NSSGA APPENDIX 1

Comments on the Revised NIOSH Roadmap for Asbestos Research

REFERENCES

1. Stanton, M. F., Layard, M. Tegeris, A., Miller, E., May, M., Morgan, E., Smith, A.: Relation of Particle Dimension to Carcinogenicity of Amphibole Asbestoses and Other Fibrous Minerals. JNCI 1981: 67:965-975.

2. Addison, J., J. M. G., Davis, Carol McIntosh, Brian Miller and Karen Niven: Variations in the Carcinogenicity of Tremolite Dust Samples of Differing Morphology. OSHA Docket H-033d Submission, April 20, 1990. 25 pages.

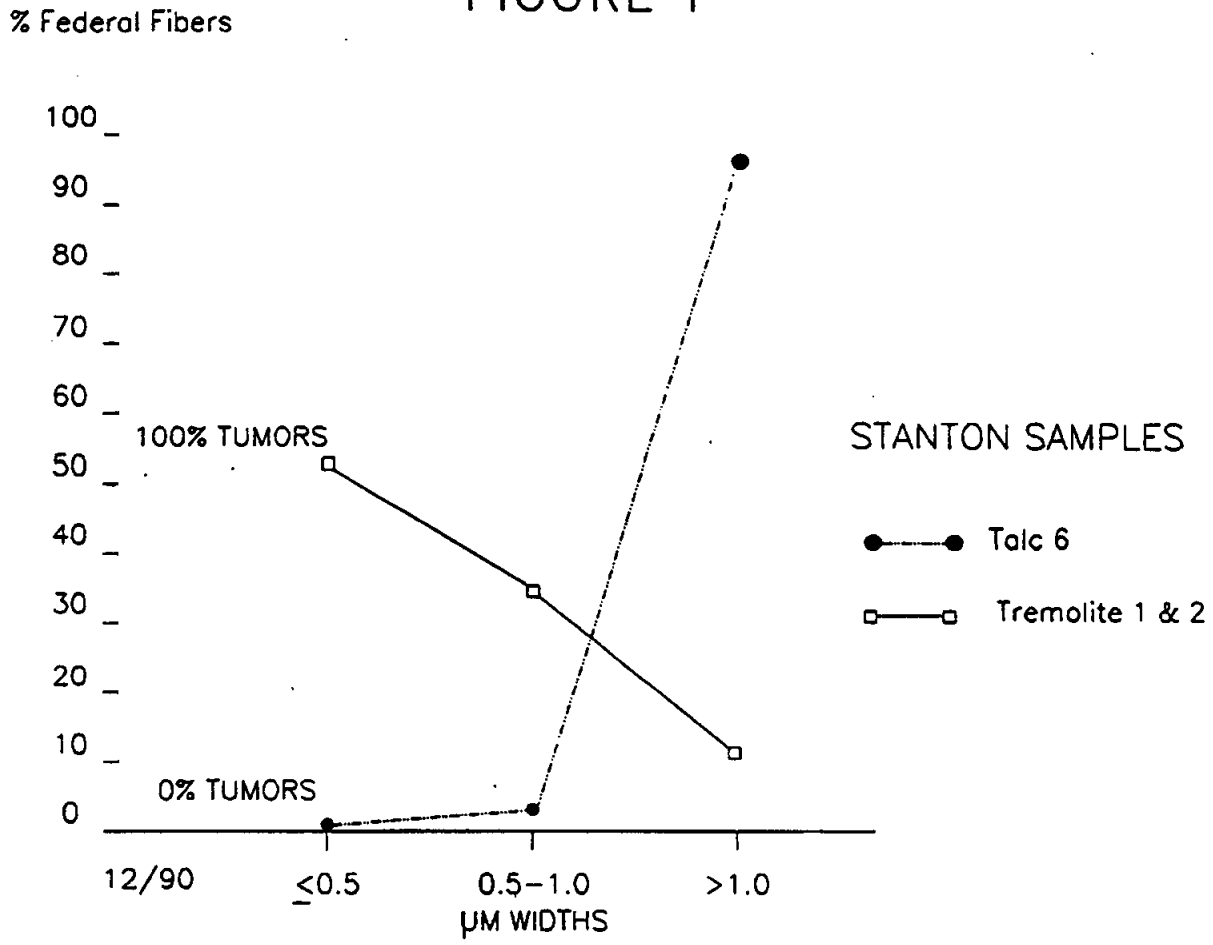
3. Wagner, J. C., M. Chamberlain, R. C. Brown, G. Berry, F. D. Pooley, R. Davis and D. M. Griffiths: Biological Effects of Tremolite. Br. J. Cancer (1982) 45:352-360.

4. Smith, William E., Hubert, D., Sobel, H., Marquet, E.: "Biologic Tests of Tremolite in Hamsters". Dust and Disease, p. 335-339, (1979).

5. Pott, F., U. Ziem, F. J. Feiffer, F. Huth and U. Mohr: Carcinogenicity Studies on Fibres, Metal Compounds and Some Other Dusts in Rats. Exp. Pathol. 1987; 32:129-152.

6. Lippmann, M.: Asbestos Exposures Indices. Env. Research 1988; 46:86-106.

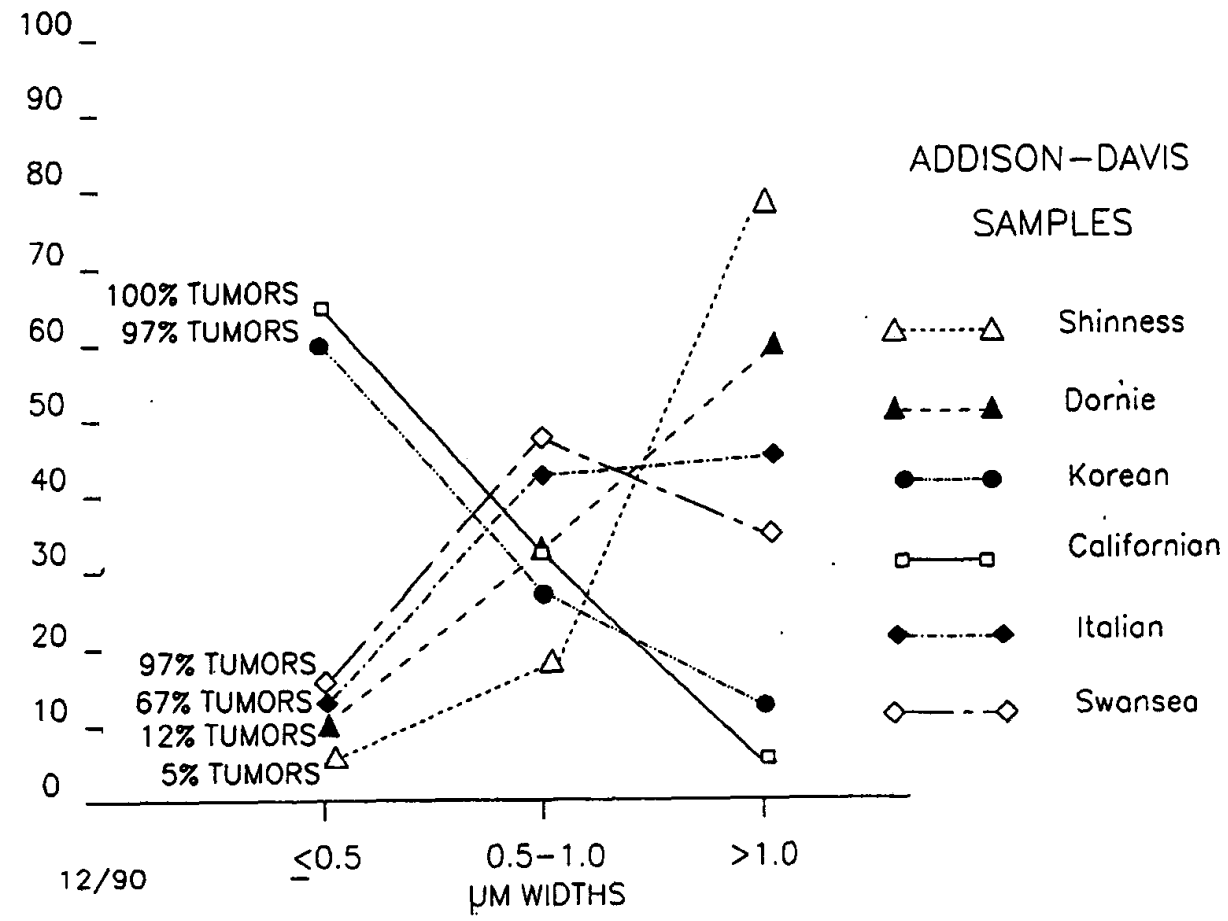
FIGURE 1



MERLE STANTON EXPERIMENTS (REFERENCE 1)

These samples were included in an expansive series of rat pleural implantation studies by Dr. Stanton for the National Cancer Institute. In this study 72 "fibrous" materials were sized and implanted in a single 40 milligram dose in female Osborne–Mendal rats. Samples designated as Tremolite 1 & 2, described as tremolite asbestos from California, was the same tremolite sample tested two separate times (% tumors the same). The Talc 6 sample was provided to Dr. Stanton along with other talc samples from a corporate source (Johns Manville) and was later positively identified as an off–the–shelf New York State tremolitic talc (Wylie, A.G. affidavit to OSHA docket H–033d, November 1, 1984) with a tremolite content of between 40 to 60 percent. No tumors were observed with Talc 6.

FIGURE 2

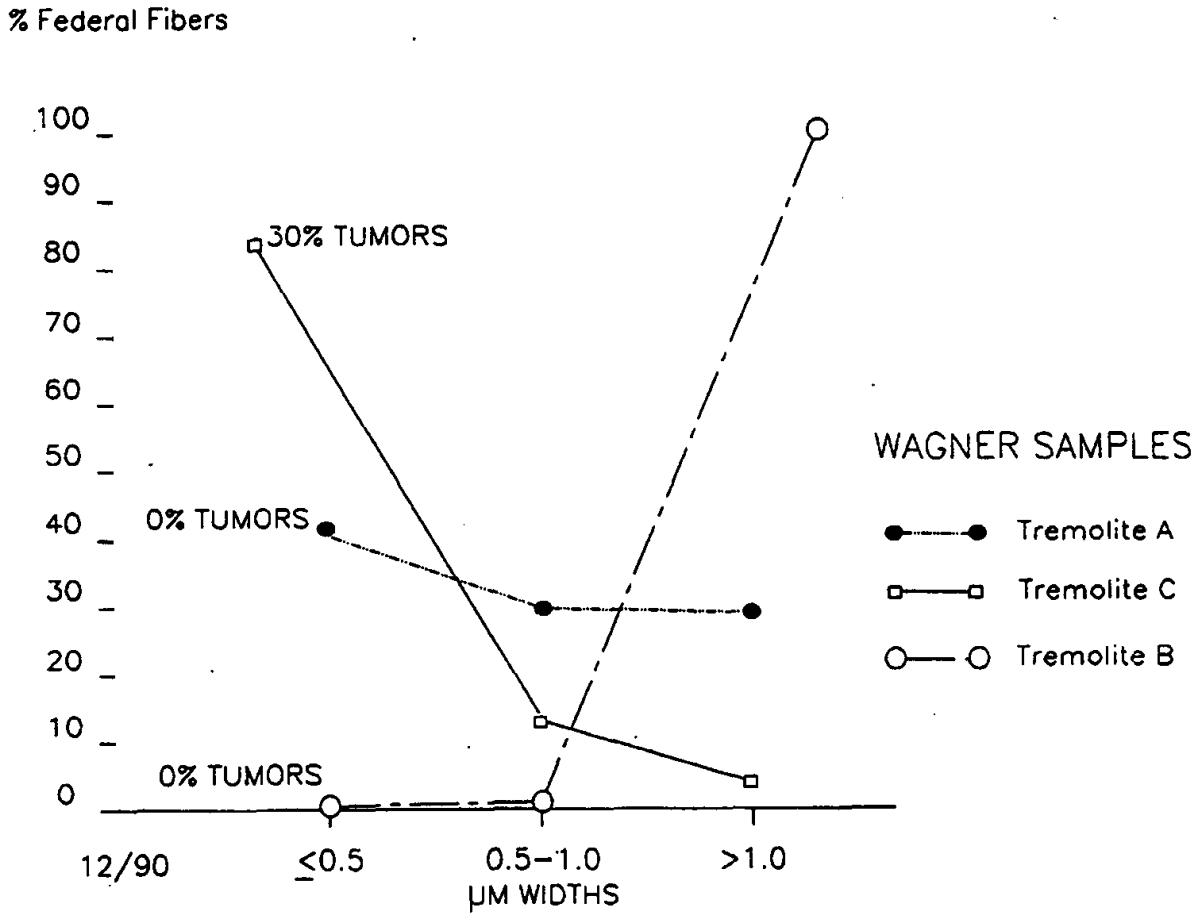


JOHN ADDISON AND J.M.G. DAVIS EXPERIMENTS (REFERENCE 2)

This study, by John Addison and John M. G. Davis from the Institute of Occupational Medicine in Edinburgh, represent the most recent tremolite animal study. The stated purpose of this intraperitoneal injection study in rats was to test the induction of mesothelioma–like tumors and survival time from a single 10 milligram dose of respirable sized tremolites of different morphological types.

This study showed that the California, Korean, and Swansea tremolite samples (described as tremolite asbestos) resulted in very short survival times and a tumor incidence in excess of 96 percent. The Italian sample, described as predominately cleavage fragment sample with acicular and asbestos particle content, resulted in a good survival time but 67 percent tumors upon sacrifice. The Dornie sample was also described as predominately a cleavage fragment sample with acicular particles and some "fibers" (identity and concentration still unclear). This sample and the Shinness sample (described as granular) showed good survival times and 12 and 5 percent tumors respectively. The authors suggest the Dornie and Shinness samples should "probably be considered harmless to human beings" given the extreme sensitivity of the intraperitoneal injection test at 10 mg.

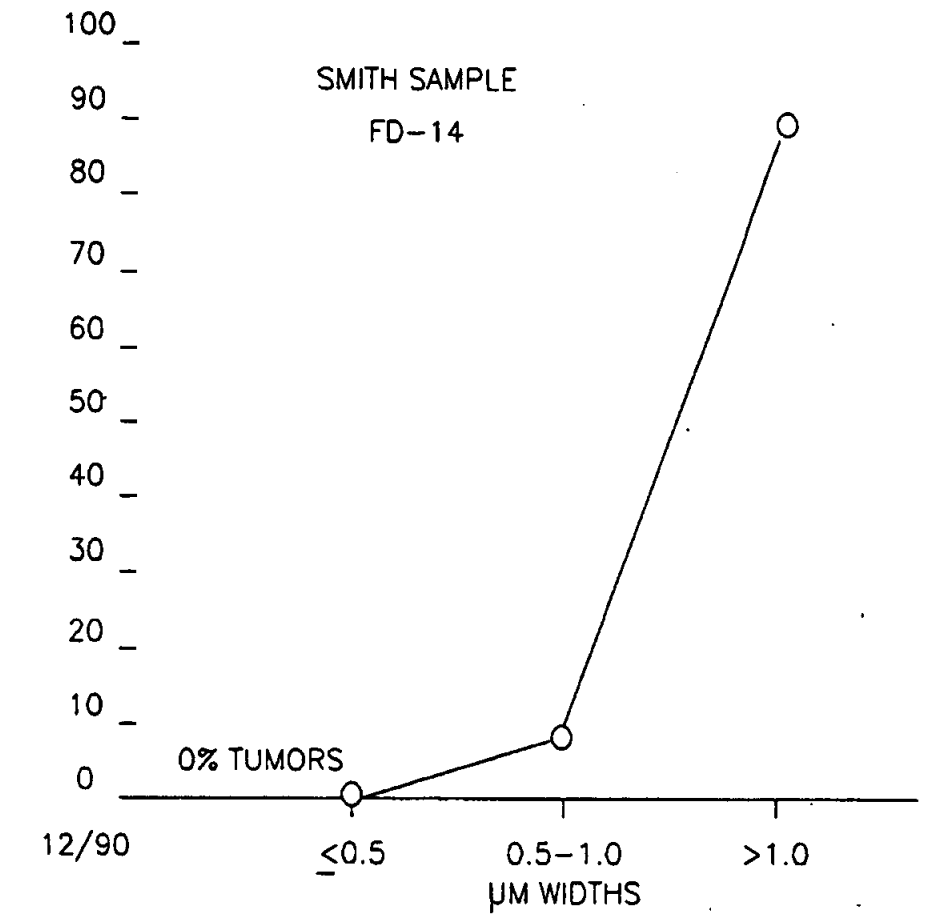
FIGURE 3



J. C. WAGNER EXPERIMENTS (REFERENCE 3)

In this study by Dr. J.C. Wagner from the MRC Pneumoconiosis Unit at University College in Cardiff England, three tremolites of differing morphology were tested in two experiments (different times). In each experiment a 20 milligram dose was injected into the right pleural cavity of rats. The author describes Sample C as a fibrous South Korean tremolite, Sample A as less fibrous and Sample B as a granular tremolite. Exposure to Sample A and B resulted in no tumors while Sample C resulted in 30 percent tumors. The author urged caution in interpreting these results because different rat strains were used and survival time was poor for the animals exposed to Sample C. The author concluded that had the animals exposed to Sample C not died early, tumor incidence would likely have been greater.

FIGURE 4



WILLIAM SMITH EXPERIMENTS (REFERENCE 4)

Dr. William Smith conducted hamster pleural injection studies of four tremolite samples of differing morphology. A 10 milligram and 25 milligram dose was singularly injected into animals in each group. These four samples were designated as FD−14, FD−275, FD−31 and FD−72. Sample FD−14 is an off−the−shelf sample of New York State tremolite talc provided by a distributor of this product (40−60% tremolite). Sample FD−275 was a respirable sized concentrate (95%+) of the tremolite in FD−14. Samples FD−72 and FD−31 were provided by Johns Manville Corporation and described as fibrous and/or asbestiform in nature. The exact origin of these latter two samples remain unclear. Of these samples, only FD−14 was available for further analysis. Tumors were observed for samples FD−31 and FD−72 but were not observed for FD−14 and FD−275.

FIGURE 5

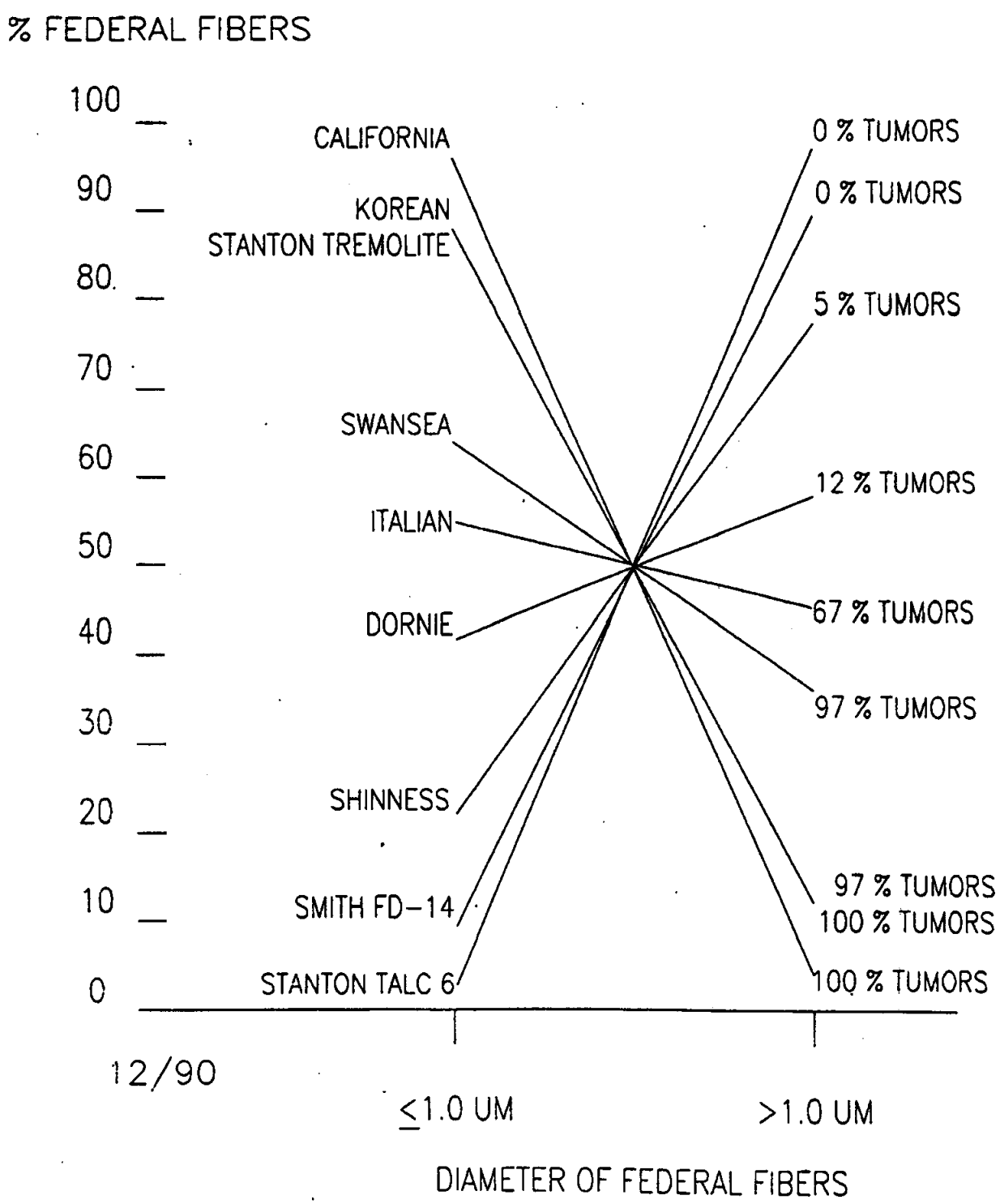

% FEDERAL FIBERS
100
90
80
70
60
50
40
30
20
10
0
CALIFORNIA
KOREAN
STANTON TREMOLITE
SWANSEA
ITALIAN
DORNIE
SHINNESS
SMITH FD-14
STANTON TALC 6
0 % TUMORS
0 % TUMORS
5 % TUMORS
12 % TUMORS
67 % TUMORS
97 % TUMORS
97 % TUMORS
100 % TUMORS
100 % TUMORS
12/90
≤1.0 UM
>1.0 UM
DIAMETER OF FEDERAL FIBERS

FIGURE 6

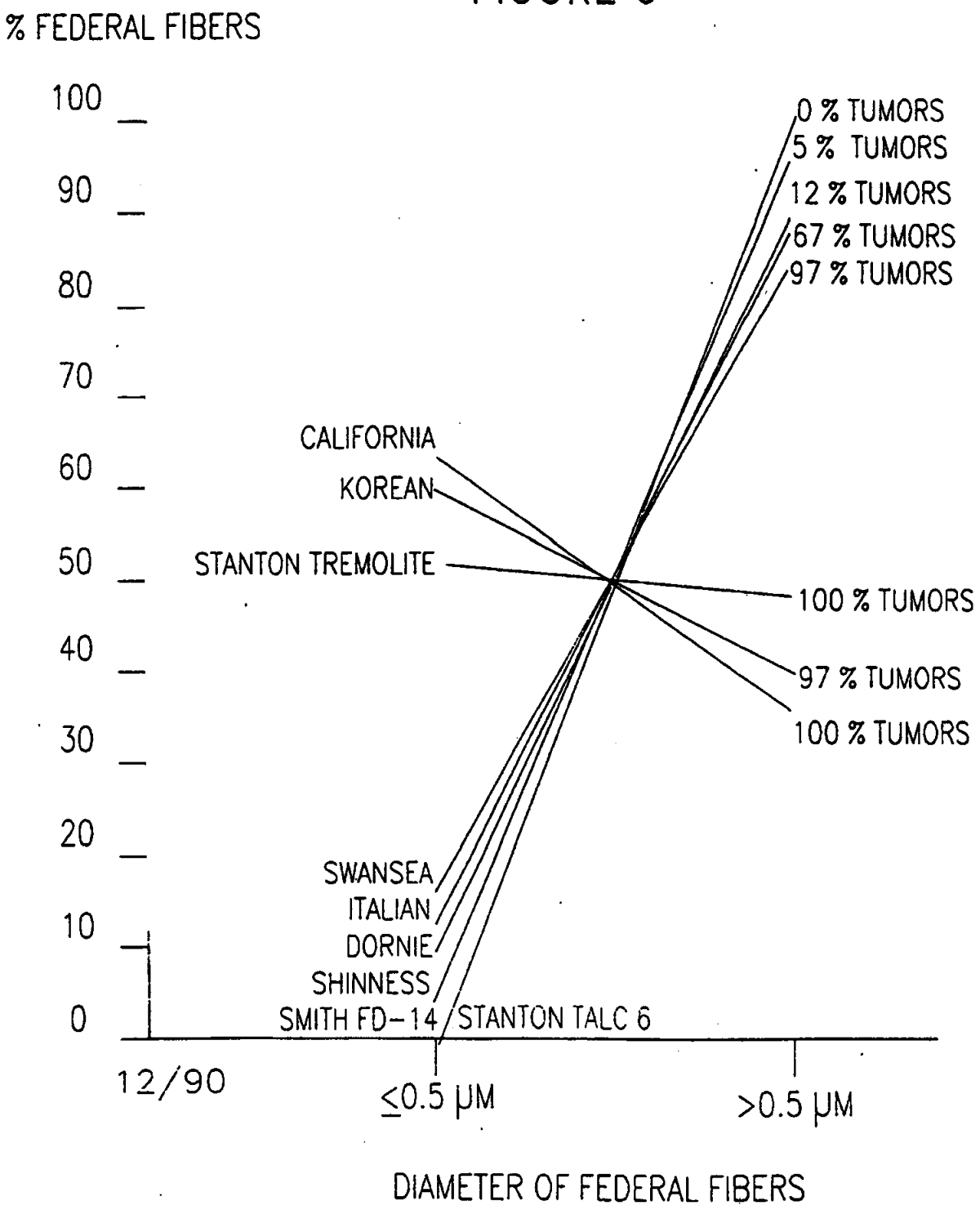
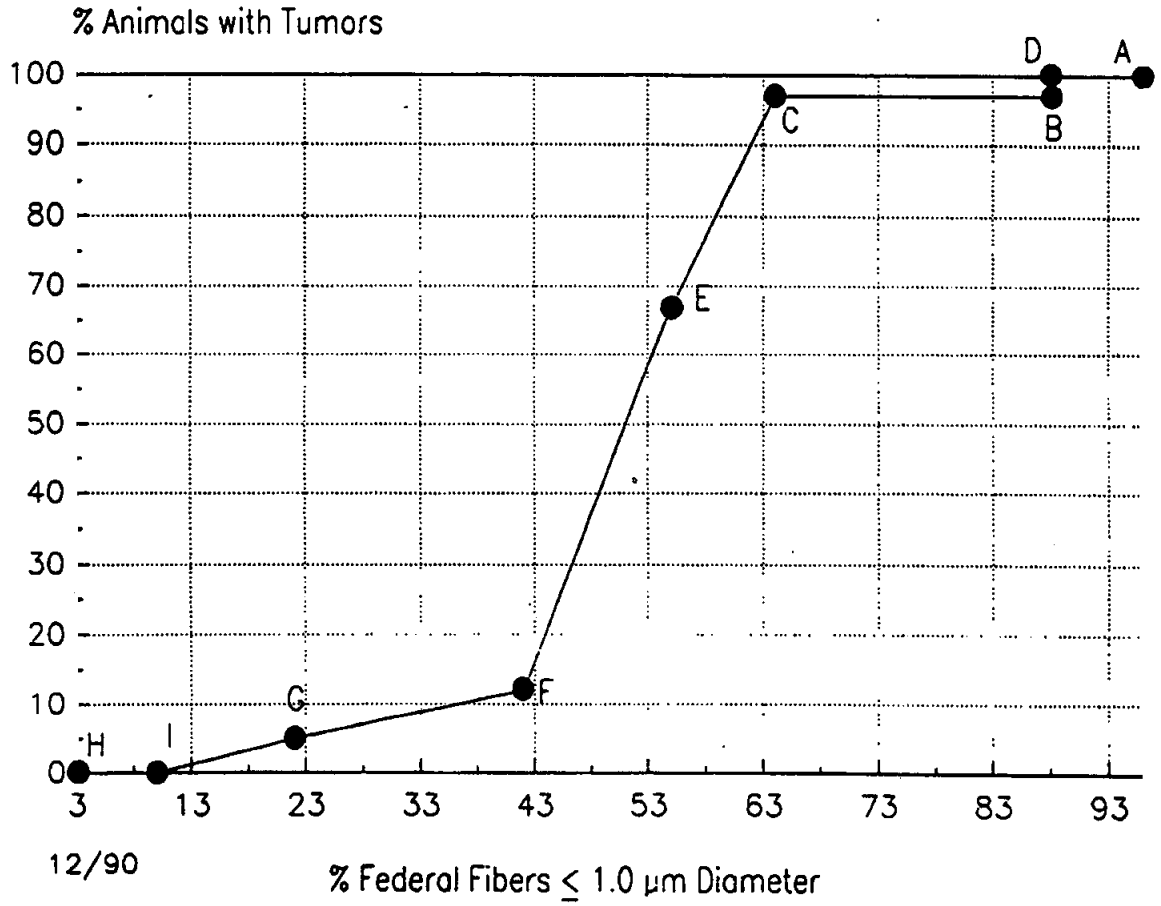

% FEDERAL FIBERS
100
90
80
70
60
50
40
30
20
10
0
0 % TUMORS
5 % TUMORS
12 % TUMORS
67 % TUMORS
97 % TUMORS
CALIFORNIA
KOREAN
STANTON TREMOLITE
100 % TUMORS
97 % TUMORS
100 % TUMORS
SWANSEA
ITALIAN
DORNIE
SHINNESS
SMITH FD-14
STANTON TALC 6
12/90
≤0.5 μM
>0.5 μM
DIAMETER OF FEDERAL FIBERS

FIGURE 7

CARCINOGENIC RESPONSE VERSUS

TREMOLITE FEDERAL FIBER WIDTH

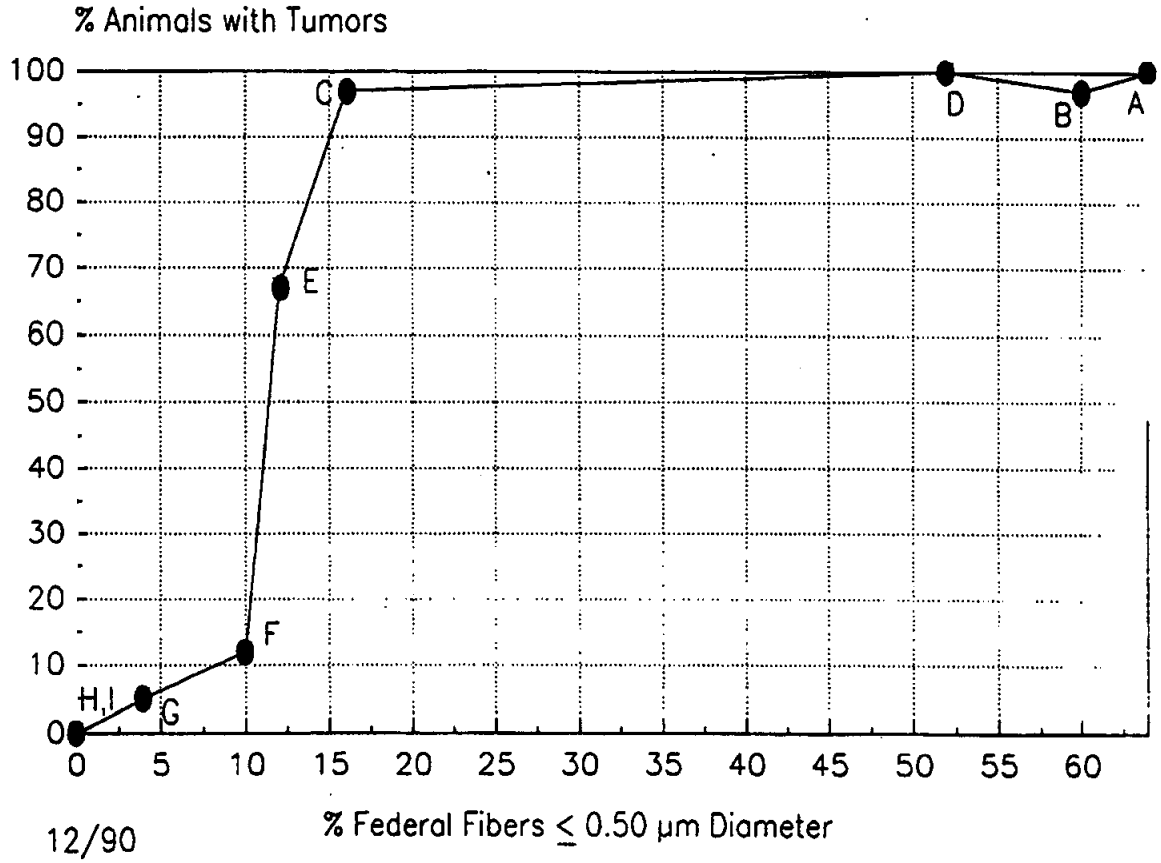


A: Addison–Davis California Tremolite Asbestos
B: Addison–Davis Korean Tremolite Asbestos
C: Addison–Davis Swansea Tremolite Asbestos
D: Stanton Tremolite Asbestos
E: Addison–Davis Italian Tremolite Asbestos/Cleavage Fragments
F: Addison–Davis Dornie Tremolite Cleavage Fragments/ Asbestos
G: Addison–Davis Shinness Tremolite Cleavage Fragments
H: Stanton Talc ō Tremolite (Non–asbestiform)
I: Smith FD–14 Tremolite (Non–asbestiform)

FIGURE 8

CARCINOGENIC RESPONSE VERSUS

TREMOLITE FEDERAL FIBER WIDTH



A: Addison–Davis California Tremolite Asbestos
B: Addison–Davis Korean Tremolite Asbestos
C: Addison–Davis Swansea Tremolite Asbestos
D: Stanton Tremolite Asbestos
E: Addison–Davis Italian Tremolite Asbestos/Cleavage Fragments
F: Addison–Davis Dornie Tremolite Cleavage Fragments/ Asbestos
G: Addison–Davis Shinness Tremolite Cleavage Fragments
H: Stanton Talc 6 Tremolite (Non–asbestiform)
I: Smith FD–14 Tremolite (Non–asbestiform)

FIGURE 9

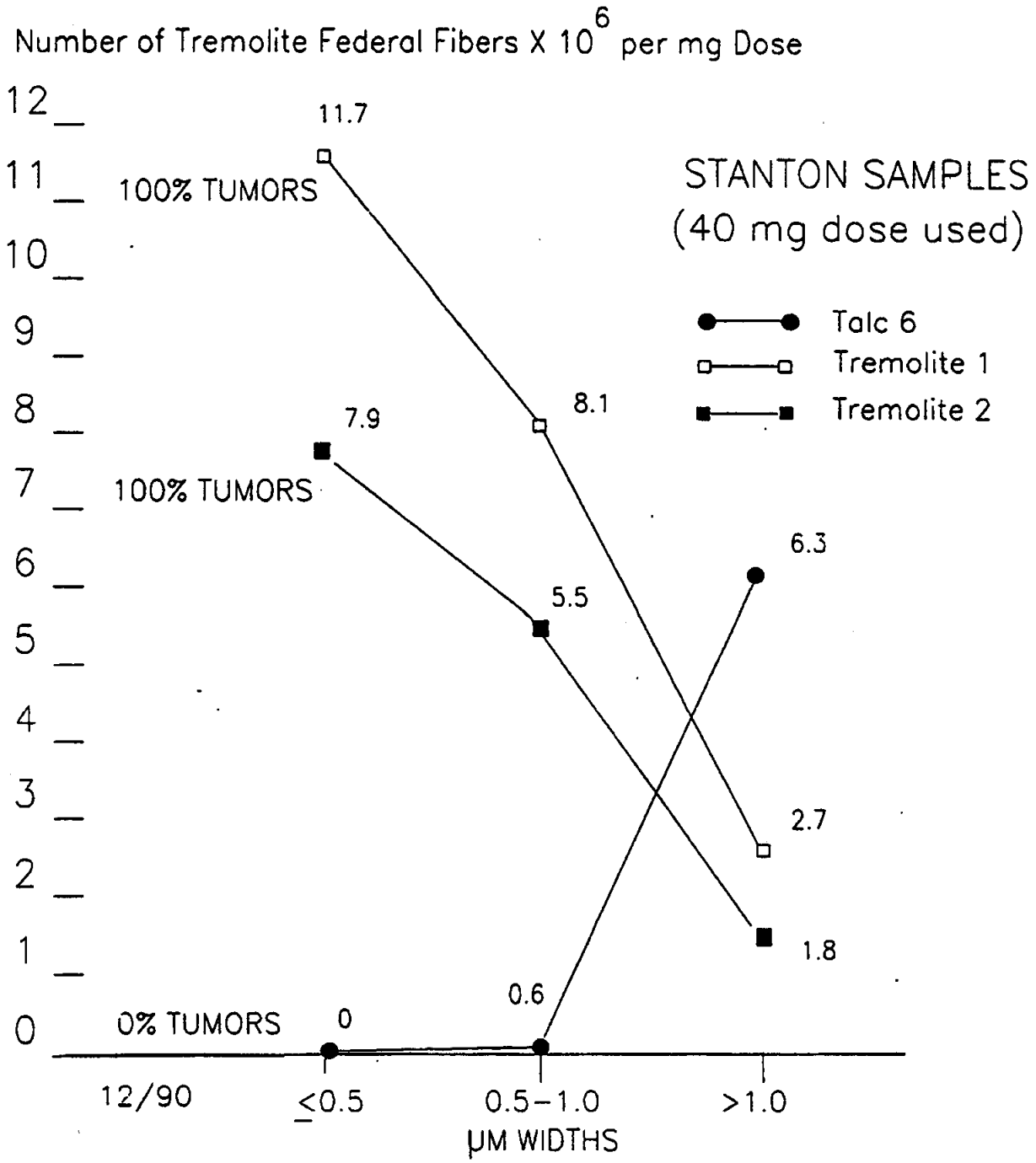

Number of Tremolite Federal Fibers X 10^6 per mg Dose
12
11
10
9
8
7
6
5
4
3
2
1
0
11.7
100% TUMORS
8.1
7.9
100% TUMORS
6.3
5.5
2.7
1.8
0.6
0
0% TUMORS
12/90
≤0.5
0.5–1.0
>1.0
μM WIDTHS
STANTON SAMPLES
(40 mg dose used)
Talc 6
Tremolite 1
Tremolite 2

FIGURE 10

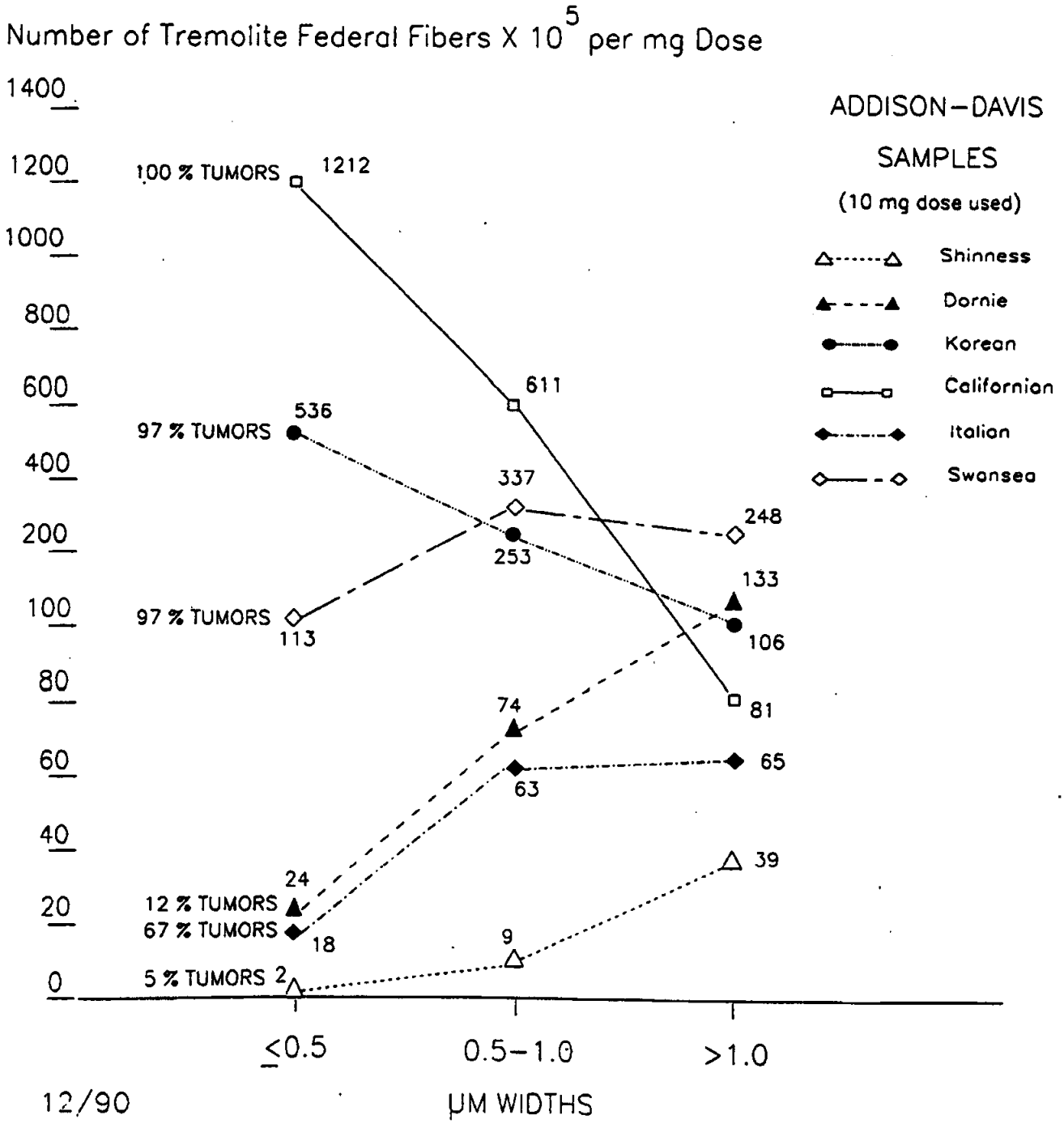
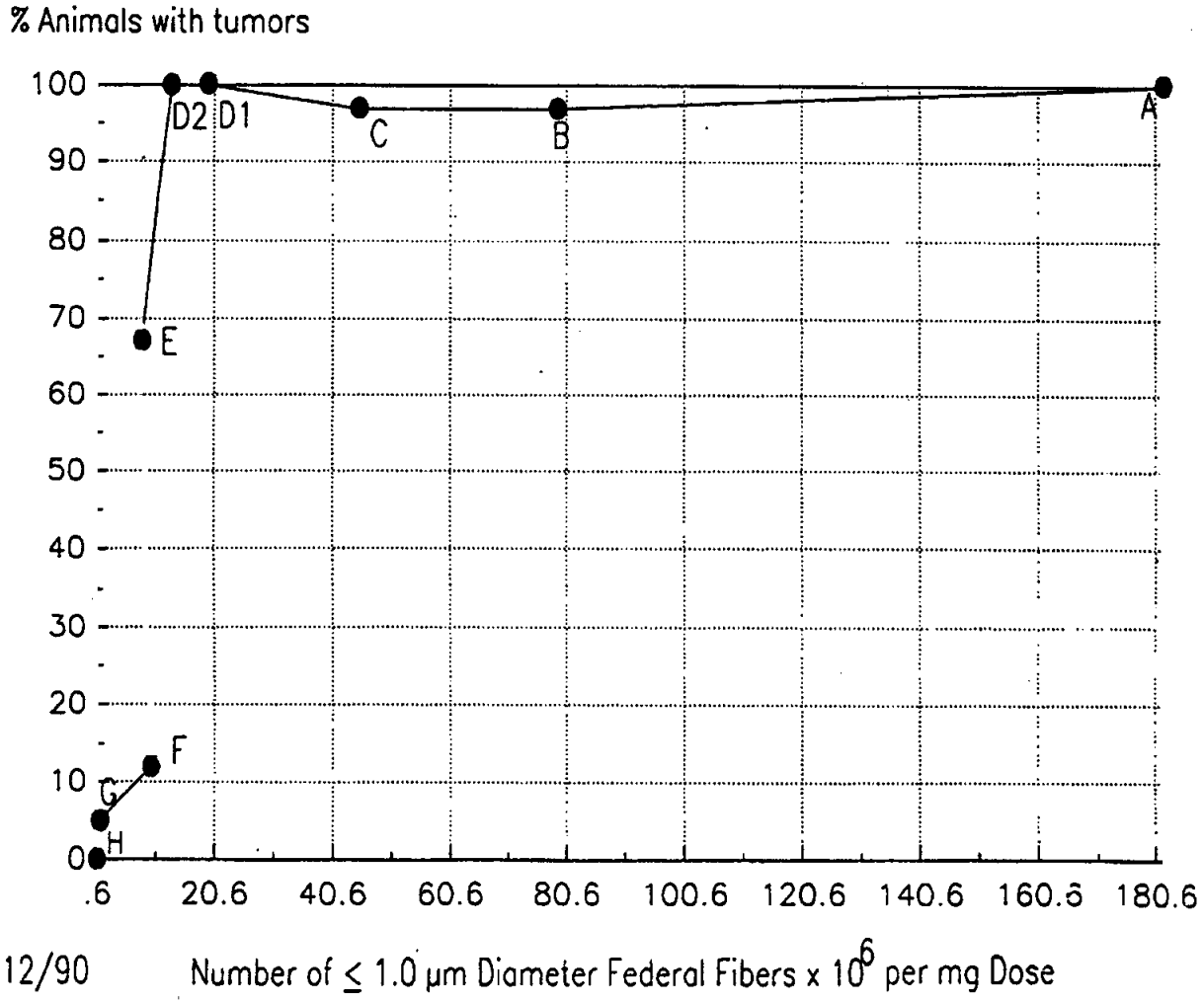

Number of Tremolite Federal Fibers X 10^5 per mg Dose
1400
1200
1000
800
600
400
200
100
80
60
40
20
0
100 % TUMORS
1212
611
81
97 % TUMORS
536
253
106
337
248
97 % TUMORS
113
133
74
65
63
24
12 % TUMORS
67 % TUMORS
18
9
39
5 % TUMORS 2
≤0.5
0.5–1.0
>1.0
12/90
μM WIDTHS
ADDISON–DAVIS
SAMPLES
(10 mg dose used)
Shinness
Dornie
Korean
Californian
Italian
Swansea

FIGURE 11

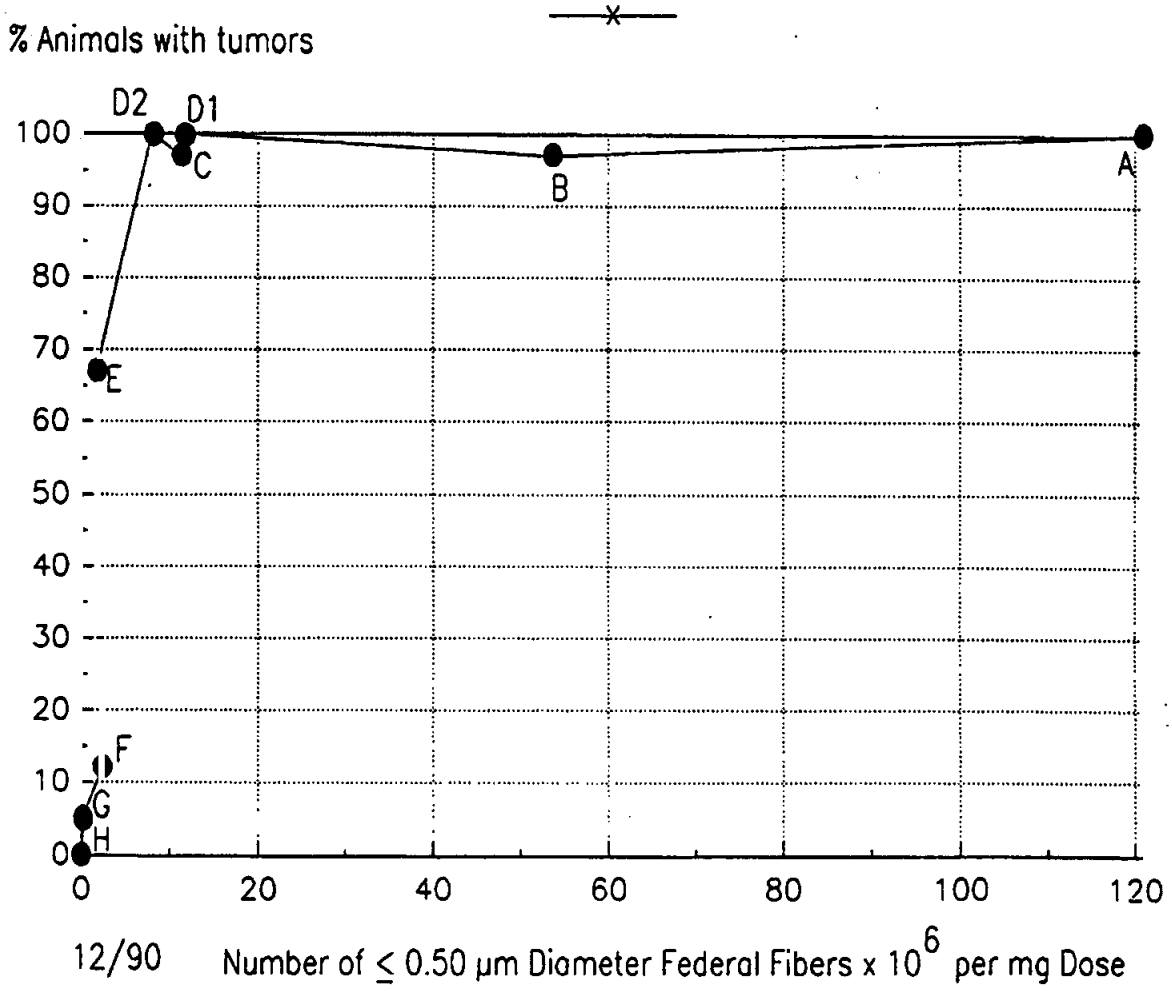
CARCINOGENIC RESPONSE VERSUS DOSE



A: Addison–Davis California Tremolite Asbestos
B: Addison–Davis Korean Tremolite Asbestos
C: Addison–Davis Swansea Tremolite Asbestos
D1: Stanton Tremolite Asbestos 1
D2: Stanton Tremolite Asbestos 2
E: Addison–Davis Italian Tremolite Asbestos/Cleavage Fragments
F: Addison–Davis Dornie Tremolite Cleavage Fragments/ Asbestos
G: Addison–Davis Shinness Tremolite Cleavage Fragments
H: Stanton Talc 6 Tremolite (Non–asbestiform)

FIGURE 12

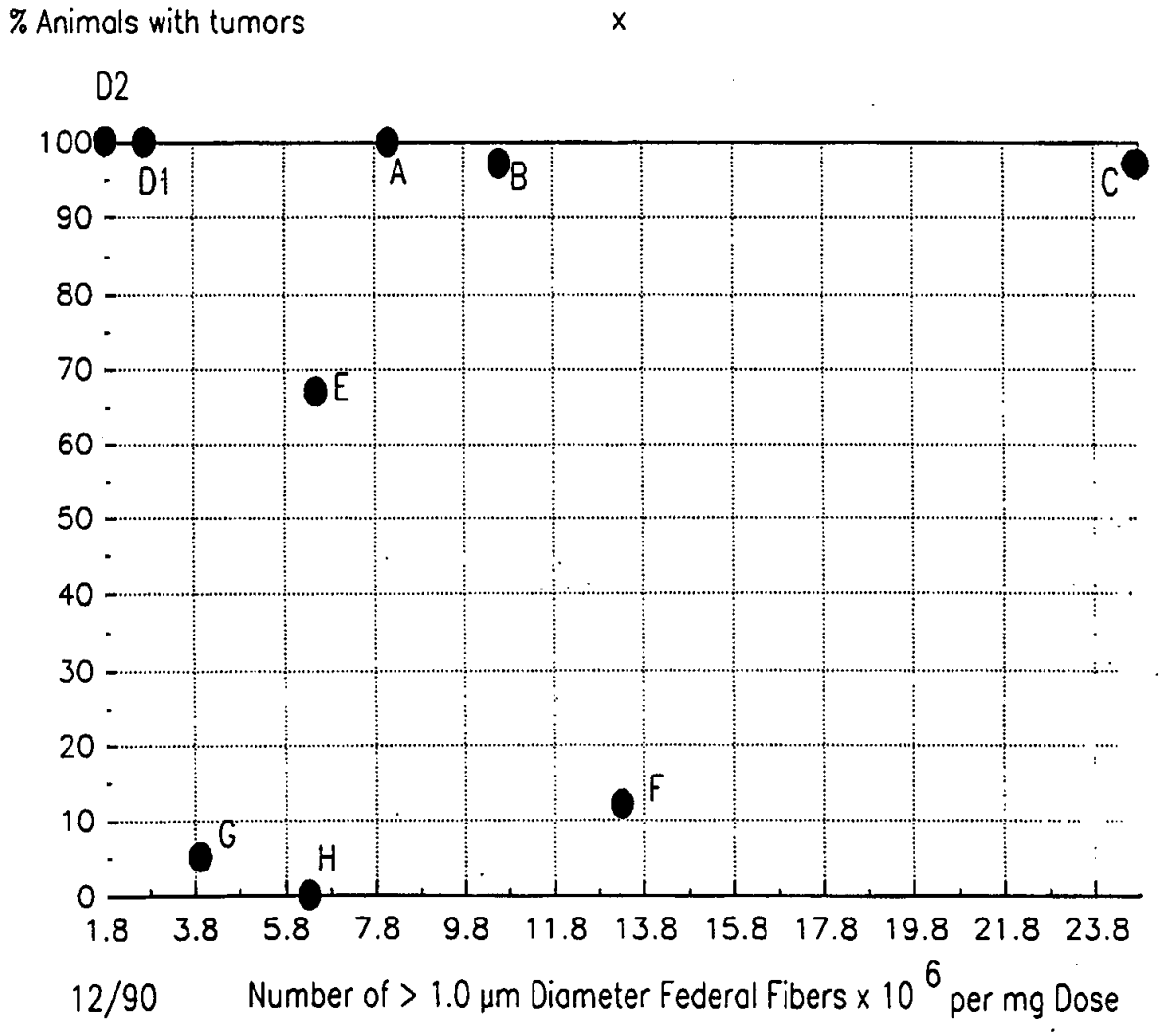
CARCINOGENIC RESPONSE VERSUS DOSE



A: Addison–Davis California Tremolite Asbestos
B: Addison–Davis Korean Tremolite Asbestos
C: Addison–Davis Swansea Tremolite Asbestos
D1: Stanton Tremolite Asbestos 1
D2: Stanton Tremolite Asbestos 2
E: Addison–Davis Italian Tremolite Asbestos/Cleavage Fragments
F: Addison–Davis Dornie Tremolite Cleavage Fragments/ Asbestos
G: Addison–Davis Shinness Tremolite Cleavage Fragments
H: Stanton Talc 6 Tremolite (Non–asbestiform)

FIGURE 13

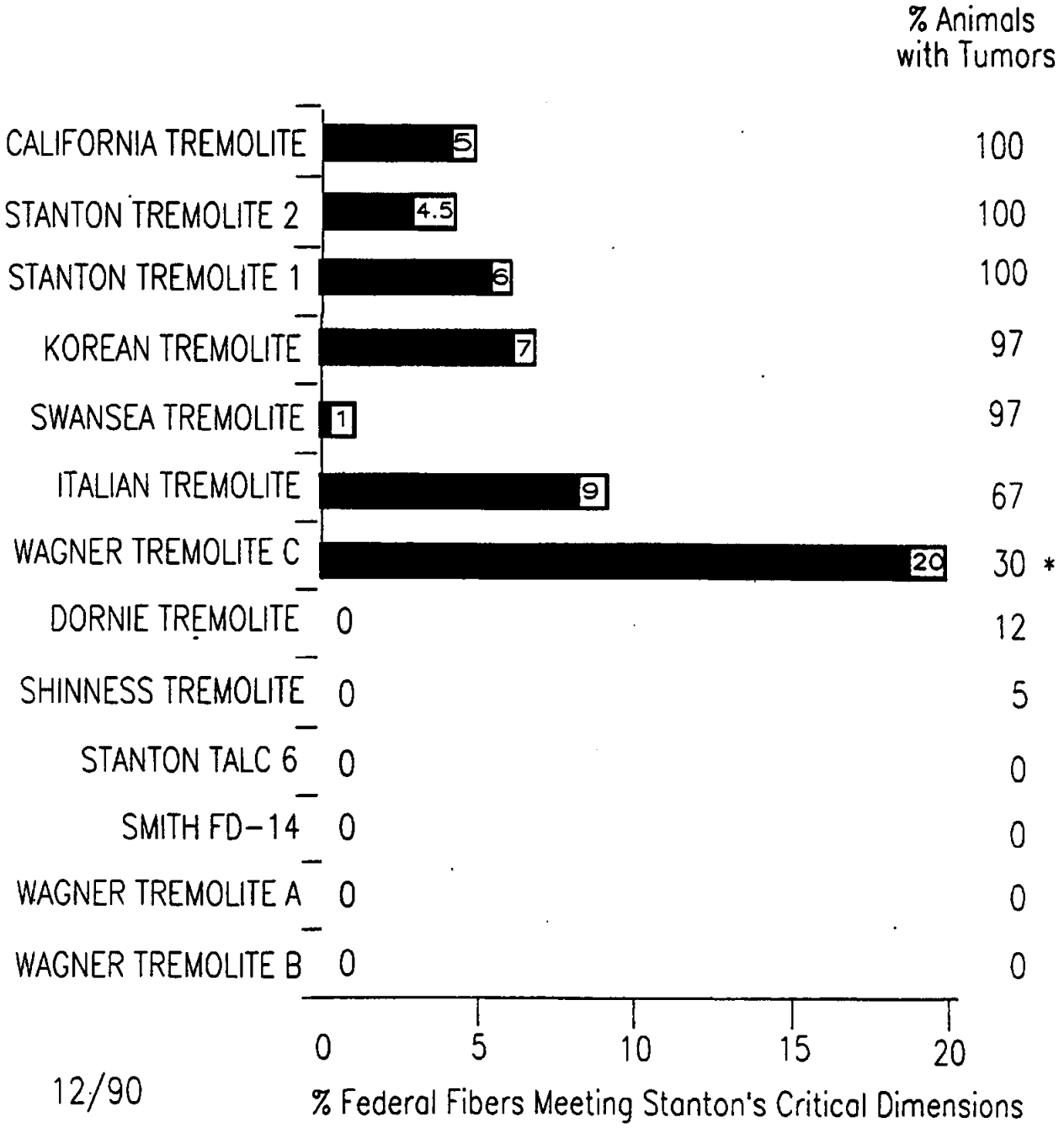
CARCINOGENIC RESPONSE VERSUS DOSE



A: Addison–Davis California Tremolite Asbestos
B: Addison–Davis Korean Tremolite Asbestos
C: Addison–Davis Swansea Tremolite Asbestos
D1: Stanton Tremolite Asbestos 1
D2: Stanton Tremolite Asbestos 2
E: Addison–Davis Italian Tremolite Asbestos/Cleavage Fragments
F: Addison–Davis Dornie Tremolite Cleavage Fragments/ Asbestos
G: Addison–Davis Shinness Tremolite Cleavage Fragments
H: Stanton Talc 6 Tremolite (Non–asbestiform)

FIGURE 14

STANTON'S CRITICAL DIMENSIONS
(<0.25 um dia.; >8.0 um long)



* Poor survival rate noted by researcher

TABLE 1

COMPARISON OF CARCINOGENIC RESPONSE TO PROPORTION OF FEDERAL FIBERS IN WIDTH CATEGORIES

SAMPLE	% FEDERAL FIBERS WITH DIAMETERS (UM) OF: ≤0.5	0.5–1.0	≤1.0	>1.0	% ANIMALS WITH TUMORS
WAGNER B	0	0	0	100	0
STANTON TALC 6	0	3	3	97	0
SMITH FD–14	0	10	10	90	0
A/D SHINNESS	4	18	22	88	5
A/D DORNIE	10	32	42	58	12
A/D ITALIAN	12	43	55	45	67
A/D SWANSEA	16	48	64	36	97
WAGNER A	41	30	71	29	0
STANTON TREM.	52	36	88	12	100
A/D KOREAN	60	28	88	12	97
A/D CALIFORNIA	64	32	96	4	100
WAGNER C *	83	14	97	3	30

A/D= ADDISON DAVIS SAMPLES

* WAGNER REPORTED POOR SURVIVAL RATES IN THIS EXPERIMENT

TABLE 2

COMPARISON OF CARCINOGENIC RESPONSE TO DOSAGE OF FEDERAL FIBERS IN WIDTH CATEGORIES

SAMPLE	* NUMBER OF FEDERAL FIBERS X 10^6 PER MG. DOSE WITH DIAMETERS (UM) OF: ≤0.5	0.5–1.0	≤1.0	>1.0	% ANIMALS WITH TUMORS
STANTON TALC 6	0	0.6	0.6	6.3	0
A/D SHINNESS	0.2	0.9	1.1	3.9	5
A/D DORNIE	2.4	7.4	9.8	13.3	12
A/D ITALIAN	1.8	6.3	8.1	6.5	67
A/D SWANSEA	11.3	33.7	45.0	24.8	97
STANTON TREM.2	7.9	5.5	13.4	1.8	100
STANTON TREM.1	11.7	8.1	19.8	2.7	100
A/D KOREAN	53.6	25.3	78.9	10.6	97
A/D CALIFORNIA	121.2	61.1	182.3	8.1	100

A/D= ADDISON DAVIS SAMPLES

* DATA NOT AVAILABLE FOR WAGNER AND SMITH EXPERIMENTS

TABLE 3

COMPARISON TO M. LIPPMANN CARCINOGENIC DIMENSIONS

	% OF FEDERAL FIBERS		RESULTS	
TREMOLITE SAMPLES	* CANCER FIBERS	* MESO-FIBERS	MG DOSE/TEST	% ANIMALS WITH TUMORS
ADDISON-DAVIS CALIFORNIA	21	0	10/IP	100
ADDISON-DAVIS KOREAN	23	1.4	10/IP	97
ADDISON-DAVIS SWANSEA	13	0	10/IP	97
STANTON TREMOLITE 1	18	?	40/PL. IMP	100
WAGNER TREMOLITE C	29	25	20/PL. I	30
ADDISON-DAVIS ITALIAN	9	0	10/IP	67
ADDISON-DAVIS DORNIE	7	0	10/IP	12
ADDISON-DAVIS SHINNESS	4	0	10/IP	5
STANTON TALC 6	3	0	40/PL. IMP	0
SMITH FD-14	0	0	20/PL. I	0
WAGNER TREMOLITE A	0	12	25/PL. I	0
WAGNER TREMOLITE B	0	0	20/PL. I	0

* LIPPMANN LUNG CANCER DIMENSIONS:

DIAMETER 0.3-0.8 MICRONS
LENGTH > 10 MICRONS

LIPPMANN MESOTHELIOMA DIMENSIONS:

DIAMETER <0.1 MICRON
LENGTH 5-10 MICRONS

IP = Intraperitoneal Injection PL. IMP = Intrapleural Implantation PL. I = Pleural Injection