/15/79	10,200 ± 2,600
02/15/79	11,100 ± 500
04/06/79	11,000 ± 500
04/60/79	11,600 ± 2,400
05/09/79	10,000 ± 1,000
05/09/79	10,700 ± 700
06/26/79	9,500 ± 500
08/28/79	10,000 ± 500
08/28/79	9,900 ± 500
10/16/79	11,500 ± 200
10/16/79	10,200 ± 100
12/03/79	9,900 ± 500
12/03/79	10,700 ± 400
01/10/80	9,400 ± 400
01/10/80	10,100 ± 600
02/27/80	12,900 ± 800
02/27/80	12,900 ± 900
04/18/80	9,100 ± 300
05/29/80	11,400 ± 1,000
05/29/80	10,200 ± 900
07/18/80	10,000 ± 2,000
	Mean = 10,272 ± 983

APPENDIX G. ANALYSIS OF DIETS AND DOSE MIXTURES

II. 1,2-Dimethylhydrazine Dihydrochloride (DMH) Solution Analysis (Hazleton Laboratories, America)

- Solutions were analyzed approximately 1 hour before dosing and the evening after dosing. A colorimetric method was followed which used pentacyanoamino ferrate as the color reagent and DMH as the standard.
- A fresh aqueous $\text{Na}_3[\text{Fe}(\text{CN})_5\text{NH}_4]$ (sodium pentacyanoamino ferrate) solution (20 mg/ml) was prepared daily.
- A fresh stock solution of DMH in 0.2 M acetate buffer pH 5.0 (200 $\mu\text{g}/\text{ml}$) also was prepared daily and kept on ice after preparation.
- A borate buffer (0.05 M) was adjusted to pH 8.5 with 0.1 M sodium hydroxide.
- The required amounts of dosing solution were prepared in glass containers with acetate buffer as the solvent.
- Aliquots of each dosing solution were taken before dosing for a qualitative determination by a UV scan from 350 nm to 220 nm, which was run on a Beckman DK-2A Spectrophotometer with acetate buffer as the reference.
- Colorimetric quantitative analysis of samples collected before and after dosing was performed by the addition of 2.5 ml of the pentacyanoamino solution (0.2 ml stock diluted with 7.8 ml borate buffer) to 0.5 ml of sample or 0.5 ml of reference (acetate buffer); 0.05 ml of 50% aqueous hydrochloric acid was added to both solutions, and they were mixed thoroughly. The color was read immediately at 536 nm on a spectrophotometer.
- The results were compared with a standard curve for DMH.

TABLE G3. ANALYSIS OF DOSE MIXTURES OF 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS (a)

Dosing Date		Sex	Gravimetric Concentration (mg/ml)	Analytical Concentration (mg/ml)	
02/22/78	Predose	Male	3.84	2.70	
		Female	7.79	2.70 4.56 5.06	
	Postdose	Male	--	2.27	
		Female	--	2.53 4.05 4.19	
	03/08/78	Predose	Male	3.87	3.85
			Female	7.73	3.92 7.40 7.54
Postdose		Male	--	1.62	
		Female	--	2.02 3.75 2.80	
03/22/78		Predose	Male	3.87	2.70
			Female	7.76	2.92 7.40 7.40
	Postdose	Male	--	2.20	
		Female	--	2.40 4.20 3.80	
	04/05/78	Predose	Male	3.88	1.27
			Female	7.66	1.20 5.20 5.30
Postdose		Male	--	2.65	
		Female	--	2.65 5.30 5.30	
04/19/78		Predose	Male	3.88	2.36
			Female	7.75	2.92 6.83 5.35
	Postdose	Male	--	2.53	
		Female	--	1.91 2.36 2.92	

(a) Values represent milligrams of 1,2-dimethylhydrazine dihydrochloride per milliliter of acetate buffer.

APPENDIX H

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

TABLE H1. FEED AND COMPOUND CONSUMPTION BY MALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS

Week	Control		Dosed Group			
	Grams Feed/Day (a)	Body Weight (grams)	Grams Feed/Day (a)	Body Weight (grams)	Dosed/Control (b) (grams)	Dose/Day (c)
7	16	152	16	156	1.0	1,053
8	17	175	18	182	1.0	965
9	16	200	17	205	1.1	843
10	16	222	18	224	1.1	823
12	17	250	17	254	1.0	681
13	17	262	17	267	1.0	642
14	16	271	17	275	1.1	629
15	16	280	17	285	1.0	586
16	16	283	17	290	1.0	581
17	18	295	15	291	0.8	515
18	14	301	17	299	1.2	554
19	17	310	17	308	1.0	552
20	17	314	18	316	1.0	556
30	18	366	18	356	1.0	502
40	16	394	17	396	1.1	437
50	18	423	18	424	1.0	431
60	17	430	17	429	1.0	386
70	17	452	18	451	1.0	393
80	18	467	16	462	0.9	343
90	17	470	17	470	1.0	368
100	16	461	16	456	1.0	351
110	16	444	15	430	0.9	339
120	17	430	15	411	0.9	361
130	15	376	16	383	1.1	410
Mean	17	334	17	334	1.0	554
SD (d)	1.0		1.0		0.1	199.7
CV (e)	5.7		6.1		8.1	36.0

- (a) Grams of feed removed from feed hopper per animal per day. Not corrected for scatter.
 (b) Grams of feed per day for the dosed group divided by that for the controls
 (c) Milligrams of short-range chrysotile asbestos consumed per day per kilogram of body weight
 (d) Standard deviation
 (e) Coefficient of variation = (standard deviation/mean) × 100

TABLE H2. FEED AND COMPOUND CONSUMPTION BY FEMALE RATS IN THE LIFETIME FEED STUDY OF SHORT-RANGE CHRYSOTILE ASBESTOS

Week	Control		Dosed Group			
	Grams Feed/Day (a)	Body Weight (grams)	Grams Feed/Day (a)	Body Weight (grams)	Dosed/Control (b) (grams)	Dose/Day (c)
7	13	124	12	129	1.0	941
8	13	135	12	139	0.9	874
9	12	143	13	149	1.0	844
10	13	153	13	156	1.0	824
12	13	163	12	168	0.9	714
13	12	167	13	172	1.0	731
14	13	170	13	175	1.0	751
15	12	175	13	180	1.0	706
16	13	174	12	180	1.0	675
17	12	181	11	180	0.9	611
18	10	182	12	181	1.2	655
19	12	187	12	185	1.0	664
20	12	188	13	189	1.1	673
30	12	206	12	204	1.0	595
40	12	220	12	223	1.0	545
50	13	247	14	244	1.0	556
60	15	262	13	269	0.9	478
70	14	290	14	291	1.0	491
80	14	311	14	316	1.0	429
90	14	326	14	331	1.0	423
100	16	332	13	328	0.8	405
110	14	324	13	308	0.9	408
120	14	326	14	312	1.0	453
130	14	303	12	291	0.9	417
140	14	293	13	279	1.0	471
Mean	13	223	13	223	1.0	613
SD (d)	1.3		0.8		0.1	160.4
CV (e)	9.6		6.2		7.9	26.1

(a) Grams of feed removed from feed hopper per animal per day. Not corrected for scatter.

(b) Grams of feed per day for the dosed group divided by that for the controls

(c) Milligrams of short-range chrysotile asbestos consumed per day per kilogram of body weight

(d) Standard deviation

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

TABLE H3. FEED AND COMPOUND CONSUMPTION BY MALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Week	Control		IR				IR/PW			
	Grams Feed/Day (a)	Body Weight (grams)	Grams Feed/Day (a)	Body Weight (grams)	IR/Control (b) (grams)	Dose/Day (c)	Grams Feed/Day (a)	Body Weight (grams)	IR/PW/Control (b) (grams)	Dose/Day (c)
8	15	134	15	136	1.0	1,103	16	148	1.1	1,110
9	16	159	16	160	1	991	17	166	1.1	1,024
10	16	183	16	180	1	889	16	195	1	828
11	16	203	16	197	1	805	16	221	1	737
12	17	218	16	216	1	761	17	234	1	733
13	16	231	17	227	1	736	18	245	1.1	746
14	17	246	14	234	0.9	611	16	254	0.9	613
15	17	256	15	245	0.9	612	16	266	0.9	591
16	16	258	16	257	1	623	17	276	1.1	606
17	16	267	17	267	1	626	16	286	1	574
18	15	278	16	276	1.1	580	17	295	1.1	567
19	17	285	17	281	1	600	17	303	1	556
20	17	294	16	290	1	567	17	312	1	559
21	15	293	17	292	1.1	572	18	319	1.1	555
31	16	344	17	333	1.1	519	18	355	1.1	495
41	17	393	16	371	1	443	16	400	1	404
51	16	402	18	396	1.1	451	19	419	1.1	447
61	17	417	16	401	0.9	388	15	417	0.9	360
71	17	443	17	424	1	408	17	441	1	376
81	17	460	18	433	1	412	18	458	1.1	402
91	16	463	17	432	1.1	384	16	462	1.1	356
101	15	452	16	423	1.1	385	16	447	1.1	355
111	16	446	16	415	1	382	17	426	1	389
121	17	423	15	393	0.9	393	17	405	1	430
131	16	394	17	359	1.1	481	15	373	0.9	406
141	16	352	18	327	1.1	546	16	354	1	440
Mean	16	319	16	306	1.0	587	17	326	1.0	564
SD (d)	0.7		0.9		0.1	194.5	1.0		0.1	200.0
CV (e)	4.6		5.6		7.0	33.1	5.8		6.8	35.5

(a) Grams of feed removed from feed hopper per animal per day. Not corrected for scatter.

(b) Grams of feed per day for the dosed group divided by that for the controls

(c) Milligrams of intermediate-range chrysotile asbestos consumed per day per kilogram of body weight

(d) Standard deviation

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

TABLE H4. FEED AND COMPOUND CONSUMPTION BY FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Week	Control		IR				IR/PW			
	Grams Feed/Day (a)	Body Weight (grams)	Grams Feed/Day (a)	Body Weight (grams)	IR/Control (b) (grams)	Dose/Day (c)	Grams Feed/Day (a)	Body Weight (grams)	IR/PW/Control (b) (grams)	Dose/Day (c)
8	12	119	11	114	0.9	990	12	116	1	1,071
9	12	131	12	126	1	952	13	130	1	967
10	12	141	11	134	0.9	842	12	140	1	847
11	11	144	12	143	1	819	12	151	1	766
12	13	154	11	149	0.9	767	12	155	0.9	765
13	12	158	12	151	1	795	13	159	1.1	791
14	12	165	11	154	0.9	696	11	164	0.9	697
15	12	166	10	157	0.8	646	11	168	0.9	663
16	11	167	12	162	1	723	12	173	1	669
17	11	169	12	166	1.1	723	12	175	1.1	694
18	12	173	11	169	1	668	11	180	1	635
19	12	175	12	171	1	693	12	182	1	636
20	12	180	12	175	1	661	11	184	1	621
21	11	178	12	175	1.1	669	12	189	1.1	627
31	11	196	12	190	1	609	12	201	1.1	597
41	11	219	11	207	0.9	511	11	223	1	512
51	13	235	13	224	1.1	599	13	241	1.1	557
61	12	259	12	251	1	472	11	257	0.9	434
71	13	280	13	272	1	467	14	277	1	490
81	13	303	13	291	1	457	14	303	1.1	453
91	12	323	13	302	1.1	435	12	313	1	397
101	12	330	13	303	1.1	438	14	320	1.2	451
111	14	329	13	303	0.9	420	15	315	1.1	467
121	13	324	12	300	0.9	410	15	315	1.1	463
131	13	308	13	268	1	490	14	301	1.1	465
141	13	286	13	255	1	515	14	287	1	473
Mean (d)	12	216	12	204	1.0	633	12	216	1.0	623
SD (d)	0.8		0.9		0.1	165.8	1.1		0.1	171.0
CV (e)	6.5		7.5		7.4	26.2	9.1		6.8	27.4

(a) Grams of feed removed from feed hopper per animal per day. Not corrected for scatter.

(b) Grams of feed per day for the dosed group divided by that for the controls

(c) Milligrams of intermediate-range chrysotile asbestos consumed per day per kilogram of body weight

(d) Standard deviation

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

TABLE H5. FEED AND COMPOUND CONSUMPTION BY MALE RATS RECEIVING DMH WITH AND WITHOUT INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Week	Control		DMH			DMH plus IR			
	Grams Feed/Day (a)	Body Weight (grams)	Grams Feed/Day (a)	Body Weight (grams)	DMH/Control (b)	Grams Feed/Day (a)	Body Weight (grams)	DMH + IR/Control (b)	Dose/Day (c)
8	15	134	15	131	1.0	15	134	1.0	1,087
9	16	159	15	150	0.9	16	154	1.0	1,030
10	16	183	16	177	1.0	16	181	1.0	876
11	16	203	16	199	1.0	16	197	1.0	798
12	17	218	17	216	1.0	16	214	1.0	741
13	16	231	16	226	1.0	16	221	1.0	718
14	17	246	17	245	1.0	15	233	0.9	638
15	17	256	17	252	1.0	15	242	0.9	620
16	16	258	16	259	1.0	16	253	1.0	638
17	16	267	14	262	0.9	15	261	1.0	591
18	15	278	16	274	1.1	17	270	1.1	619
19	17	285	17	282	1.0	17	277	1.0	619
20	17	294	17	294	1.0	17	281	1.0	605
21	15	293	15	290	1.0	17	288	1.1	595
31	16	344	17	340	1.0	17	332	1.1	521
41	17	393	16	390	0.9	16	370	1.0	429
51	16	402	19	416	1.1	18	390	1.1	465
61	17	417	16	421	0.9	15	402	0.9	370
71	17	443	18	446	1.0	17	423	1.0	395
81	17	460	16	452	0.9	17	426	1.0	402
91	16	463	16	462	1.0	16	437	1.0	373
101	15	452	15	461	1.0	16	421	1.1	390
111	16	446	17	447	1.0	17	407	1.0	421
121	17	423	18	410	1.1	17	387	1.0	443
131	16	394	17	374	1.1	16	362	1.0	430
Mean	16	318	16	315	1.0	16	303	1.0	593
SD (d)	0.7		1.0		0.1	0.9		0.1	198.2
CV (e)	4.6		6.3		5.7	5.6		6.7	33.5

(a) Grams of feed removed from feed hopper per animal per day. Not corrected for scatter.

(b) Grams of feed per day for the dosed group divided by that for the controls

(c) Milligrams of intermediate-range chrysotile asbestos consumed per day per kilogram of body weight

(d) Standard deviation

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

TABLE H6. FEED AND COMPOUND CONSUMPTION BY FEMALE RATS RECEIVING DMH WITH AND WITHOUT INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Week	Control		DMH			DMH plus IR			
	Grams Feed/Day (a)	Body Weight (grams)	Grams Feed/Day (a)	Body Weight (grams)	DMH/Control (b)	Grams Feed/Day (a)	Body Weight (grams)	DMH + IR/Control (b)	Dose/Day (c)
8	12	119	12	115	1.0	11	110	0.9	1,013
9	12	131	12	126	0.9	12	120	0.9	964
10	12	141	12	137	1.0	11	133	1.0	859
11	11	144	11	145	1.0	11	137	1.0	803
12	13	154	11	152	0.9	11	144	0.9	784
13	12	158	12	152	1.0	11	144	0.9	754
14	12	165	12	161	1.0	10	151	0.8	691
15	12	166	12	160	1.0	10	153	0.9	682
16	11	167	12	162	1.0	12	160	1.0	741
17	11	169	10	164	0.9	11	162	1.0	661
18	12	173	12	168	1.0	12	166	1.0	723
19	12	175	13	173	1.1	12	170	1.0	714
20	12	180	12	179	1.0	12	170	1.0	714
21	11	178	11	174	1.0	12	173	1.1	685
31	11	196	11	196	1.0	12	190	1.1	617
41	11	219	11	217	0.9	11	204	1.0	546
51	13	235	14	239	1.1	13	224	1.0	593
61	12	259	13	261	1.0	11	247	0.9	451
71	13	280	13	285	1.0	13	267	1.0	492
81	13	303	13	303	1.0	14	280	1.1	495
91	12	323	13	316	1.0	13	293	1.0	444
101	12	330	13	325	1.1	14	294	1.1	462
111	14	329	16	314	1.1	15	284	1.1	513
Mean	12	204	12	201	1.0	11	190	1.0	670
SD (d)	0.8		1.2		0.1	1.1		0.1	157.2
CV (e)	6.2		10.2		6.5	9.6		8.2	23.5

(a) Grams of feed removed from feed hopper per animal per day. Not corrected for scatter.

(b) Grams of feed per day for the dosed group divided by that for the controls

(c) Milligrams of intermediate-range chrysotile asbestos consumed per day per kilogram of body weight

(d) Standard deviation

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

APPENDIX I

**PATHOGEN BURDEN IN RATS IN THE LIFETIME FEED
STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS**

APPENDIX I. PATHOGEN BURDEN

A. Pathogen Burden Summary: F₀

Sections of brain, heart, lung, spleen, liver, kidney, small intestine, large intestine, salivary gland, urinary bladder, harderian gland, skin, anus, and trachea from eight male and eight female rats were examined microscopically (Tables I1-I3).

Evidence of mild respiratory disease was present in all sections of lung examined. In some rats, small foci of mononuclear cells were present adjacent to the bronchial tissue, and in other rats, small cuffs of lymphoid cells were evident, particularly at the bifurcation of the bronchi. These lesions were very mild.

A section of kidney from one female rat revealed an area of early nephritis with a focal area of regenerative tubule epithelium. This wedge-shaped lesion, producing an area of depression on the capsule, may have resulted from an infarction.

The remaining tissues were not remarkable.

TABLE II. INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F₀ RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS

Organ and Description	Animal Number	Male								Female								
		1 7	1 8	1 9	1 0	1 1	1 2	1 2	1 3	1 4	1 5	1 6	1 7	1 8	1 9	1 0	1 1	1 2
Brain		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Heart		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Lung Minimal peribronchial lymphoid hyperplasia Artificial collapse		1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Spleen		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Liver		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Kidney Regenerative tubule epithelium Early interstitial nephritis		X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
Small intestine		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Large intestine		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Salivary gland		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urinary bladder		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Harderian gland		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Skin		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Anus		X	X	O	X	X	X	X	X	X	O	X	X	X	X	X	X	X
Trachea		X	X	X	O	X	X	X	X	X	X	X	X	X	X	X	X	X

Type of Finding:

- O = Tissue Absent
- X = Tissue Examined and Not Remarkable
- A = Autolysis
- P = Finding Present

Degree of Finding:

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

TABLE 12. MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F₀ RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS

Animal/Specimen Number (a)	Microorganisms Identified (b)
117/3701	3 + Coliform; 1 + <i>Proteus morganii</i>
118/3702	1 + Coliform; 1 + <i>Proteus vulgaris</i>
119/3703	3 + Coliform (3 types)
120/3704	2 + Coliform (2 types)
121/3705	3 + Coliform (2 types)
122/3706	4 + Coliform (2 types); 4 + <i>Proteus vulgaris</i>
123/3707	4 + Coliform; 4 + <i>Proteus vulgaris</i>
124/3708	No growth
125/3709	1 + Coliform
126/3710	1 + Coliform; 1 + <i>Proteus vulgaris</i>
127/3711	2 + Coliform; 1 + <i>Proteus vulgaris</i>
128/3712	2 + Coliform (2 types)
129/3713	1 + Coliform
130/3714	3 + Coliform (2 types); 1 + <i>Proteus vulgaris</i>
131/3715	2 + Coliform (2 types)
132/3716	2 + Coliform (2 types)

(a) Date of specimen: 9/28/77

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

TABLE 13. MURINE VIRUS ANTIBODY DETERMINATION IN F₀ RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS

Sample Number	Complement Fixation	
	Sendai	LCM
701	-	-
702	-	-
703	-	-
704	-	-
705	-	-
706	-	-
707	-	-
708	-	-
709	-	-
710	-	-
711	-	-
712	-	-
713	-	-
714	-	-
715	-	-
716	-	-
Significant titer	10	10

APPENDIX I. PATHOGEN BURDEN

B. Pathogen Burden Summary: F₁

Sections of brain, heart, lung, spleen, liver, kidney, small intestine, large intestine, salivary gland, urinary bladder, harderian gland, skin, anus, and trachea were examined from four males and four females in the untreated control group and four males and four females in the 1% SR chrysotile group that were killed for pathology burden (Tables I4 and I5).

Evidence of early spontaneous respiratory disease was present in the lungs of all rats examined. In one control male and two SR chrysotile males, only small foci of mononuclear cells were present adjacent to the bronchioles. In the remaining rats, minimal-to-slight peribronchial lymphoid hyperplasia was present. Agonal hemorrhage occurred in one control female.

In sections of kidney, foci of regenerative tubule epithelium and foci of mononuclear cells were noted in one control male. Foci of mineralization were noted at the corticomedullary junction of two females in the control and SR chrysotile groups.

Focal nonsuppurative tracheitis occurred in one control male.

The remaining tissues examined were not remarkable.

TABLE 14. INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F₁ RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS

Organ and Description	Animal Number	Untreated Control								Short-Range							
		Male				Female				Male				Female			
		1	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2
		9	9	9	0	0	0	0	0	0	0	0	0	0	1	1	1
		7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2
Brain		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Heart		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Lung																	
Foci of mononuclear cells		P							P								
Peribronchial lymphoid hyperplasia			1	2	2	2		1	2	1	1	1	1	2	1	2	2
Agonal hemorrhage										P							
Spleen		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Liver		X	X	X	X	X	X	X	X			X	X	X	X	X	X
Nonsuppurative pericholangitis										1	1						
Kidney		X	X	X		X	X	X	X			X	X		O		X
Foci of regenerative tubule epithelium					P												
Foci of mononuclear cells					P												
Foci of mineralization										P	P			P		P	
Small intestine		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Large intestine		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Salivary gland		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urinary bladder		X	X	O	X	X	X	X	X	X	X	X	X	X	X	X	X
Harderian gland		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Skin		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Anus		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Trachea		X	X	X		X	X	X	X	X	X	X	X	X	X	X	X
Focal nonsuppurative tracheitis					P												

Type of Finding:

- O = Tissue Absent
- X = Tissue Examined and Not Remarkable
- A = Autolysis
- P = Finding Present

Degree of Finding:

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

TABLE 15. MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F₁ RATS IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS

Animal/Specimen Number (a)	Microorganisms Identified (b)
197/3880	3+ Group D Streptococcus; 1+ Micrococcus; 1+ Coliform; 1+ <i>Proteus vulgaris</i>
198/3881	1+ Coliform; 4+ Group D Streptococcus; 3+ Micrococcus
199/3882	1+ Coliform; 3+ Group D Streptococcus; 3+ Micrococcus
200/3883	1+ Coliform; 3+ Group D Streptococcus; 3+ Micrococcus
201/3884	1+ Coliform; 3+ Group D Streptococcus; 3+ Micrococcus
202/3885	1+ Coliform; 1+ <i>Proteus vulgaris</i> ; 3+ Group D Streptococcus; 3+ Micrococcus
203/3886	1+ Coliform; 4+ Group D Streptococcus
204/3887	1+ Coliform; 1+ <i>Proteus vulgaris</i> ; 4+ Group D Streptococcus; 1+ Micrococcus
205/3888	1+ <i>Proteus vulgaris</i> ; 4+ Group D Streptococcus; 4+ <i>Staphylococcus epidermidis</i> ; 3+ Micrococcus
206/3889	1+ Coliform; 4+ Group D Streptococcus; 4+ <i>Staphylococcus epidermidis</i> ; 1+ <i>Proteus vulgaris</i>
207/3890	4+ Group D Streptococcus; 3+ Micrococcus
208/3891	1+ Coliform; 3+ Group D Streptococcus; 3+ <i>Staphylococcus epidermidis</i>
209/3892	1+ Coliform; 3+ Micrococcus; 1+ <i>Proteus vulgaris</i> ; 3+ <i>Staphylococcus epidermidis</i> ; 3+ Group D Streptococcus
210/3893	1+ Coliform; 3+ <i>Staphylococcus epidermidis</i>
211/3894	No growth
212/3895	1+ Coliform; 1+ <i>Proteus vulgaris</i> ; 3+ <i>Staphylococcus epidermidis</i>

(a) Date of specimen: 1/26/78

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

APPENDIX J

**PATHOGEN BURDEN IN RATS IN THE LIFETIME FEED
STUDIES OF INTERMEDIATE-RANGE
CHRYOTILE ASBESTOS**

APPENDIX J. PATHOGEN BURDEN

I. Pathogen Burden Procedures

A. Types of Specimens Obtained:

1. Feces: flotation Bac-T and stereomicroscopic dissection
2. Blood: smear and staining (intracellular parasites)
3. Tracheal wash: mycoplasma
4. Body tissue: gross necropsy, histopathologic examination, and Bac-T
5. Blood serum: viral antibody profile
6. Scotch Tape impression slides: microscopic for ectoparasites

B. Methods

1. Fecal Flotation: modified zinc sulfate concentration method

- a. Zinc sulfate (USP) solution ($ZnSO_4$) at a specific gravity of 1.118 and a small aliquot of fecal material (15:1) are mixed in a standard centrifuge tube until well suspended.
- b. $ZnSO_4$ is added to the suspension until the tube is in a near overflow position.
- c. A slide coverslip is placed over the top of the centrifuge tube and allowed to stand for a minimum of 5 minutes.
- d. The slide coverslip is then removed and placed on an appropriately sized microscope slide for examination. (One drop of Iodine Stain for wet-mount fecal examination was employed infrequently in some cases.)
- e. Composite fecal samples for flotation were obtained from three sites: lower colon, cecum, and jejunum.
- f. Fecal samples from these sites were also dissected and examined under a stereomicroscope for the presence of endoparasites.
- g. Fecal samples from the colon were transported to the diagnostic microlaboratory in buffer glyceriated saline and cultured in the appropriate media for isolation and identification of enteric pathogens.

2. Blood

- a. Whole blood films (two each) were made of each animal by the blood smear technique. These films were in turn stained (Wright's) and microscopically examined for the presence of blood parasites.
- b. Approximately 1 ml of whole blood for serum harvest was obtained for viral antibody profile using aseptic technique. Whole blood samples were centrifuged. The serum was harvested, diluted 1:5 in 1N saline, and heat inactivated before shipment to an outside commercial laboratory for analysis.

APPENDIX J. PATHOGEN BURDEN

3. Tracheal Wash (Lung)

Aseptic tracheal washes with physiologic saline (one per animal) were obtained and placed in appropriate media for mycoplasma culture and identification.

4. Body Tissue

a. Aseptically obtained sections of spleen and lung were placed in appropriate media and cultured for the presence of pathogenic organisms.

b. Body tissues as outlined for each 840 series study (16 tissues) were examined grossly at necropsy and placed in 10% neutral buffered formalin for histopathologic examination.

5. Scotch Tape Impression Slides

Ordinary scotch tape was pressed firmly against both the anus (perianal fold) and the hair covering at the anterior dorsum aspect of the neck. The tape was then applied to an ordinary microscopic slide for low-power microscopic examination for ectoparasites and/or migratory intestinal parasites (pinworms).

II. Pathogen Burden Summary: F₀

Sections of brain, heart, lung, spleen, liver, kidney, small intestine, large intestine, salivary gland, urinary bladder, harderian gland, skin, anus, and trachea from eight male and eight female rats were examined microscopically (Tables J1 and J2).

Evidence of early chronic respiratory disease was present in all animals: minimal-to-moderate peribronchial lymphoid hyperplasia (six males, seven females); focal accumulations of mononuclear cells (two males); focal accumulations of alveolar macrophages (one female); and minimal lymphoid hyperplasia (one female).

Lymphoid hyperplasia was present in the spleen and cervical lymph nodes of a single female.

In sections of liver, minimal nonsuppurative pericholangitis was present in two males. In sections of kidney, minimal focal interstitial nephritis, characterized by focal accumulations of mononuclear inflammatory cells, was present in two males and one female.

The remaining tissues were not remarkable.

TABLE J1. INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F₀ RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Organ and Description	Animal Number	Male								Female								
		1 3	1 3	1 3	1 3	1 3	1 3	1 3	1 3	1 3	1 3	1 3	1 3	1 3	1 3	1 3	1 3	
Brain		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Heart		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Lung														X				
Peribronchial lymphoid hyperplasia			1		2	2	1	2	3	1	1	1	1			2	1	2
Artifactual collapse			P				P						P					
Foci of mononuclear cells		P		P														
Perivascular lymphoid hyperplasia																		1
Accumulations of alveolar macrophages																	P	
Spleen		X	X	X	X	X	X	X	X	X	X			X	X	X	X	X
Lymphoid hyperplasia												P						
Liver		X	X			X	X	X	X	X	X	X	X	X	X	X	X	X
Nonsuppurative pericholangitis				1	1													
Kidney		X	X	X	X		X		X	X	X	X	X			X	X	X
Focal interstitial nephritis						1		1						1				
Small intestine		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Large intestine		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Salivary gland		X	O	X	X	X	X	X	X	X	X	X	X	X	O	X	X	X
Urinary bladder		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Harderian gland		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	O
Skin		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Anus		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Trachea		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Cervical lymph nodes																		
Lymphoid hyperplasia												P						

Type of Finding:

- O = Tissue Absent
- X = Tissue Examined and Not Remarkable
- A = Autolysis
- P = Finding Present

Degree of Finding:

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

TABLE J2. MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F₀ RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Animal/Specimen Number (a)	Microorganisms Identified (b)
133/3726	1 + Coliform
134/3727	1 + Coliform
135/3728	1 + Coliform; 1 + <i>Proteus vulgaris</i>
136/3729	1 + Coliform
137/3730	1 + Coliform; 1 + <i>Proteus vulgaris</i>
138/3731	1 + Coliform
139/3732	1 + Coliform
140/3733	1 + Coliform
141/3734	No growth
142/3735	2 + Coliform
143/3736	1 + Coliform; 1 + <i>Proteus vulgaris</i>
144/3737	1 + Coliform
145/3738	1 + Coliform
146/3739	1 + Coliform
147/3740	2 + Coliform; 1 + <i>Proteus vulgaris</i>
148/3741	1 + Coliform

(a) Date of specimen: 10/13/77

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

APPENDIX J. PATHOGEN BURDEN

III. Pathogen Burden Summary: F₁

Sections of brain, heart, lung, spleen, liver, kidney, small intestine, large intestine, salivary gland, urinary bladder, harderian gland, skin, and anus were examined from four males and four females in the control and dosed groups of the F₁ generation which were killed for pathology burden (Tables J3-J5).

Evidence of early chronic respiratory disease, consisting of minimal-to-slight peribronchial lymphoid hyperplasia, was present in nearly all animals.

In sections of kidney, small foci of regenerative tubule epithelium were noted in the cortex of one dosed male. Small foci of mineralization were noted in the medullary of one dosed and two control females.

The remaining tissues examined were not remarkable.

TABLE J3. MURINE VIRUS ANTIBODY DETERMINATION IN F₁ RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Sample Number	Complement Fixation	
	Sendai	LCM
197	-	-
198	-	-
199	-	-
200	-	-
201	-	-
202	-	-
203	-	-
204	-	-
205	-	-
206	-	-
207	-	-
208	-	-
209	-	-
210	-	-
211	-	-
212	-	-
Significant titer	10	10

TABLE J4. INDIVIDUAL HISTOPATHOLOGIC FINDINGS IN F₁ RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Organ and Description	Animal Number	Untreated Control								Intermediate-Range							
		Male				Female				Male				Female			
		2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
1	1	1	1	2	2	2	2	1	1	1	2	2	2	2	2		
		3	4	5	6	1	2	3	4	7	8	9	0	5	6	7	8
Brain		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Heart		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Lung										X							
Peribronchial lymphoid hyperplasia		1	1	1	2	1	1	1	1	1		2	1	1	1	1	2
Spleen		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Liver		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Kidney		X	X	X	X		X	X	X	X	X	X			X	X	X
Foci of regenerative tubule epithelium													P				
Foci of mineralization							P								P		
Small intestine		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Large intestine		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Salivary gland		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urinary bladder		X	X	X	X	O	O	O	X	X	X	X	X	X	X	O	X
Lacrimal gland		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Skin		X	X	X	X	X	O	X	X	X	O	X	X	X	X	X	X
Anus		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Type of Finding:

- O = Tissue Absent
- X = Tissue Examined and Not Remarkable
- A = Autolysis
- P = Finding Present

Degree of Finding:

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

TABLE J5. MICROSCOPIC EXAMINATION FOR ENDOPARASITES AND BACTERIA IN F₁ RATS IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS

Animal/Specimen Number (a)	Microorganisms Identified (b)
213/3897	4 + Group D Streptococcus; 1 + Micrococcus; 3 + Coliform; 1 + <i>Pseudomonas aeruginosa</i>
214/3898	1 + Coliform; 4 + Group D Streptococcus; 3 + Bacillus; 1 + <i>Proteus vulgaris</i>
215/3899	1 + Coliform; 4 + Group D Streptococcus; 1 + Micrococcus; 4 + Diphtheroids
216/3900	1 + Coliform; 4 + Group D Streptococcus; 1 + Micrococcus; 4 + Diphtheroids; 1 + <i>Staphylococcus epidermidis</i>
217/3901	1 + Coliform; 4 + Group D Streptococcus; 4 + Diphtheroids
218/3902	2 + Bacillus; 3 + Group D Streptococcus; 1 + <i>Pseudomonas aeruginosa</i>
219/3903	1 + Coliform; 4 + Group D Streptococcus; 3 + Micrococcus; 4 + Diphtheroids; 1 + <i>Proteus vulgaris</i> ; 1 + <i>Pseudomonas aeruginosa</i>
220/3904	3 + Bacillus; 4 + Group D Streptococcus; 3 + Micrococcus; 1 + <i>Pseudomonas aeruginosa</i>
221/3905	3 + Coliform; 4 + Group D Streptococcus; 1 + Micrococcus; 4 + Diphtheroids; 1 + <i>Proteus morganii</i>
222/3906	1 + Coliform; 1 + <i>Proteus morganii</i> ; 4 + Group D Streptococcus; 3 + Micrococcus; 3 + Diphtheroids
223/3907	1 + Bacillus; 4 + Group D Streptococcus; 1 + Micrococcus
224/3908	1 + Coliform; 4 + Diphtheroids; 4 + Group D Streptococcus; 2 + Micrococcus
225/3909	1 + <i>Proteus vulgaris</i> ; 4 + Group D Streptococcus; 1 + Coliform; 1 + Micrococcus
226/3910	1 + Micrococcus; 4 + Group D Streptococcus; 1 + <i>Pseudomonas aeruginosa</i>
227/3911	1 + Coliform; 4 + Group D Streptococcus; 3 + <i>Proteus vulgaris</i> ; 1 + Micrococcus
228/3912	1 + Coliform; 1 + Micrococcus; 1 + <i>Proteus vulgaris</i> ; 4 + Group D Streptococcus

(a) Date of specimen: 2/9/78

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

APPENDIX K

**CLINICAL SIGNS IN RATS IN THE
LIFETIME FEED STUDIES OF SHORT-RANGE
CHRYSOTILE ASBESTOS**

TABLE K2. SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF SHORT-RANGE CHRYSOTILE ASBESTOS: SHORT-RANGE (a)
(Continued)

	<u>Weeks 95-99</u>		<u>Weeks 100-104</u>	
	Male	Female	Male	Female
Depressed	3	6	7	11
Labored respiration				1
Wheezing	1		1	
Abdomen distended and/or firm			1	
Palpable mass in abdomen	5	5	9	4
Nodule(s)			1	1
Tissue mass (abscessed)--head, back, ear, abdomen, axilla, neck, inguinal, side, lower midline, or flank	3	5		6
Unkempt			2	
Cold to touch		2	1	1
Rough haircoat	1			
Prostrate in cage	1		1	2
Alopecia		1		
Urine stains		1		1
Malocclusion				1
Loss of righting reflex	1		1	2
Loss of equilibrium			2	3
Muscle tone flaccid	2	1	1	1
Paralysis or partial paralysis in hindlegs	2		3	
Inactive	1		1	
Extremities appeared yellow			1	
Discharge from anus	1			
Right hindleg was stiff, swollen, immobile; sores on surface	1			

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

APPENDIX L

**CLINICAL SIGNS IN RATS IN THE
LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE
CHRYSOTILE ASBESTOS**

TABLE L1. SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: UNTREATED CONTROL (a)

	<u>Weeks 63-67</u>		<u>Weeks 68-73</u>		<u>Weeks 74-78</u>		<u>Weeks 79-83</u>	
	Male	Female	Male	Female	Male	Female	Male	Female
Number of animals killed in moribund condition					2	1		1
Number of animals with no clinical signs reported					1			
Thin						1		1
Wheezing								1
Tissue mass--chest								1
Loss of equilibrium or righting reflex					1			
Small size						1		
Lying in cage					1			
Spinning					1			
			<u>Weeks 84-88</u>		<u>Weeks 89-93</u>			
			Male	Female	Male	Female		
Number of animals killed in moribund condition			4	4	1	1		
Number of animals with no clinical signs reported			1					
Pale			1	1				
Thin			1	2				
Hunched			1					
Eyes								
Pale			1	2		1		
Dark red stains around				1				
Squinted				1				
Head tilt				2	1			
Head swollen					1			
Wheezing					1			
Labored respiration				1				
Palpable mass in abdomen			1				1	
Tissue mass--inguinal, side of body, or leg			2	1				
Loss of equilibrium or righting reflex				1				
Ataxia				1				
Depressed				1				
Loss of pain perception				1				
Circling				1				
Low feed consumption					1			
Urine stains				1				

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

TABLE L2. SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: DMH (a)
(Continued)

	<u>Weeks 84-88</u>		<u>Weeks 89-93</u>	
	Male	Female	Male	Female
Inactivity and/or depression	3	4	1	
Abdomen distended (bloated) and/or firm			1	
Palpable mass in abdomen	1	12	3	4
Tissue mass--head, inguinal, neck, ear, throat, back, perineal, or abdomen	6	4	2	1
Nodule		1	2	1
Rough haircoat	2		2	
Swelling around vagina		1		
Discolored discharge around vagina				1
Urine stains	1	1		
Discolored (red) discharge or stains around anus	2		1	1
Nodule protruding from anus	2	1	1	1
Body (extremities) had yellow appearance	1	1		
Muscle tone flaccid				1
Soft feces	3		1	

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

TABLE L3. SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE RANGE (a)

	<u>Weeks 63-67</u>		<u>Weeks 68-73</u>		<u>Weeks 74-78</u>		<u>Weeks 79-83</u>	
	Male	Female	Male	Female	Male	Female	Male	Female
Number of animals killed in moribund condition		1	1	11	11	7	2	2
Number of animals with no clinical signs reported			1	1	8	6		1
Pale				1				
Thin							1	
Hunched							1	
Eyes								
Pale		1					1	
Bloody crust surrounding both eyes				1		1		
Lacrimating						1		
Labored respiration					1		1	
Wheezing					1			
Depression							1	
Ataxia					1			
Loss of equilibrium							1	
Discharge (red) from anus					1			
Stains on fur--paws, nose, or eye		1						
Rough haircoat							1	
Abdomen distended and/or firm		1		1				
Tissue mass--axilla								1
	<u>Weeks 84-88</u>		<u>Weeks 89-93</u>		<u>Weeks 94-98</u>		<u>Weeks 99-103</u>	
	Male	Female	Male	Female	Male	Female	Male	Female
Number of animals killed in moribund condition	7	6	8	9	6	11	11	13
Number of animals with no clinical signs reported				1				
Pale	2		2			4	6	8
Thin	4	2	2	3	4	2	8	4
Hunched	1	2	2					
Eyes								
Pale	1	4	4	1		5		
Bloody crust surrounding both eyes	1							
Squinted	1				1			
Opaque	1							
Head tilt	1		1	1		3	1	1
Malocclusion				1		1		
Labored respiration	1	1		1	1	1	1	
Wheezing	1	1		1	1			
Chest firm				1				
Salivating					2			
Alopecia				2				
Inactive						3	1	2
Depression	3	1	2	1	2	5	4	3
Loss of equilibrium						2	1	2
Loss of righting reflex					1	1		
Discharge (red) from anus			1					
Discharge (red) from vagina								1
Nodule		2	2					1
Unkempt					1		2	1
Bloody crust on paws								1
Stains on fur--paws, nose, or eye	1				1		1	
Rough haircoat	2		1					

TABLE L3. SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: INTERMEDIATE RANGE (a) (Continued)

	<u>Weeks 84-88</u>		<u>Weeks 89-93</u>		<u>Weeks 94-98</u>		<u>Weeks 99-103</u>	
	Male	Female	Male	Female	Male	Female	Male	Female
Abdomen distended and/or firm	1		2					
Abdomen dark			2					
Palpable mass in abdomen	3	2	3	1		6	3	7
Tissue mass--head, neck, axilla, chest, mouth, neck, shoulder, hip, or lower midline	2	3		3	2	2	4	2
Cold to touch	1							
Animal prostrate in cage								2
Extremities yellow	1							
Scrotum dark			2					
Muscle tone flaccid	1		3			1		
Spastic movement					1			
Paralysis--flaccid							1	
Protruding mass from vagina								1

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

TABLE L4. SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBOUND KILL IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: IR + DMH (a)
(Continued)

	<u>Weeks 84-88</u>		<u>Weeks 89-93</u>	
	Male	Female	Male	Female
Head tilt	1			1
Dark red crust in ear or red discharge from ear			1	
Wheezing	1		2	
Labored respiration	1			
Rapid respiration	1			
Depression or inactivity	1		2	1
Circling	1			
Tissue mass--inguinal, axilla, chest, perineal, ear, head, neck, or side of body		3	4	1
Abdomen distended (bloated)	2		1	
Palpable mass in abdomen	4	9	4	3
Nodule			1	
Nodule protruding from anus	4	1		
Discharge (red) from anus	1	1	1	
Discolored discharge from vagina				1
Fecal stains or soft feces	1		1	
Rough haircoat	3	1	2	1
Cold to touch		1		
Left leg had bloody crust and discharge			1	
Yellowish appearance or extremities yellow	1	2		
Muscle tone flaccid		1		1
Discolored urine				2

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

TABLE L5. SUMMARY OF CLINICAL SIGNS OBSERVED IN RATS BEFORE MORIBUND KILL IN THE LIFETIME FEED STUDIES OF INTERMEDIATE-RANGE CHRYSOTILE ASBESTOS: IR/PW (a)

	<u>Weeks 63-67</u>		<u>Weeks 68-73</u>		<u>Weeks 74-78</u>		<u>Weeks 79-83</u>	
	Male	Female	Male	Female	Male	Female	Male	Female
Number of animals killed in moribund condition	0	1	2	0	1	3	3	2
Number of animals with no clinical signs reported			1		1	2	2	1
Thin								1
Hunched								1
Bloody crust surrounding eye(s)						1		1
Eye lacrimating								1
Labored respiration		1					1	
Wheezing						1		1
Tissue mass--ear, back, side of body, or chest			1			1		
Depression		1						
Animal appeared paralyzed							1	
Prostrate in cage		1						
Rough haircoat								1
	<u>Weeks 84-88</u>		<u>Weeks 89-93</u>		<u>Weeks 94-98</u>		<u>Weeks 99-103</u>	
	Male	Female	Male	Female	Male	Female	Male	Female
Number of animals killed in moribund condition	1	3	0	3	3	3	2	3
Number of animals with no clinical signs reported				1				
Pale						1	1	2
Thin		3			1	2	1	2
Hunched		2						
Eye(s) pale				2	3			1
Bloody crust surrounding eye(s)				1				
Red discharge from nose	1							
Bloody crust around nose		1						
Head tilt						1		
Wheezing	1	1						1
Abdomen distended (bloated) and dark					1			
Palpable mass or masses in abdomen				2	1		1	1
Tissue mass--ear, back, side of body, or chest		1		1	1	2	1	3
Lack of coordination or equilibrium		1				1		
Depression or inactivity		1		2	2	1		
Muscle tone flaccid						1		
Prostrate in cage								1
Urine stains		1				2		
Discolored urine				1				
Discharge (red) from vagina								1

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

APPENDIX M

DATA AUDIT SUMMARY

APPENDIX M. DATA AUDIT SUMMARY

The experimental data from the lifetime feed studies of chrysotile asbestos (short-range and intermediate-range fibers) in F344/N rats conducted at Hazleton Laboratories, Inc., were audited for completeness, consistency, and accuracy of the experimental data and for consistency of scientific procedures with Good Laboratory Practices. The in-life phase of the study was completed before NTP's requirement for full compliance with Good Laboratory Practices regulations in October 1981. The experimental data audit was performed by Dynamac Corporation in March 1984. The audit team consisted of the following: Ms. Shirley Corson, Pathology; Mr. Chris Dippel, Toxicology and Chemistry; Mr. James Konz, Pathology; Mr. Curt Lunchick, Toxicology; Mr. James Plautz, Toxicology and Chemistry; Dr. Ronald Schueler, Pathology; and Dr. Karen Whitkin, Toxicology.

The full report of the audit of the chrysotile asbestos studies is on file at the National Toxicology Program, NIEHS. The audit consisted of (a) review of records for the in-life portion of the study, including clinical observations and body weight data for 10% of the animals, mortality records for 20% of the animals, and all environmental records; (b) review of chemistry data including fiber characterization, fiber distribution (homogeneity) and concentration in diet preparation method development, and diet analysis for 10% of the samples; and (c) review of pathology data consisting of (i) a 20% random sample of individual animal pathology records (IADR's), (ii) slide/block match for a 20% random sample of animals in all groups, and (iii) wet tissues for a 10% random sample of animals in groups 82M, 82F, 93M, 93F, 95M, and 95F.

The audit identified no major problems with the conduct of the study or with collection or reporting of the experimental data. The analytical chemistry data for chrysotile asbestos were adequate and supported the stated conclusions of the Technical Report. Although dosing records were present for the two groups receiving DMH, records for preparation and analysis of DMH dose solutions were not available for audit. Animals were identified by ear tags. Although ear tags were missing from wet tissues in approximately 10% of the bags opened, in all the remaining wet tissue bags the tag number corresponded with the bag number. Apparent discrepancies between gross observations during necropsy and microscopic diagnoses were infrequent and consisted predominantly of minor tissue alterations with no impact on study interpretation. For seven rats (081M-one, 082M-four, 082F-one, 092F-one), cecal or colon "nodules" were noted, apparently by the pathology technician ("trimmer"). Pathologic changes, however, were not observed on microscopic examination, although lymphoid nodules (normal structure) were sometimes present. For one rat (091M), two colon "polyps" were described but microscopic examination revealed two lymphoid nodules. The remaining wet tissue (colon) did not show evidence of any polyps. Thus, the apparent discrepancies in gross microscopic correlation for the intestine can be explained by prominent lymphoid structures, which are a normal component of the intestine. The slide/block match was generally good. One or two slides for each of three rats were labeled with the wrong slide number but were appropriately identified by animal and histology number. For each of two other rats, one slide was identified by the incorrect histology number but matched the appropriately labeled block.

In conclusion, no discrepancies were found that would influence the final interpretation of this experiment.

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