NSSGA APPENDIX 1

Comments on the Revised NIOSH Roadmap for Asbestos Research
REFERENCES


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-Mendel 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 (Wyile, 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.
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 tremolite 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.
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

0 % TUMORS
0 % TUMORS
5 % TUMORS

12 % TUMORS

67 % TUMORS
97 % TUMORS

97 % TUMORS
100 % TUMORS
100 % TUMORS

SWANSEA
ITALIAN
DORNIE
SHINNESS
SMITH FD-14

STANTON TALC 6

12/90

≤1.0 UM

>1.0 UM

DIAMETER OF FEDERAL FIBERS
% FEDERAL FIBERS

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

DIADEMETE OF FEDERAL FIBERS

12/90 ≤0.5 μM >0.5 μM
FIGURE 7

CARCINOGENIC RESPONSE VERSUS
TREMOLITE FEDERAL FIBER WIDTH

% Animals with Tumors

% Federal Fibers ≤ 1.0 μm Diameter

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 & Tremolite (Non-asbestiform)
I: Smith FD—14 Tremolite (Non—asbestiform)
FIGURE 8

CARCINOGENIC RESPONSE VERSUS TREMOLITE FEDERAL FIBER WIDTH

% Animals with Tumors

% Federal Fibers ≤ 0.50 μm Diameter

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 $\times 10^6$ per mg Dose

12 _
11 _
10 _
9 _
8 _
7 _
6 _
5 _
4 _
3 _
2 _
1 _
0 _

100% TUMORS

STANTON SAMPLES
(40 mg dose used)

- - - - - - Talc 6
□ □ □ □ □ Tremolite 1
■ ■ ■ ■ ■ Tremolite 2

0% TUMORS

12/90 ≤ 0.5 0.5 - 1.0 > 1.0

μM WIDTHS

11.7
7.9
5.5
8.1
6.3
2.7
1.8
FIGURE 11

CARCINOGENIC RESPONSE VERSUS DOSE

% Animals with tumors

12/90 Number of ≤ 1.0 μm Diameter Federal Fibers x 10^6 per mg 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 Toic 6 Tremolite (Non-asbestiform)
FIGURE 12

CARCINOGENIC RESPONSE VERSUS DOSE

% Animals with tumors

D2  D1  C  B  A

0  20  40  60  80  100  120

12/90  Number of ≤ 0.50 μm Diameter Federal Fibers x 10^6 per mg 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 Telc 6 Tremolite (Non–asbestiform)
FIGURE 13

CARCINOGENIC RESPONSE VERSUS DOSE

% Animals with tumors

D2
100
90
80
70
60
50
40
30
20
10
0

D1
A
B
C

1.8 3.8 5.8 7.8 9.8 11.8 13.8 15.8 17.8 19.8 21.8 23.8

12/90 Number of > 1.0 μm Diameter Federal Fibers x 10^6 per mg 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 Taic 6 Tremolite (Non-asbestiform)
### FIGURE 14

**STANTON'S CRITICAL DIMENSIONS**

(<0.25 um dia.; >8.0 um long)

<table>
<thead>
<tr>
<th>Material</th>
<th>% Animals with Tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>CALIFORNIA TREMOLITE</td>
<td>100</td>
</tr>
<tr>
<td>STANTON TREMOLITE 2</td>
<td>100</td>
</tr>
<tr>
<td>STANTON TREMOLITE 1</td>
<td>100</td>
</tr>
<tr>
<td>KOREAN TREMOLITE</td>
<td>97</td>
</tr>
<tr>
<td>SWANSEA TREMOLITE</td>
<td>97</td>
</tr>
<tr>
<td>ITALIAN TREMOLITE</td>
<td>67</td>
</tr>
<tr>
<td>WAGNER TREMOLITE C</td>
<td>30 *</td>
</tr>
<tr>
<td>DORNIE TREMOLITE</td>
<td>12</td>
</tr>
<tr>
<td>SHINNESS TREMOLITE</td>
<td>5</td>
</tr>
<tr>
<td>STANTON TALC 6</td>
<td>0</td>
</tr>
<tr>
<td>SMITH FD-14</td>
<td>0</td>
</tr>
<tr>
<td>WAGNER TREMOLITE A</td>
<td>0</td>
</tr>
<tr>
<td>WAGNER TREMOLITE B</td>
<td>0</td>
</tr>
</tbody>
</table>

12/90 % Federal Fibers Meeting Stanton's Critical Dimensions

* Poor survival rate noted by researcher
**TABLE 1**

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

<table>
<thead>
<tr>
<th>SAMPLE</th>
<th>% FEDERAL FIBERS WITH DIAMETERS (UM) OF:</th>
<th>% ANIMALS WITH TUMORS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤0.5</td>
<td>0.5–1.0</td>
</tr>
<tr>
<td>WAGNER B</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>STANTON TALC 6</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>SMITH FD–14</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>A/D SHINNESS</td>
<td>4</td>
<td>18</td>
</tr>
<tr>
<td>A/D DORNIE</td>
<td>10</td>
<td>32</td>
</tr>
<tr>
<td>A/D ITALIAN</td>
<td>12</td>
<td>43</td>
</tr>
<tr>
<td>A/D SWANSEA</td>
<td>16</td>
<td>48</td>
</tr>
<tr>
<td>WAGNER A</td>
<td>41</td>
<td>30</td>
</tr>
<tr>
<td>STANTON TREM.</td>
<td>52</td>
<td>36</td>
</tr>
<tr>
<td>A/D KOREAN</td>
<td>60</td>
<td>28</td>
</tr>
<tr>
<td>A/D CALIFORNIA</td>
<td>64</td>
<td>32</td>
</tr>
<tr>
<td>WAGNER C</td>
<td>*</td>
<td>83</td>
</tr>
</tbody>
</table>

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**

<table>
<thead>
<tr>
<th>SAMPLE</th>
<th>≤0.5</th>
<th>0.5–1.0</th>
<th>≤1.0</th>
<th>&gt;1.0</th>
<th>% ANIMALS WITH TUMORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stanton Talc 6</td>
<td>0</td>
<td>0.6</td>
<td>0.6</td>
<td>6.3</td>
<td>0</td>
</tr>
<tr>
<td>A/D Shinness</td>
<td>0.2</td>
<td>0.9</td>
<td>1.1</td>
<td>3.9</td>
<td>5</td>
</tr>
<tr>
<td>A/D Dornie</td>
<td>2.4</td>
<td>7.4</td>
<td>9.8</td>
<td>13.3</td>
<td>12</td>
</tr>
<tr>
<td>A/D Italian</td>
<td>1.8</td>
<td>6.3</td>
<td>8.1</td>
<td>6.5</td>
<td>67</td>
</tr>
<tr>
<td>A/D Swansea</td>
<td>11.3</td>
<td>33.7</td>
<td>45.0</td>
<td>24.8</td>
<td>97</td>
</tr>
<tr>
<td>Stanton Trem. 2</td>
<td>7.9</td>
<td>5.5</td>
<td>13.4</td>
<td>1.8</td>
<td>100</td>
</tr>
<tr>
<td>Stanton Trem. 1</td>
<td>11.7</td>
<td>8.1</td>
<td>19.8</td>
<td>2.7</td>
<td>100</td>
</tr>
<tr>
<td>A/D Korean</td>
<td>53.6</td>
<td>25.3</td>
<td>78.9</td>
<td>10.6</td>
<td>97</td>
</tr>
<tr>
<td>A/D California</td>
<td>121.2</td>
<td>61.1</td>
<td>182.3</td>
<td>8.1</td>
<td>100</td>
</tr>
</tbody>
</table>

A/D = Addison Davis Samples  
* Data not available for Wagner and Smith Experiments
# Table 3

**Comparison to M. Lippmann Carcinogenic Dimensions**

<table>
<thead>
<tr>
<th>Tremolite Samples</th>
<th>% of Federal Fibers</th>
<th>Results</th>
<th>% Animals with Tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>* Cancer Fibers</td>
<td>* Meso-Fibers</td>
<td>mg Dose/Test</td>
</tr>
<tr>
<td>Addison-Davis California</td>
<td>21</td>
<td>0</td>
<td>10/IP</td>
</tr>
<tr>
<td>Addison-Davis Korean</td>
<td>23</td>
<td>1.4</td>
<td>10/IP</td>
</tr>
<tr>
<td>Addison-Davis Swansea</td>
<td>13</td>
<td>0</td>
<td>10/IP</td>
</tr>
<tr>
<td>Stanton Tremolite 1</td>
<td>18</td>
<td>?</td>
<td>40/Pl. Imp</td>
</tr>
<tr>
<td>Wagner Tremolite C</td>
<td>29</td>
<td>25</td>
<td>20/Pl. I</td>
</tr>
<tr>
<td>Addison-Davis Italian</td>
<td>9</td>
<td>0</td>
<td>10/IP</td>
</tr>
<tr>
<td>Addison-Davis Dornie</td>
<td>7</td>
<td>0</td>
<td>10/IP</td>
</tr>
<tr>
<td>Addison-Davis Shinness</td>
<td>4</td>
<td>0</td>
<td>10/IP</td>
</tr>
<tr>
<td>Stanton Talc 6</td>
<td>3</td>
<td>0</td>
<td>40/Pl. Imp</td>
</tr>
<tr>
<td>Smith FD-14</td>
<td>0</td>
<td>0</td>
<td>20/Pl. I</td>
</tr>
<tr>
<td>Wagner Tremolite A</td>
<td>0</td>
<td>12</td>
<td>25/Pl. I</td>
</tr>
<tr>
<td>Wagner Tremolite B</td>
<td>0</td>
<td>0</td>
<td>20/Pl. I</td>
</tr>
</tbody>
</table>

* 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