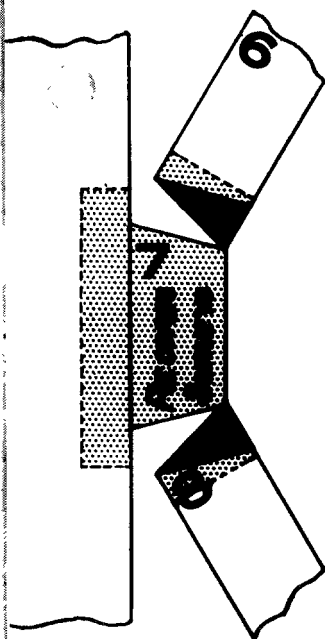


**HOW TO USE
THESE SEPARATORS**

Use one page for
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Select appropriate
tab, add further
identification if
desired, and cover
it with scotch
tape.

Cut off and discard
all tabs except the
one covered by tape.



TABBED SEPARATOR SHEET
Form NEW-69B
(9-56)

TO : Petitions Control Branch, HFF-334

DATE: October 7, 1974

Attn: Dr. C. Miles

FROM : Residue Analysis & Methods Investigations Branch, HFF-144

SUBJECT: Johns-Manville (J-M) 9/27/74 Letter and Data on Analyses of Tremolite (T) in Food.

In previous data on the above subject, discussed at the 9/12/74 meeting, we inquired of J-M what did a zero fiber count mean in terms of ppm or ppb T in food. Furthermore, we suggested that some finite fiber count related to food content would be more significant experimentally. J-M agreed to perform a number of spiking experiments of meat and salt with standard T and determine recovery data by measuring fiber count.

I. Spiked Meat

Based on a 100 ppb T spiking of meat, assaying, millipore filtering and microscopic count showed 70 fibers vs a theoretical level of 98 or 72% recovery.

II. Spiked Salt

Based on a 1 ppb T spiking of salt, dissolving, millipore filtering and microscopic count showed an average (2 trials) of 3825 fibers vs a theoretical level of 4100 fibers or 94% recovery.

IV. Spiked Salt

Again, spiking of salt with a 0.1 ppb T level, dissolving, millipore filtering and microscopic count showed a fiber level of 290 vs theoretical 656 fibers or 45% recovery.

In the following we have attempted to relate a zero fiber count sensitivity (or a minimum sensitivity count) to some detection limit of Tremolite in food based on paper wrapping of meat or packaging salt. We will have to defer this evaluation to W. Eisenberg (Microanalytical Branch, HFF-127) who, being more familiar with the optical microscopic counting procedures used for the T fibers, can prescribe fiber count sensitivities for these analyses which will permit more accurate detection limits for the spiking experiments carried out by Johns-Manville.

The relationship of the above data to J-M's original "zero fiber" count, if acceptable, presents some problems in the above spiked samples.

I.a. A zero or single fiber count or 100% recovery could be equated to $\frac{1}{100} \times 100 \text{ ppb} = 1 \text{ ppb}$ detection limit - based on the 98 fiber spiking.

b. Based on the 70% recovery, zero count would equate to $\frac{100}{70} \approx 1.4 \text{ ppb}$.

c. If a 10 fiber count were the sensitivity variation, then the detection limit would be $\frac{100}{10} = 10 \text{ ppb}$.

II.a. A zero or single fiber count sensitivity could be equated to $\frac{1}{4000} = 0.25 \text{ ppt}$ detection limit based on the 4000 fiber spiking.

b. A 100 fiber count sensitivity would provide a detection limit of 10 ppt.

IV.a. A zero fiber count sensitivity could be equated to $\frac{0.1}{10} = 0.3 \text{ ppt}$.

b. A 100 fiber count sensitivity would provide a detection limit of 0.9 ppt.

A. Holtz

A. Holtz

*The analyses performed by John Marville
discussed in this memo demonstrate a
sensitivity level of practical detection of
10 ppb in water and 10 ppt in salt.*

W. V. Enenberg Oct 16, 1971

John S-Manville

Research & Development Center

Denver, Colorado 80217
(303) 770-1000

September 27, 1974

Dr. Corbin Miles (HFF-335)
Food & Drug Administration
200 C Street, S.W.
Washington, D.C. 20204

Dear Corbin:

At our last meeting with you on September 12, 1974, you raised a question regarding the limits of detectability of tremolite in various food samples. The main reason for your question was to be able to specify a reasonable lower limit to 0 fiber counts.

In order to answer your question, we agreed to perform the following three tests:

1. Determine the limit of detectability of tremolite in salt spiked with tremolitic talc.
2. Determine the limit of detectability of tremolite in meat spiked with tremolitic talc.
3. Determine the limit of detectability of tremolite in salt spiked with ash from paper manufactured with tremolitic talc.

The details of the experiments are attached. All of the counting was done by the optical microscope at 500X magnification. The samples were prepared by filtering on a 47 mm diameter, 0.2 micrometer millipore filter. The maximum amount of total material which can be deposited on this filter is 0.5 mg. Any greater concentrations result in too great a probability of fibers being hidden behind other particles.

The results that we have obtained indicate that tremolite can be detected at a level of about 20 ppm in any residue. The detectability in any foodstuff will, therefore, depend upon the amount of ash remaining when the food is ignited.

D. Corbin Miles, FDA
Washington, D.C.

September 27, 1974
Page 2

As an example, if a food yields 1 per cent ash, then the limit of detectability of tremolite in the food could be 200 parts per billion. In the case of the spiked salt, the limit of detectability is about 0.1 parts per billion.

We hope that this information has answered your questions. If we can be of any further assistance, please do not hesitate to contact either Rich Zyzenski or myself.

As you requested, under separate cover we are also sending several paper samples made with various amounts of tremolitic talc.

Very truly yours,

Dr. James P. Leineweber
Manager, Applied Research


Richard J. Zyzenski
Research Engineer

LS

Attachment

Attachment
Dr. Corbin Miles, FDA

SUPPLEMENTARY FDA WORK

Item I: 150 gm of meat was spiked with 0.0060 gm of F-1 talc standard (0.25 per cent tremolite). This produced the equivalent of 100 ppb tremolite/meat. Based on the original fiber count of 41,000 tremolitic fibers/mg of F-1 standard, there were approximately 246,000 fibers contained in the ash. The 150 gm of meat ashed down to 1.25 gm. For petrographic slide preparation, 0.5 mg of this ash was dispersed on a 47 mm millipore filter. Assuming a homogeneous mix of ash and fibers, there should have been approximately 98 tremolite fibers deposited on the millipore filter. Optical examination observed 70.

Item II: 250 gm of salt was spiked with 0.1 mg of F-1 standard. In the 0.1 mg of talc, there were approximately 4,100 fibers. This corresponds to 1 ppb tremolite/salt. The salt was completely dissolved and filtered through a 0.2 μ millipore filter. If no fibers were lost during the procedure, all of the 4,100 fibers should have been collected on the filter. Optical examination observed 4,200 tremolite fibers on one sample and 3,450 fibers on another.

Item III: A paper containing 3 per cent CYCLO-FIL talc was ashed and prepared for tremolite fiber count. The count was 390,770 $\pm$ 30 per cent tremolite fibers per mg/ash.

Then 0.1 mg of this paper ash was mixed with 250 gm of salt and the procedure for the recovery of insolubles was performed. If no fibers were lost during preparation, there should have been approximately 39,000 fibers collected on the filter. Optical examination revealed 35,000.

Item IV: 400 gm of salt was spiked with 16 micrograms of F-1 standard. This introduced approximately 656 tremolite fibers into the salt. This corresponds to approximately 0.1 ppb tremolite/salt. The salt was dissolved and filtered through 0.2 millipore. Optical examination observed 290 fibers.

R. J. Zazenski
9-27-74

0
MEMORANDUM OF CONFERENCE

September 12, 1974

Between: Corbin I. Miles, GRAS Review Branch, DFCA/HFF
William V. Eisenberg, Microanalytical Branch, DM/HFF
Albert Holtz, Organic and Additives Branch, DCP/HFF

and

Richard Carter, Johns-Manville
Richard Lamar, Johns-Manville
Jim Leineweber, " "
Richard Zazenski, " "

Subject: Response to FDA Questions on Migration Data Discussed on
February 27, 1974.

Mr. Carter requested this meeting to explain the details of J-M's response to questions raised by FDA personnel on February 27, 1974. J-M's written response to these questions, dated September 4, 1974, was received by FDA personnel on September 9, 1974, and represented the total substance of this meeting.

The above FDA personnel were generally satisfied with J-M's response to questions, as presented in the September 4, 1974 memorandum. Mr. Eisenberg suggested, however, that the following further studies be conducted by J-M, to demonstrate the lowest limits of detection for tremolitic talc in various food samples. The suggested studies were as follows:

1. Determine the limit of detectability and recovery of tremolite in salt (as a representative of other dry packaged foods) by spiking a sample of salt with a small measured amount of standardized talc.
2. Determine the same limit of detectability and recovery for a meat sample, in the same manner as above.
3. Repeat the above test (1) with tremolite from ashed paper made with tremolitic talc. The intent of this study was to distinguish any difference between standard tremolitic talc and tremolitic talc after ashing.

All persons at this meeting agreed that these studies were necessary to characterize the limits of detectability expressed in previous J-M data. Dr. Miles also expressed the urgency required for completion of these studies, so that these findings could be incorporated into a presently drafted FDA regulation on this matter. Mr. Carter thought that this additional work could be reported within three weeks.

cc: HFF-300
HFF-330
HFF-335
HFF-144
HFF-127
CIM:Miles:dbb:10-9-74

Corbin I. Miles, Ph.D., HFF-335

Johns-Manville Corporation

Greenwood Plaza
Denver, Colorado 80217

Environmental Affairs Department

September 4, 1974

Dr. Corbin I. Miles
GRAS Review Branch
Division of Food and Color Additives
Bureau of Foods
Food and Drug Administration
200 C Street, S.W.
Washington, D. C. 20204

Dear Corbin:

As you will recall, on December 21, 1973, Johns-Manville Products Corporation submitted written comments to the Food and Drug Administration in response to FDA's Notice of Proposed Rulemaking relating to asbestos particles in food and drugs, as published in the Federal Register on September 28, 1973 (hereinafter referred to as the "proposal").

On February 27, 1974, Dick Lamar and Jim Leineweber of our Research and Development Center and myself met with you, Al Holtz and Bill Eisenberg to review eleven questions raised by FDA with respect to our December 21, 1973 submission.

On April 2, 1974, I forwarded a letter to you outlining our understanding of the eleven questions posed, setting forth answers to those questions where information was readily available and outlining what we proposed to do to provide the requested information for the remaining questions.

Attached to this letter, is a memorandum listing each question posed and the information requested by FDA and Johns-Manville's responses thereto. Included in this memorandum, for the purpose of clarity and continuity, are those questions previously answered in part or in full in my April 2, 1974 letter.

The necessary research work undertaken to provide FDA with the information requested has taken a considerable amount of time. This was due to the nature of the work involved

Dr. Corbin I. Miles
Page 2
September 4, 1974

and the considerable demands placed on our Research facilities and personnel with respect to other important projects.

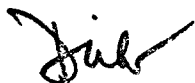
Additionally, our Research personnel place considerable importance on the integrity of the research work undertaken in response to FDA's questions and the necessity to obtain valid results.

The results of the research work undertaken in response to FDA's questions confirm the conclusion reached by Johns-Manville in our submission dated December 21, 1973, that tremolite does not migrate from paper packaging materials containing tremolitic talc to the food or drug contents during commercial handling and shipping. It is our hope that FDA will reach the same conclusion from the attached memorandum, and as a result, will not impose any restriction on the use of talc containing tremolite in food and drug packaging applications.

As we discussed in our telephone conversation yesterday, I am not enclosing the original photographs or charts, as we do not have any additional copies. I will bring the originals with me for our meeting at 2:30 P.M. on September 12. Dick Lamar, Jim Leineweber and Rich Zazenski from our Research and Development Center will accompany me at this meeting.

I look forward to seeing you on September 12 and hope it will be a most productive meeting for all concerned. We will be prepared to answer questions which you and your associates may have with respect to the attached memorandum.

Very truly yours,



Richard P. Carter, Director
Government Relations

RPC/emr

Attach.

MEMORANDUM PREPARED BY JOHNS-MANVILLE PRODUCTS CORPORATION
IN RESPONSE TO ELEVEN QUESTIONS POSED BY THE FOOD AND
DRUG ADMINISTRATION AT A MEETING HELD ON FEB. 27, 1974

These questions and the answers thereto relate to the comments dated December 21, 1973, submitted by Johns-Manville Products Corporation to the Food and Drug Administration in response to FDA's Notice of Proposed Rulemaking relating to asbestos particles in food and drugs, as published in the Federal Register on September 28, 1973.

The questions raised by FDA and Johns-Manville's responses thereto are as follows:

QUESTION 1

WHAT IS THE RELATIONSHIP BETWEEN THE FIBER COUNT AND THE SURFACE AREA OF THE CONTAINER (FOOD CONTACT AREA)?

The areas for the various food containers are as follows:

Salt shaking or scuffing test	18.18 sq. in.
Macaroni container	88.0 sq. in.
Carnation dried milk	138.0 sq. in.
Quick rice	160.0 sq. in.
Cornflakes	304.0 sq. in.
Morton's salt	45.0 sq. in.

In the case of the five packaged food items, TEM and petrographic analyses could not detect the presence of tremolite in any of the food that was packaged in tremolitic talc containing paper. Thus, the ratio of fibers to food contact area is zero for each item. There was no migration.

In the case of the four test containers (salt packaged in tremolitic-talc containing paper) that were shipped by truck approximately 4,000 miles, petrographic analysis revealed no evidence of the presence of any chrysotile or tremolite fibers due to migration. TEM examination of all four samples indicated only the possibility of one tremolite fiber in one of the test contents. For all practical purposes, the ratio of fibers to surface area for each of these samples is 0 fibers/18.18 sq. in. (Each container had an effective contact area of 18.18 sq. in. and a void space of 15 percent interior container volume to allow free movement of contents within the container.)

QUESTION 2

WHAT ARE THE LOWER LIMITS OF DETECTABILITY BY TEM, PETROGRAPHIC AND XRD METHODS FOR TREMOLITE AND CHRYSOTILE IN TALC?

The work which was undertaken to respond to this question should be qualified in one important aspect. We have interpreted the

limits of identification to mean the levels at which positive identification can be made by each method. As a review of the data below will indicated, this is an important consideration.

A. Petrographic identification of tremolite and chrysotile in comminuted talc using Johns-Manville's modified FDA method at a magnification of 500X.

1. Tremolite - In general, positive identification of tremolite can be made on fibers as small as 2.5 x 7.5 microns. However, in some samples examined, positive identification can be made on fibers as small as 1.5 x 5 microns. Unlike "fibrous talc", the Becke line can be followed readily if there is a mis-match in indices of refraction. However, by our method, we use an index oil of 1.622 to match the gamma index at the position of inclined extinction which can vary from 14 to 20 degrees (gamma index relative to the Z direction). Tremolite is also non-pleochroic whereas actinolite and ferroactinolite can be highly pleochroic, accompanied by higher indices of refraction. An experienced petrographer will also look for good cleavage along (110), parting along (100), and twinning along (100), and sometimes along (001). At a position of 90 degrees from inclined extinction, the fiber will show high relief since alpha index is indicated and is on the order of 1.599.
2. Chrysotile - The identification of chrysotile is very much like tremolite since positive optical identification can be made on fibers as small as 2.5 x 7.5 microns. The technique involves using 1.566 oil to capture the gamma index in parallel extinction in which the fiber will disappear or show Christiansen effect in plane polarized light. At 90 degrees from the gamma position, the fiber will show high relief since the alpha index is 1.549 or less. Maximum interference color (Birefringence) is shown at 45 degrees. It is not unusual for chrysotile to show undulatory extinction. Fibrous talc also shows parallel extinction, but the relief is high in either direction; but a match with the 1.556 oil can occur anywhere from 45 to 80 degrees.

B. TEM detectability

1. Tremolite - Tremolite fibers cannot be positively identified by TEM. Usually, tremolite is verified by chemical, optical or X-ray diffraction methods and then dense asbestiform amphibole morphology is viewed by TEM as tremolite. The electron diffraction pattern of tremolite is similar to all other mono-clinic amphiboles. (See Figure No. 1, attached). Using the RCA EMU 3B, it is possible to see tremolite on the order of a few hundred Angstrom units. However, it appears to be the nature of tremolite to remain on the coarse side when compared to chrysotile.

2. Chrysotile - Chrysotile fibers can be positively identified by morphology and electron diffraction. (See Figure No. 2, attached). The electron diffraction pattern is distinctive since alternate rows of Laue spots are not spots but rather elongated streaks. The morphology is most unusual since chrysotile is characterized by an internal low density tubular structure which is sometimes beaded. The most narrow of individual fibrils of chrysotile are on the order of 250 Angstrom units. Below this width, the mineral ceases to be chrysotile. The most common magnification employed for the study of chrysotile and asbestiform amphiboles is 8000X. The negative is enlarged 2.5 times to provide an 8.5 x 10-in. print at a magnification of 20,000X.

C. XRD identification

Qualitative evaluations at 2°/minute and quantitative evaluations at 1/4°/minute were performed using Ni filtered CuK radiation.

1. Tremolite - With qualitative examination through the 9.4 A peak area, detection could be made at the level of 0.5% tremolite in talc. However, quantitative evaluation could not be made below 1.0% even though samples containing 0.0, 0.25, and 0.5% tremolite were compared to background counts, with none having counts above background.
2. Chrysotile - While 1.0% chrysotile can be detected by XRD under the 7.3 A peak, positive identification by this means may be difficult because of the conflict between major chlorite peaks and serpentine peaks. The former appear at 7.3 and 3.65 A and would obscure chrysotile concentrations. Serpentine has a minor peak at 2.15 A which differs slightly from the minor 2.10 A peak, but neither would be apparent at low concentrations of either mineral or combinations of the two. In the absence of chlorite, 1% chrysotile (in talc) was measurable, but small quantities of chrysotile in the presence of serpentine would not be detected.

From the foregoing, we believe the following conclusions can be substantiated:

- (1) Individual tremolite particles 2.5 x 7.5 microns can be positively identified petrographically and under some circumstances, particles as small as 1.5 x 5 microns can also be identified.

- (2) Tremolite particles cannot be positively identified as such by TEM, since they cannot be distinguished positively from other amphibole minerals.
- (3) Tremolite particles can be detected at the 0.5% level by XRD but their quantity cannot be determined accurately below 1.0%.
- (4) Chrysotile fibers 2.5 x 7.5 microns can also be positively identified petrographically.
- (5) Chrysotile can be positively identified by TEM morphology and electron diffraction, with the lower limit of fibril width being of the order of 250 Angstrom units. Below this figure, the mineral ceases to be chrysotile.
- (6) The chrysotile content of talc can be determined at the 1.0% level only if the commonly associated minerals, chlorite and serpentine, are not also present. If they are present, chrysotile may not be positively identified.

QUESTION 3

PROVIDE VALIDATION AND RECOVERY DATA FOR TREMOLITE AND CHRYSOTILE IN SPIKED SAMPLES OF TALC - SAMPLES OF TREMOLITE AND CHRYSOTILE-FREE TALC TO WHICH KNOWN AMOUNTS OF TREMOLITE AND CHRYSOTILE HAVE BEEN ADDED.

The following data contains our findings with respect to Petrographic, TEM and XRD examination of a series of standards made from amphibole-free talc and varying percentages of tremolite. In addition, XRD examination of similar talc - chrysotile standards was made, but a set of talc - chrysotile standards suitable for Petrographic and TEM examination was not available. Because little, if any, chrysotile-containing talc is used by the pulp and paper industry, it was decided that the very time consuming preparation of such standards was not warranted in view of the detection data already made available.

A. Tremolite validation

The following tabulation sets forth tremolite content vs. numbers of "fibers" in talc samples. In all cases, the number of tremolite particles should be read as $\pm 20\%$. So-called fibers are tremolite particles having a 3:1 aspect ratio and a length of at least 5 microns counted at 500X.

<u>Sample</u>	<u>Percent Tremolite By Weight</u>	<u>No. of Tremolite "Fibers" per mg of Talc</u>
F-1 Standard	0.25%	41,000
F-2 Standard	0.50%	61,000
F-3 Standard	1.00%	111,000
F-4 Standard	2.00%	207,000
F-5 Standard	4.00%	400,000
F-6 Standard	16.00%	1,800,000
Tremolite-free Talc	--	0

The slight lack of linearity is due to the difficulty in obtaining sufficiently dispersed slides to permit unhindered counting, i.e., a top layer of particles obscuring lower layers, and the counting precision noted above.

Figures 3 and 4, attached, are electron photomicrographs (TEM) of two of the above materials. Figure 3 is the tremolite-free talc at 20,000X as reproduced here. Figure 4 is the same talc spiked with 0.5% tremolite (F-2 Standard). There are three (3) tremolite "fibers" present and these are the most dense in the entire print. Other similar looking particles in both pictures are talc platelets on edge. Each tremolite particle identified represents 1,100 particles per mg of sample.

Figure 5, attached, is a composite XRD tracing covering the same series of samples used for the petrographic examination. The various levels of tremolite added, from 0 to 16% by weight, are indicated along with the height of the 9.4 Å peak for each. For samples having no or 0.25% tremolite, there is no discernible peak. At 0.5%, an identifiable peak appears which becomes more prominent as the percentage of tremolite increases.

This latter phenomenon can be used to estimate the amount of tremolite present when compared to a sample containing a known and discernible amount of tremolite. This is done by determining the number of counts or units of area under the peak. Figure 6, attached, is a plot of counts vs. tremolite content of the same standards, extended in this case to include one having 50% tremolite. All counts are corrected for background. The lowest level having a count above background is 1.0%. Above this point, the relationship between point count and tremolite content is seen to be quite linear, and it could be used as a reliable means of assessing tremolite content above that level.

B. Chrysotile

As noted previously, no comparable series of chrysotile-spiked samples suitable for petrographic and TEM examination is available. Differences in the manner of dispersion of the fibers, makes samples for microscopy much more difficult to prepare than those for XRD. Some samples for XRD were prepared for this study.

Figure 7, attached, is a composite XRD tracing of talc, and talc with chrysotile added in the amounts of 1.2 and 2.2% respectively. It should be noted that the 7.3 Å peak is sufficiently well developed to indicate that a quantitative evaluation could be made at about 1%.

However, It must be emphasized that chlorite and serpentine produce identical to similar peaks if present. As an illustration, Figure 8, attached, is an XRD tracing for a mixture of 60% chrysotile and 40% serpentine (without talc) showing the peaks between 2.10 and 4.57 Å. Only the peaks at 2.10 Å for chrysotile and 2.15 Å for serpentine are distinguishable. However, if these were included in a mixture which was mainly talc, they would no longer be discernible.

The above leads to the conclusion that chrysotile can be positively and quantitatively identified by petrographic or TEM means. However, a quantitative gravimetric evaluation must take into account that chlorite and/or serpentine minerals cannot be present.

QUESTION 4

A REQUEST WAS MADE THAT, WHEREVER POSSIBLE, WE RETAIN ALL SAMPLES, PREPARATIONS, SLIDES, ETC.

Wherever possible, we are doing this. Petrographic slides, however, are not permanent. Immersion oils change with age and exposure to air. We are retaining the negatives for all TEM's.

QUESTION 5

IN OUR SALT-SCUFFING TESTS, DO WE HAVE DATA FOR 10 CPS TESTS SIMILAR TO 19 CPS TESTS? DO WE HAVE TEM TEST RESULTS AT 10 CPS? DO WE HAVE RETAINED ASH SAMPLES?

The data on the 10 cps test is as follows:

<u>Sample</u>	<u>% Talc in Paper</u>	<u>Residue Due To Scuffed Paper (gms)</u>	<u>Number of Talc Particles*</u>	<u>Number Of Chrysotile & Tremolite Fibers</u>
RS 73242-2A	1.0	0.00000	0	0
RS 73242-2B	1.0	0.00000	0	0

*Residue viewed petrographically at 500X

These results are discussed on pages 3 and 4 of Report No. E414-2, Preliminary Studies of Food Contamination by Contact with Paper (Exhibit I, Johns-Manville submission dated December 21, 1973). There are no TEM results at 10 cps, as there are none for any of the artificial test results. TEM analysis began on samples that had actually endured road travel and on the analysis of actual food contents.

Except for TEM negatives, we have not retained ash samples of any work prior to March 1, 1974. Whenever possible, we are doing so now.

Although FDA requested that we repeat these salt-scuffing tests, based on the research work undertaken in preparation of our submission dated December 21, 1973, and based on the additional work reported herein, we have reached the conclusion that it is futile to run additional artificial scuff tests at this time. An artificial test is generally any test which simulates an actual occurrence. It is usually run on a smaller scale and at accelerated times. Before any laboratory test can be designed to simulate an actual or large-scale occurrence, all of the parameters and variables must be known so that they can be scaled down correctly. Only by knowing these parameters and variables, can one even begin to design and build a simulated model which will produce valid test results.

In the case of the artificial scuff tests, we were requested by FDA to run and re-run paper samples on the artificial scuff tests. It was assumed that a test of this nature would simulate the vibrating action which food packages undergo during normal commercial shipping and handling. This is a dangerous assumption. The simple procedure of placing a test container on a vibrating table, vibrating at an arbitrarily chosen amplitude and frequency for an arbitrarily chosen period of time, simply cannot be said to simulate actual shipping and handling. Any conclusions or correlations between this artificial test and actual road travel would be completely unfounded. Yet, in the months of study on this subject, many people have tried to compare the two. Such erroneous assumptions can lead to mistaken conclusions.

Based on the research work completed thus far, we have concluded that the only data which warrants consideration is that data which is supplied by examining actual food contents and test contents that undergo actual road travel. For these reasons,

the results and conclusions discussed in Report No. E414-6, Lack Of Food Contamination By Contact With Paper Due To Shipping (Exhibit II, Johns-Manville submission dated December 21, 1973), and the data furnished in response to Question 9 herein, should be regarded with the utmost importance.

QUESTION 6

PROVIDE A DESCRIPTION OF OUR METHOD AND A SAMPLE CALCULATION OF OUR XRD ANALYSIS OF FOOD PACKAGING PAPER FOR TALC CONTENT.

XRD analysis of food packaging paper for talc content is performed by scanning the paper over the 9.4 A peak and computing the percent of talc present from the ratio of the area count obtained for the unknown paper to the area under the peak of a standard paper of known talc content. Papers of verified talc contents ranging from 0.53% to 12% talc are used for standards.

A. Sample Calculation: Unknown Paper Sample

Scan 200 sec from 9.9° to 8.23° 2θ = 64,056 counts

Background Determination:

Count for 100 seconds at 9.9° 2θ = 25,394 counts

Count for 100 seconds at 8.23° 2θ = 24,187 counts

49,581 counts (total background count)

64,056 counts (total sample counts)

-49,581 counts (total background counts)

14,475 counts contributed by talc in paper sample

B. Standard Sample: 2.5 Percent Talc

The same procedure determines that the 2.5 percent standard has a total count due to the talc of 15,069 counts.

The percent talc in the unknown paper sample is computed by:

$$\frac{14,475 \text{ counts (unknown sample)}}{15,069 \text{ counts (2.5 percent standard)}} \times 2.5\% \text{ talc} =$$

2.4% talc in unknown paper sample

QUESTION 7

IN TABLE IV-A ON PAGE 11, REPORT NO. E414-2 (Exhibit I, JOHNS-MANVILLE SUBMISSION DATED DECEMBER 21, 1973), THE SIX-HOUR RESULTS APPEAR OUT OF LINE. CAN THIS ANOMALY BE EXPLAINED?

As for the irregularity of the six-hour results, we can only suggest the possible source of error, since a definite explanation is not known. We strongly believe the anomaly is a result of a human error, probably committed early in the weighing procedure. The belief that the anomaly is due to human error, is strongly supported by the other data. Since six out of seven data points form a definite, regular curve, and since the irregular data point is not at either end of the curve, but somewhere in between, scientific logic suggests that the point should be disregarded and labeled as a procedural error.

QUESTION 8

PROVIDE VALIDATION OF THE MEAT WRAPPING AND SAMPLING TESTS AND THE SENSITIVITY OF THESE TESTS. IN ADDITION, RELATE ANY MIGRATION TO MEAT SURFACE OR MEAT WEIGHT.

This question relates to the McCrone meat wrapping studies (Exhibit E, Johns-Manville submission dated April 20, 1973) in which talc-containing papers were placed in contact with raw meat. Subsequent examination of the meat, both in thin sections and after ashing, showed no migration of tremolite.

The question raised by FDA was whether talc containing tremolite would have been detected if present in the meat in McCrone's studies. The answer is essential to the validity of McCrone's finding that no migration of tremolite had occurred.

An experimental plan, a copy of which is attached hereto as Figure 9, was devised to confirm the presence or absence of tremolitic talc on meat under known conditions. Preliminary experiments indicated that there is no practical way to determine the lowest level of detectability, which was one element of the FDA question, because we could not uniformly spread extremely small amounts of tremolitic talc over a known area. Applications of the order of 0.1 to 0.2 mg/cm² are so apparent, however, that the limit of detectability is probably at least three orders of magnitude lower, i.e., 0.0001 to 0.0002 mg/cm². We were unable to devise a means of applying such small amounts.

Test Results

Using the procedure described in Figure 9, samples were prepared from three steaks, the first a control having no contact with tremolitic talc except what might have come from the wrappings and mask, the second having an applied dose of 0.12 mg/cm² of J-M CYCLO-SORB, and the third having an applied dose of 0.16 mg/cm² of J-M CYCLO-FIL. Samples of all paper in

contact with the meat were also obtained to identify any source that could have lead to contamination of the control.

The three samples of raw meat scrapings were examined by optical microscope at 500X. Results are reported as follows:

<u>Sample Number</u>	<u>Sample</u>	<u>Talc</u>	<u>Tremolite</u>
4384-38-4 (Fig. 10)	Meat Control	None detected	None detected
4384-38-5 (Fig. 10)	Meat with 0.12 mg/cm ² CYCLO-SORB	Present	Present
4384-38-6 (Fig. 11)	Meat with 0.16 mg/cm ² CYCLO-FIL	Present	Present

Three pictures, attached, as Figures 10 and 11, are photomicrographs of the three meat samples above, taken at 500X. It should be noted that talc and tremolite particles are readily visible in the samples to which CYCLO-SORB and CYCLO-FIL were applied, but neither talc nor tremolite could be confirmed in the blank. The CYCLO-FIL-dosed sample also illustrates the problem mentioned earlier of obtaining even distribution of dispersion of very small amounts of talc, in this case 0.16 mg/cm², and obtaining representative samples therefrom. The fibrous material in all of these pictures is part of the raw meat structure.

Meat and paper samples were then ashed for 16 hours at 800°F. There was considerable difficulty in reducing the carbonaceous content of these samples to low enough levels to permit reliable examination, but this was finally achieved. Optical microscopy results are as follows:

<u>Sample Number</u>	<u>Sample</u>	<u>Talc</u>	<u>Tremolite</u>
4384-38-4	Meat Control	None detected	None detected
4384-38-5	Meat w/CYCLO-SORB	Present	Present
4384-38-6	Meat w/CYCLO-FIL	Present	Present
4384-38-1	Mask Paper	Trace	None detected
4384-38-2	Outside Wrapper	Trace	None detected
4384-38-3	Meat Contact Wrap	None detected	None detected

The final part of FDA's question relates to number of tremolite particles applied meeting the standard of 5 μ length with a 3:1 aspect ratio. The 0.12 mg/cm² CYCLO-SORB applied is estimated to contain 390,000 ($\pm$ 20 percent) tremolite particles meeting the above criteria. The 0.16 mg/cm² CYCLO-FIL applied is estimated to contain 1,250,000 ($\pm$ 20 percent) tremolite particles meeting the criteria. No attempt was made to enumerate talc particles in either case, since such particles do not generally fit the criteria. However, many millions of particles can be seen and particle size analysis indicates that there are many millions more that are sub-optical microscopic.

Based on the high numbers and degree of detectability of both talc and tremolite particles on meat samples and ash in this study, it is concluded that McCrone's finding, that migration of tremolite from the tremolitic talc-containing wrappings did not take place, is valid. Had even a very low order of migration taken place, it would have been detectable.

QUESTION 9

PERFORM BOTH SCUFFING AND SHIPPING TESTS USING PAPER WITH HIGH LOADINGS OF TREMOLITIC TALC (PAPER WITH THE HIGHEST LEVEL OF TREMOLITIC TALC THAT IS COMMERCIALY USED FOR FOOD PACKAGING WRAP)

See our answer to Question 5 as to why we did not perform additional scuffing tests.

As requested by FDA, salt shipping tests were repeated, employing papers with high loadings of tremolitic talc. To briefly review the test, it consists of lining salt-filled glass jars with test papers and shipping them by truck approximately 4,000 miles (For a more complete description of the test procedure utilized, see Johns-Manville's submission dated December 21, 1973). By utilizing this procedure, we can duplicate, if not exceed in stringency, the conditions under which food packages are shipped.

The test results reported hereinafter were obtained from papers with exceptionally high loadings of tremolitic talc. The papers used to line the salt-filled glass jars contained 9%, 14% and 20% of Johns-Manville's CYCLO-FIL talc. The 9% and 14% CYCLO-FIL papers were obtained from a Johns-Manville customer which purchases CYCLO-FIL. The 20% CYCLO-FIL papers were previously made by Johns-Manville for testing purposes, using CYCLO-FIL. Therefore, we knew that tremolite was present in all of the paper used to line the salt-filled glass jars, as CYCLO-FIL contains approximately 30% tremolite. To confirm the presence of talc in the paper used in this test, the analytical method

set forth in our answer to Question 6 of this memorandum was utilized. Our XRD analysis of these papers confirmed the presence of talc.

It is essential to note that after an exhaustive search, we were unable to locate any food packaging paper containing loadings of talc in excess of the paper utilized in the salt shipping tests reported in Exhibit II to our December 21, 1973 submission. As noted in our December 21, 1973 submission, papers with high talc loadings would normally not be used for direct food packaging applications. However, FDA requested that we specifically subject highly loaded talc papers to the salt shipping test. Therefore, these highly loaded talc papers, which are manufactured for such purposes as writing paper, textbooks, etc. (as indicated by our customers), were utilized.

A misunderstanding which may have arisen from our December 21, 1973 submission should be clarified. High brightness talc (i.e., CYCLO-FIL) is used in the manufacture of fine paper products as a high-brightness filler and opacifying pigment. Its loading ranges may vary from 2% to 15% by weight. CYCLO-FIL and other related ultra-fine particle size white pigments are used to increase opacity and brightness and in many instances to improve the printing characteristics of the paper. The ultra-fine particle size also develops a unique synergistic effect when blended with TiO_2 . It not only acts as a spacing mechanism, but also attracts the TiO_2 to the platey planar surface, thus resulting in increased efficiency from TiO_2 usage.

However, it is important to emphasize that high brightness fillers and pigments are used only for fine paper products, such as printing (magazine) paper, writing paper, labels, etc. Costs prohibit its use in paper whose application does not warrant high brightness and opacity, such as newspaper, cardboard, paper bags, etc. Most paper which is used in food packaging applications would fall into this second lower grade category. There is no need to load this paper that comes into direct contact with food with high brightness fillers and pigments, because it is rare that this paper is ever used for outside labeling. However, this lower grade paper (lower grade so far as brightness and ink receptivity are concerned) is generally then wrapped with a bright, high grade paper, which is then suitable for labeling and attractiveness. Therefore, papers that are loaded with high concentrations of high brightness pigments and fillers are used only indirectly so far as food wrapping applications are concerned. This type of paper is normally not used in a direct food-contact basis. As a result

of all of our research efforts and investigations, we have been unable to locate food packaging paper containing more than 1.5% talc. Such paper was utilized in the scuffing and salt shipping tests reported in Exhibits I and II of our December 21, 1973 submission.

The salt shipping tests which were repeated with highly loaded talc paper, utilized the identical test procedure employed in the tests described in our December 21, 1973 submission. The results reported in Table 1 below were obtained by employing the TEM at 11,000X. The proposed FDA criteria for identifying asbestos fibers (as published in the Federal Register on September 28, 1973) was employed.

Table 1

Examination of Shipped Test Sample Residues By
Transmission Electron Microscopy - Plain Uncoated Paper

<u>Sample No.</u>	<u>Percent Talc in Paper</u>	<u>11,000X TEM Plate No.</u>	<u>Chrysotile</u>	<u>Tremolite</u>
4385-78-7	9	2282A	0	0
		B	0	0
		C	0	0
		D	1 Bundle *	0
			10 μ long	
		E	1 Fiber *	0
			10 μ long	
4385-78-10	14	2283A	0	0
		B	0	0
		C	0	0
		D	0	0
		E	0	0
4385-78-12	20	2284A	0	0
		B	0	0
		C	0	0
		D	0	0
		E	0	0

Table 2, following, reports shipping test results using the same papers, after they were coated with a thin film of Flexbond 811 prior to testing. As indicated in our April 20 and December 21, 1973 submissions, paper food containers are normally either lined on the inside with plastic (such as polyethylene) or coated with a thin film of wax or plastic. This is done for two reasons: (1) to help keep the food fresh, and (2) to prevent the paper from absorbing moisture, oils, taste and fragrance from the food. Because this is a real situation, we decided to simulate this type of container to see if it was possible for the salt to abraid through the coating, thus exposing the paper to the food. The Flexbond 811 employed in this test was a polyvinyl acetate co-polymer.

*Most likely due to contamination, as bundles of chrysotile are not found in Johns-Manville's

EXHIBIT 1-12

Table 2

Examination of Shipped Test Sample Residues by TEM
Papers Coated with Flexbond 811

<u>Sample No.</u>	<u>Percent Talc in Paper</u>	<u>8,000X TEM Plate No.</u>	<u>Chrysotile</u>	<u>Tremolite</u>
Salt Blank		2293A	0	0
		B	0	0
		C	0	0
4385-78-7F	9	2290A	0	0
		B	0	0
		C	0	0
4385-78-10F	14	2291A	0	0
		B	0	0
		C	0	0
4385-78-12F	20	2292A	0	0
		B	0	0
		C	0	0

CONCLUSIONS:

1. The results reported in Tables 1 and 2 clearly indicate that even the most severe of actual shipping and handling conditions are not severe enough to cause destruction of food packaging paper. Since the paper is not degraded, there is no migration of tremolite fibers.
2. The above conclusion is supported by shipping test results on test papers that had as little as 0.25% tremolitic talc to as much as 20% tremolitic talc.
3. The results also indicate that the migration of paper additives, such as tremolitic talc, depends on the strength of the paper and not the amount of additives that are contained in the paper. Since we have determined that the paper itself must be physically degraded in order for migration to occur, and since we have found that actual shipping and handling conditions are not severe enough to cause commercial paper to degrade, the fact remains that regardless of the quantity of tremolitic talc which commercial food packaging paper may contain, there should be no fear of tremolite migration and contamination. The conditions are simply not present to cause such an occurrence. To visibly demonstrate this conclusion, we have attached SEM photographs displaying the surface of one of the test papers (14% talc by weight). Figure 12

attached, is a picture of the surface of the paper before going through the shipping test. Figure 13, attached, is a picture of the surface of the paper after testing. Both pictures are virtually identical and indicate that the paper obviously was not degraded.

QUESTION 10

WHAT ARE THE EFFECTS OF ASHING TREMOLITE AND CHRYSOTILE?
WHAT HAPPENS WHEN PAPER CONTAINING TALC, TREMOLITE AND
CHRYSOTILE IS INCINERATED?

When any sample containing tremolite or chrysotile is ashed, the purpose is to eliminate any carbonaceous material which might mask the sample and hinder its examination. However, in order not to affect the tremolite or chrysotile, a temperature is selected which is a safe distance below that which would alter the lattice crystals. For our own analytical preparations, we use 800°F. In an oxygen rich atmosphere, this temperature is sufficient to oxidize the carbon which may be present in the form of cellulose or any other organic materials. However, this temperature is well below that which would affect the asbestos. Chrysotile will remain unaffected until 1382°F and tremolite will withstand temperatures to 1796°F. At these respective temperatures, the minerals will lose their bound water and the crystal lattices would collapse.

QUESTION 11

EXPLAIN THE HIGH TALC CONTENT IN THE SALT BLANK AND REPEAT THE TEST RESULTS.

When we initially began our test program to study the possible migration of tremolite from tremolitic-talc containing paper, laboratory work was performed in an area which also houses many talc-related testing equipment. Therefore, it is very likely that the first few test results (artificial scuff test results) were artificially high in talc content due to airborne contamination. When the first salt blank was reported to contain approximately 8,000 talc platelets in its residue, the laboratory work was immediately moved to an area which would be less likely to contain airborne contamination. Future salt blanks showed a decrease in talc content down to ranges of 700 to 1000 platelets per membrane. In an effort to further decrease this level, modifications were designed into the testing procedure to reduce as much as possible the open-air time exposure of all test components. This last measure reduced the background count to less than 500. The very fact that we could not completely

eliminate the talc background indicates that TEM evaluations of actual test samples may have detected talc platelets which did not come from migration.

However, since our December 21, 1973 submission, time has permitted the set-up of a "clean room", in which the background count of airborne contamination is essentially zero. The test results reported in response to Question 9 herein, were obtained from samples which were completely prepared for microscopy in this "clean room".

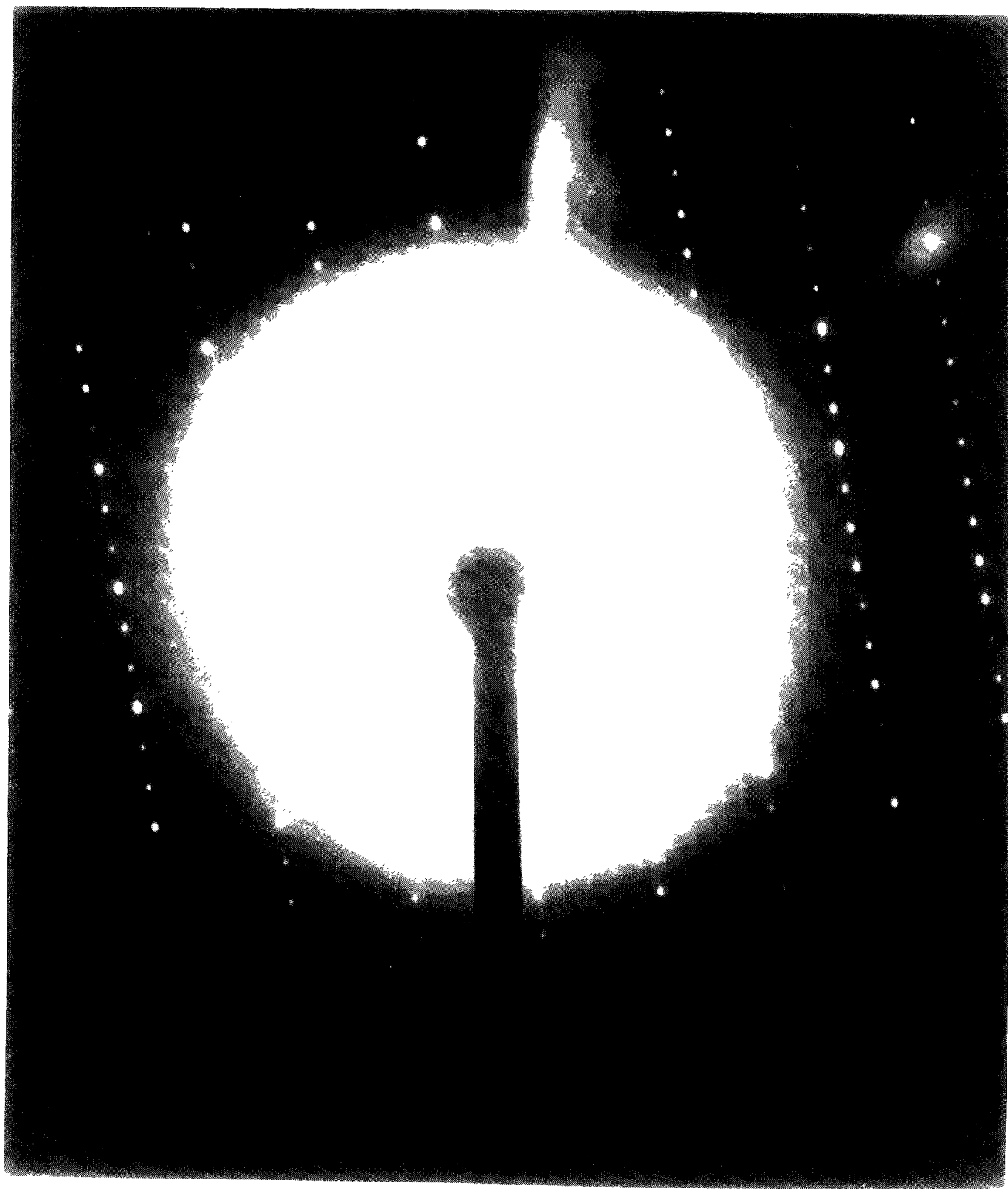


Figure No 1

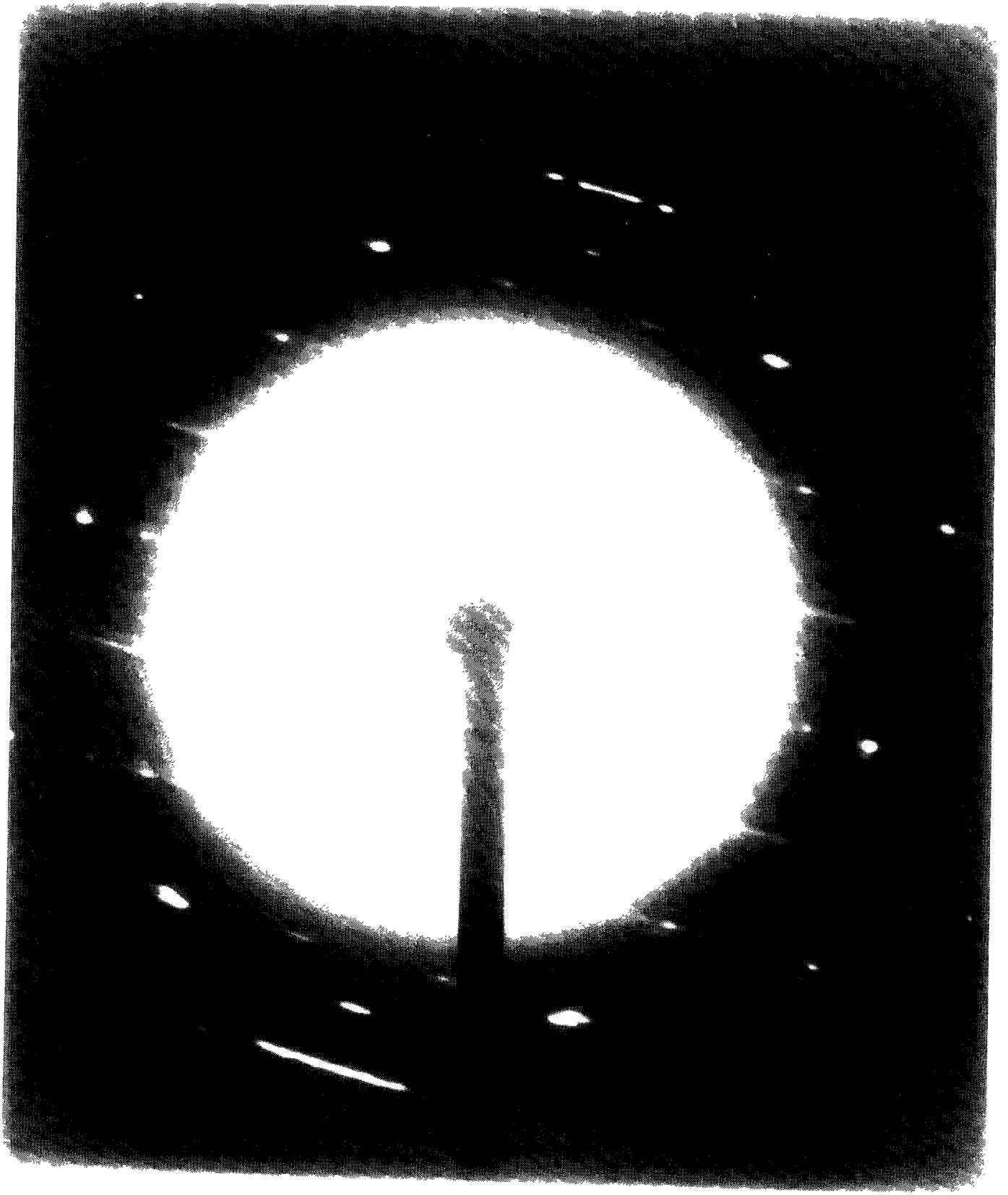


Figure No. 2

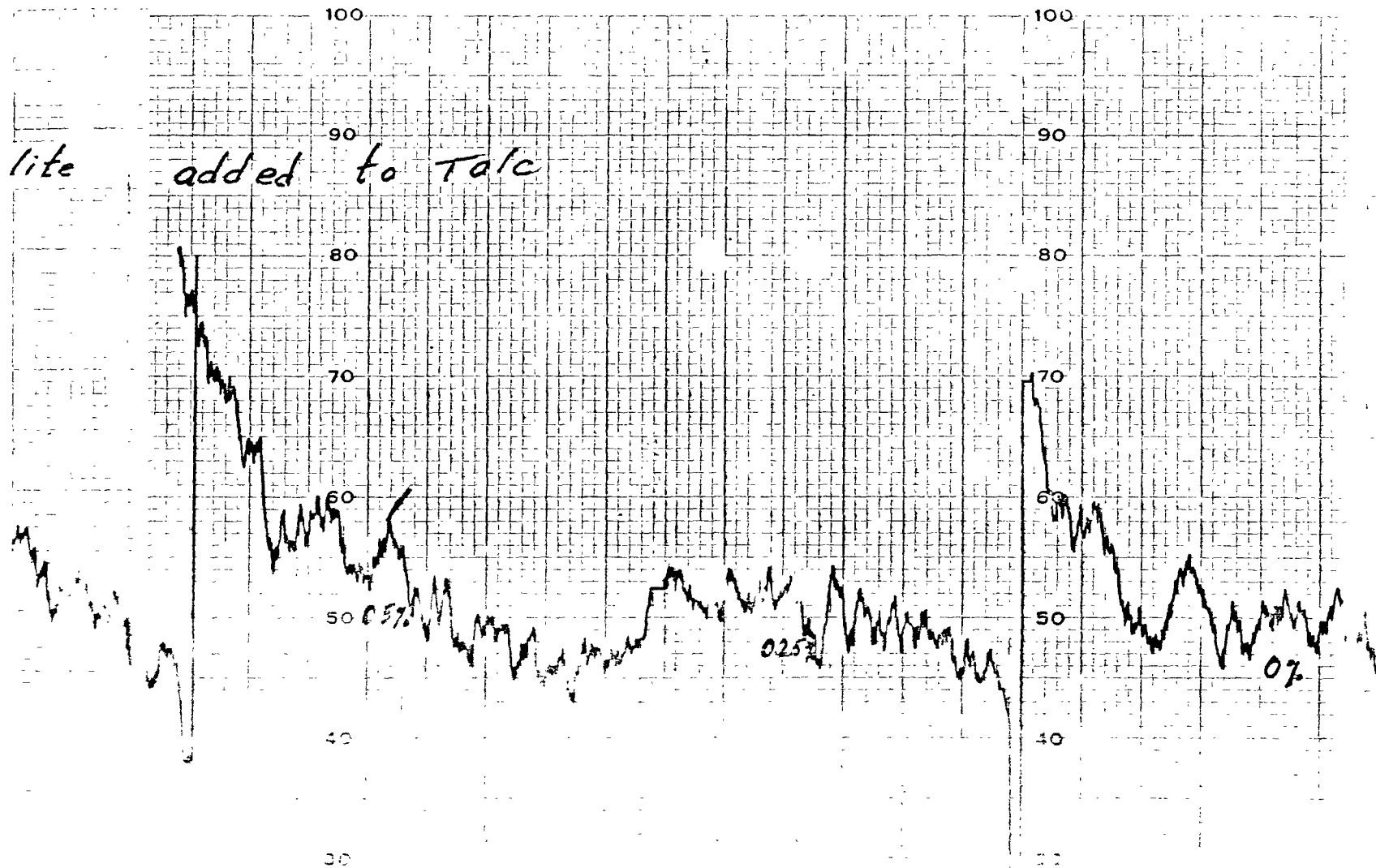


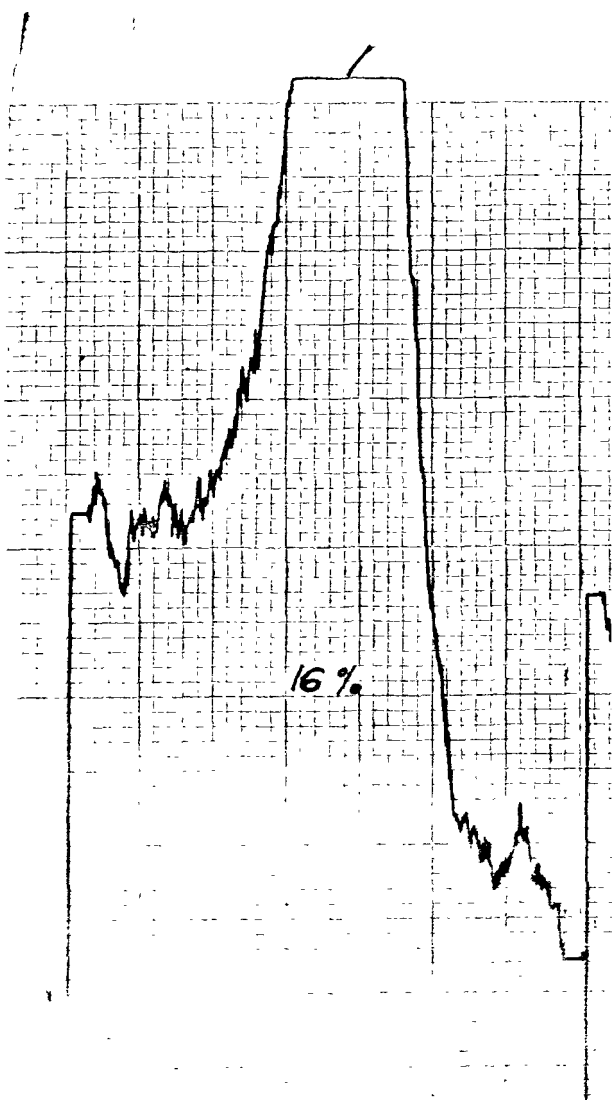
Figure No. 3



Figure No. 4

Figure No. 5





100

90

80

70

60

50

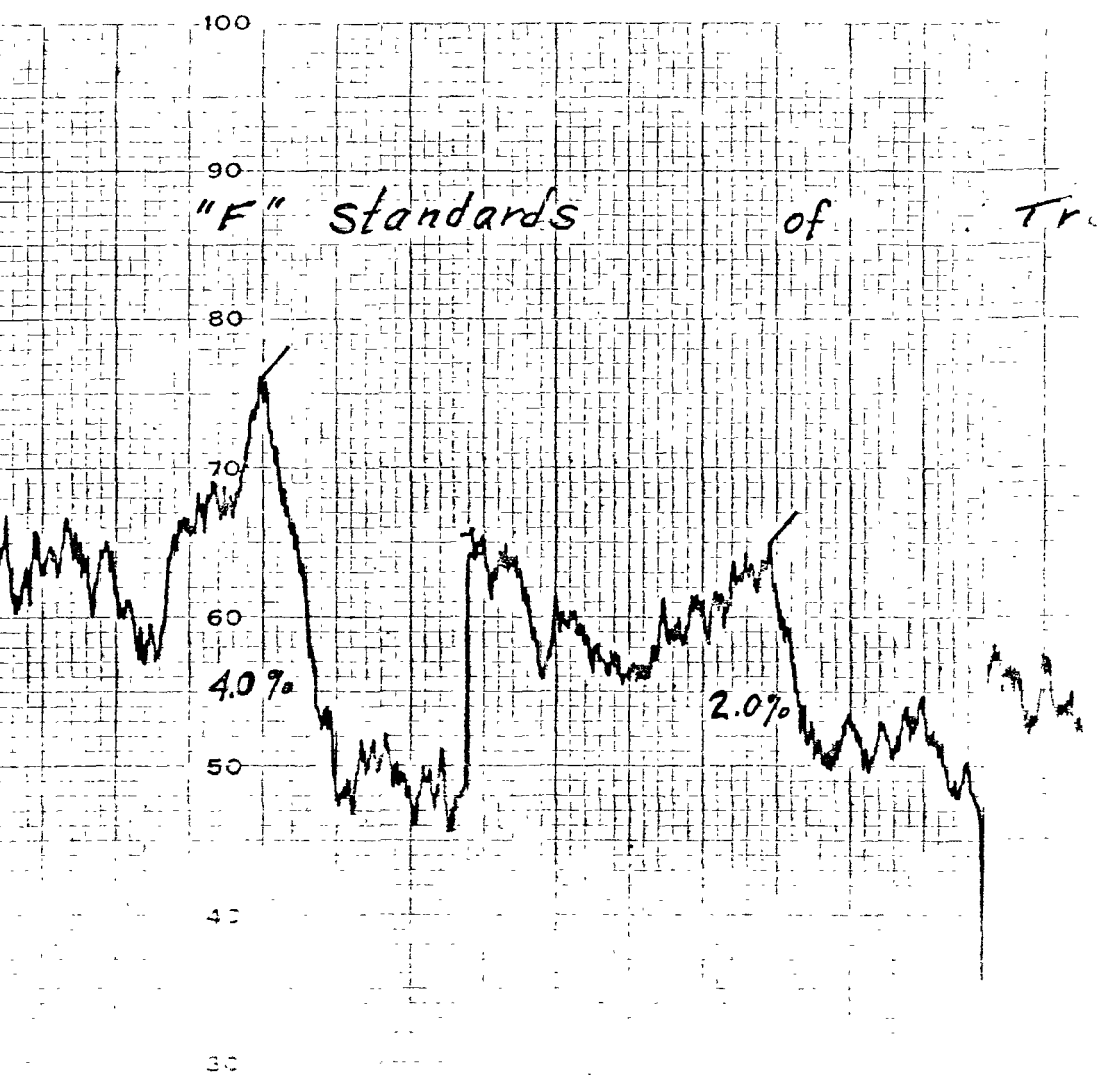
40

30

"F" standards of Tr.

4.0%

2.0%



Counts
(units)

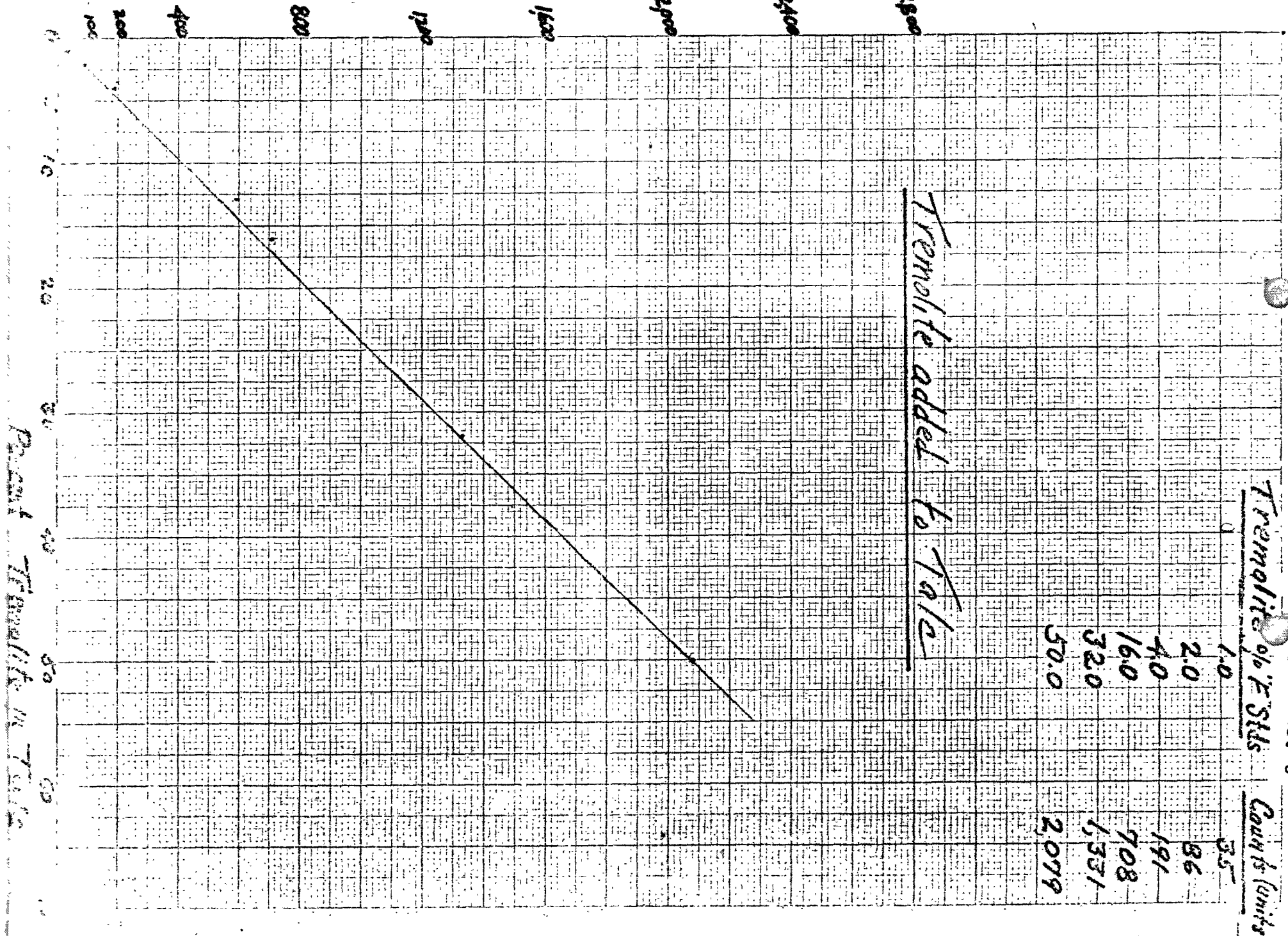
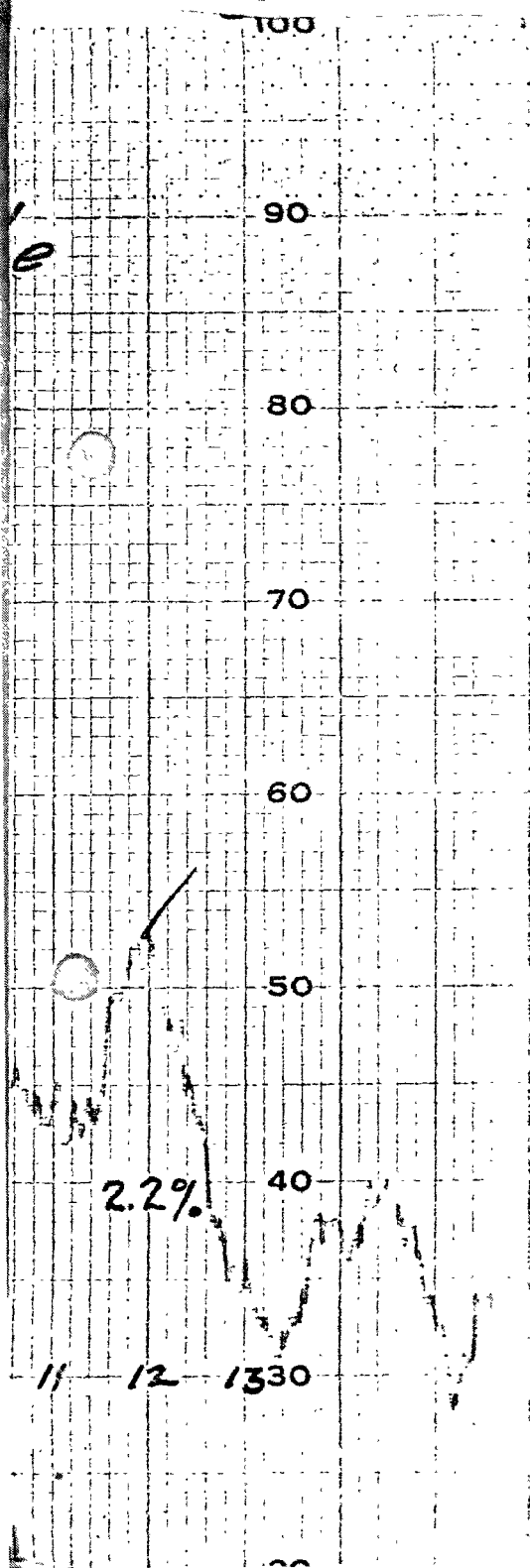


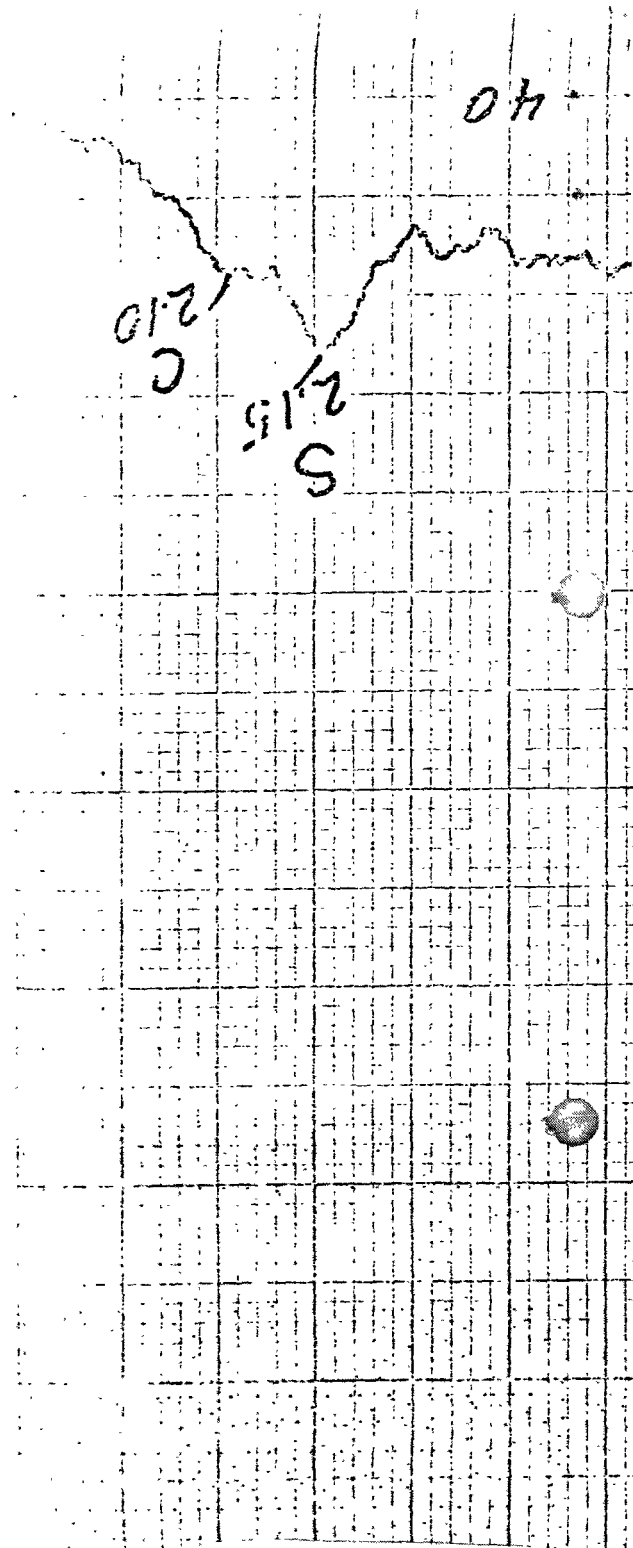
Figure No. 6

Figure No. 7



[illegible]

Figure No. 8



EXPERIMENTAL PLAN TO CONFIRM PRESENCE OF TALC ON MEAT

I. Raw Materials

1. CYCLO-SORB (~5% Tremolite)
2. CYCLO-FIL (~30% Tremolite)
3. Lean Beefsteak

II. Sample Preparation

1. Make a mask with 5 x 10 cm rectangular opening (50 cm²) using butcher paper or plastic.
2. Put talc into a clean pepper shaker (small holes).
3. Shake talc onto a tared paper and determine shaking needed to achieve approximate weight per unit area desired, perhaps 0.1 mg/cm².
4. Now put a weighed amount of talc into a clean shaker.
5. Place the mask on the meat and coat the exposed area as evenly as possible at about the desired dose.
6. Freeze the meat (uncovered).
7. Determine weight of talc used by difference.
8. When meat is solidly frozen scrape talc coated area with edge of a sharp tablespoon or knife to approximate depth of 1 mm.
9. Examine scrapings by optical microscopy at 500X. If talc and tremolite are seen make photographic record.
10. Low temperature ash scrapings.
11. Determine optically presence or absence of talc and tremolite and estimate number of particles of latter.

III. Report

1. Note presence or failure to confirm presence of tremolite and talc.
2. If present, calculate numbers of particles of tremolite per cm² relative to weight of talc applied.



Cyclo-SORB 4384-38-5



MEAT BLANK 4384-38-4

50x



4384-38-6 Cyclo-Fil

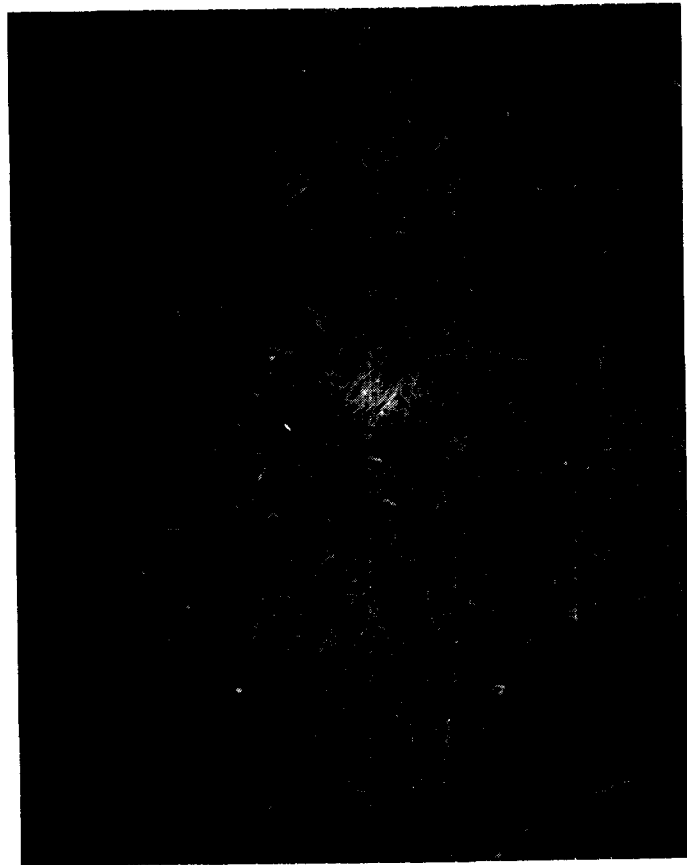


Figure No. 12



Figure No. 13

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

TO : Petitions Control Branch (HFF-334),
Attn: Dr. C. Miles FCA

DATE: May 3, 1974

FROM : Organic and Additives Chemistry Branch (HFF-144)

SUBJECT: Johns-Manville Corporation (J-M) 4/2/74
Data on talc-Asbestos (T-A) Program.

We have reviewed J-M's response to the FDA questions raised on the above subject matter at the 2/27/74 meeting. Our following comments will cover the J-M answers and proposals as numbered in their reply.

1. (a) The food contact area of the purchased containers are provided. However since there was no detection of either tremolite (T) or chrysotile (C) fibers there was no migration.

(b) The above "no detection" values will be clarified in the following data. The method of measurement under (a) should be identified.

2. (a) Comparison of lower limits of detectability of (T) and (C) by transmission electron microscopy (TEM), petrographic (P) and X-Ray Diffraction (XRD) methods will be carried out on T and C spiked talc. The relationship and results of the 3 methods will be submitted along with XRD patterns and TEM prints. A statistical analysis of the methods has been prepared.

(b) The TEM analysis on the 10 or 13 cps samples cannot be run since they have not been retained. However the optical test result data may be available and should be submitted if possible.

(c) Under (9) scuffing and shipping tests on high talc papers will be run. Possibly TEM analysis on these samples may be helpful.

3. The protocol outlined under (2) should cover our request for "Recovery and validation data ---- for the entire analysis at low levels of spiking"

4. J-M will attempt - wherever possible - to retain all samples, preparations, slides etc. which would permit FDA to check all data and our method(s) if necessary.

5. As noted under 2(b) the 10 or 19 cps. samples are not available. J-M does not confirm our request for a repetition of this test.

6. The complete description of J-M's XRD analysis will be submitted along with sample calculation(s) of their results on a food packaging paper.

7. This covers our No. 8 question concerning the 6 hour anomalous decrease of the talc particles in Table IV-A, Report E414-2. J-M has no explanation for this result.

8. J-M will repeat their meat sampling test - which initially showed no migration. Therefore the spiking and recovery studies with the Cyclo-Sorb and Cyclo-Fil should cover detection at the lowest sensitivity possible.

9. Since the original scuffing and shipping tests were run with papers of lower level talc content, J-M has agreed to obtain paper samples with up to 20% Cyclo-Fil and repeat the salt-scuffing and shipping tests previously covered.

We would suggest that the scuffing trials attempt to compare the 19 10 cps. trials. Furthermore these results should be evaluated with the IEM and P methods if possible.

10. J-M interpreted our question on the effects of ashing on paper containing T and C fibers to be related to the environmental effects. Our question was directed towards the possible effects on the analysis of samples and not on environment.

11. They have not been able to repeat the high talc concentrations in their salt blanks as were noted in Appendix 1, pl2, Table IV-B. These results will be submitted.

The above data also contain a statistical analysis on the lower limits of detectability. This section should be evaluated by HFF-127.

A. Holtz
A. Holtz

Johns-Manville Corporation

Greenwood Plaza
Denver, Colorado 80217

Environmental Affairs Department

April 2, 1974

Dr. Corbin I. Miles
GRAS Review Branch
Division of Food and Color Additives
Bureau of Foods
Food and Drug Administration
200 C Street, S.W.
Washington, D.C. 20204

Dear Corbin:

I deeply apologize for the long delay in my response to you since our meeting on February 27. This delay has been caused by the extensive travel schedules of myself and our research personnel. However, much of the work which we discussed at the meeting has been underway for several weeks.

In accordance with the agreement reached at our meeting, outlined below is our understanding of the eleven questions posed by you, Al Holtz and Bill Eisenberg. Following the listing of each question, we have attempted to answer those questions where information was readily available. In all other cases, we have outlined what we proposed to do to provide the information requested.

The questions raised were as follows:

- (1) What is the relationship between the fiber count and the surface area of the container (food contact area)?

The areas for the various food containers are as follows:

Salt shaking or scuffing test	18.18 in. ²
Macaroni container	88.0 in. ²
Carnation Dried Milk	138.0 in. ²
Quick Rice	160.0 in. ²
Corn Flakes	304.0 in. ²
Morton's Salt	45.0 in. ²

Dr. Corbin I. Miles
Page 2
April 2, 1974

In the case of all packaged foods we observed no fibers of either tremolite or chrysotile in the ash residues. In all cases the ratio is therefore 0/area. There is no migration.

- (2) What are the lower limits of detectability by TEM, petrographic, and XRD methods for tremolite and chrysotile in talc?

It was indicated that FDA wants to see a comparison of TEM results with petrographic fiber counts and XRD analyses on various talc samples containing various amounts of tremolite. Further, FDA would like to see positive TEM results on control samples to assure proper functioning of the instrument.

To respond to this question, we need to standardize the TEM with talcs containing known amounts of tremolite and to compare tremolite content by XRD with fiber counts by the FDA petrographic method. We are presently working with "spiked" samples of a talc that is free from either tremolite or chrysotile and have added to it known percentages of these two asbestos minerals. These "spiked" samples are then being analyzed by XRD, TEM and petrographic methods to determine the lower limit of detectability by each method and the relationship and results among the three methods. We will provide XRD patterns and TEM photographic prints to support the study. A statistical analysis of the methods used has been prepared.

- (3) We were requested to provide validation and recovery data (a materials balance) on "spiked" samples - samples of tremolite free talc to which we have added known amounts of tremolite.

The approach outlined in response to question (2) above will be followed. This work will be carried out at levels as close to the lower limits of detectability as possible, as determined by our statistician.

Dr. Corbin I. Miles
Page 3
April 2, 1974

- (4) A request was made that wherever possible we retain all samples, preparations, slides, etc.

Wherever possible, we are doing this. Petrographic slides, however, are not permanent. Immersion oils change with age and exposure to air. We are retaining the negatives for all TEM's.

- (5) In our salt-scuffing tests, do we have data for 10 cps tests similar to 19 cps tests? Do we have TEM test results at 10 cps? Do we have retained ash samples?

Ash samples have not been retained. We have no TEM's for this series - just optical test results.

- (6) Provide a description of our method and a sample calculation of our XRD analysis of food packaging paper for talc content.

A detailed description of our XRD procedure is being prepared.

- (7) In Table IV-A on page 11, Report E414-2, the six-hour results appear out of line. Can this anomaly be explained?

This result is an anomaly. We can explain it in no other way.

- (8) It was requested that we provide validation of the meat wrapping and sampling tests and the sensitivity of these tests. In addition, relate any migration to meat surface or meat weight.

It should be noted that McCrone's results showed no migration. Our proposed response, is to dust a known area of raw meat with a weighed amount of talc. We then propose to scrape the meat to remove the talc, ash this residue and then make a petrographic count of the ash to determine talc and tremolite content. Tests will be run using both J-M CYCLO-SORB and CYCLO-FIL.

- (9) It was requested that we perform both scuffing and shipping tests using paper with high loadings of tremolitic talc (paper with the highest level of tremolitic talc that is commercially used).

We have obtained samples of paper that are reported to contain up to 20% CYCLO-FIL. This will be confirmed by XRD analysis. If confirmed, we will repeat the salt-scuffing and shipping tests previously reported, using these papers.

- (10) What are the effects of ashing tremolite and chrysotile? What happens when paper containing talc, tremolite and chrysotile is incinerated?

DTA and TGA data clearly showed the temperatures at which the hydroxyl bonds are broken in these minerals. Tremolite goes to diopside, chrysotile to forsterite and talc to clino-enstatite. After burning paper containing these minerals, they would all be altered. As indicated at our meeting, a good incineration system would provide heat in excess of 1,000 degrees and at 700 degrees, tremolite and chrysotile are destroyed.

We are presently preparing an environmental impact analysis report for use as back-up for FDA's environmental impact statement. A reference being used is: "Incinerator Guidelines" by Demarco, Kelbe, Leckman and Newton; 1969, U.S. Department of Health, Education and Welfare, Public Health Service.

- (11) Explain the high talc content in the salt blank and repeat the test results.

This test was repeated several times and with each repeat test we failed to find the high talc concentrations originally found in the blank. Documentations of these results will follow.

During the meeting, you requested a statistical analysis on the lower limits of detectability as prepared by our statistician. This document is attached hereto.

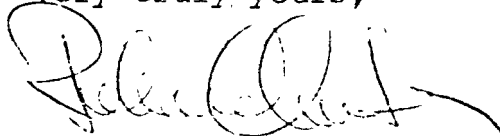
As we indicated at the meeting, it will require a period of approximately two months to perform all the necessary work to respond to all of the above requests. Hopefully, this information should be available by the latter part of May. We appreciate very much your indication that FDA will make no final determination with respect to the proposed talc regulations until this work is completed.

Dr. Corbin I. [redacted]les
Page 5
April 2, 1974

Unless I hear otherwise from you in the near future,
we will proceed with the work outlined herein.

Again, thank you very much for your cooperation and
assistance in this matter.

Very truly yours,

A handwritten signature in dark ink, appearing to read "Richard P. Carter", with a stylized flourish extending to the right.

Richard P. Carter, Director
Government Relations

RPC/emr

Attachs.

April 2, 1974

FIBER COUNTING STATISTICS

In all counting techniques it must be recognized that a single numerical value reported represents an estimate of the true value from some range of possible values. The range is dependent upon such factors as how large a number is expected and the number of fields counted. For low concentrations, it is valid to assume that the particles, or fibers, will follow a Poisson distribution.

Based upon the above assumption, there are several ways in which the statistics of counting fibers can be analyzed, and a complete study of the problem will be presented at a later date. For preliminary consideration the attached graph shows the expected variability for counting fibers in a one milligram sample of talc. It is based on the assumptions that the sample covers an area of 324 mm^2 , one "field" represents 0.096 mm^2 , and that the number of fibers in 100 fields are counted. The limits shown around the "expected value line" are the 95% confidence limits, i.e., one can be 95% certain that the true value will fall between these limits.

NUM OF FIBERS PER MG

1 mg CN 324 mm²
fields 0.09621 mm²

0.00075% concentration

500
1000
1500
2000
2500
3000
3500
4000
4500
5000
5500
6000
6500
7000
7500
8000
8500
9000
9500
10000

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

FIBERS COUNTED PER 100 FIELDS



April 3, 1974

Mr. Richard Carter, (Course 4)
c/o J. Lee Saville
Cottonwood Plaza
Durango, Colorado 81301

Dear Mr. Carter:

Not long ago received your letter regarding your understanding of the substance
of our January 27, 1974 report. I am enclosing my draft of the final
report which called and points requiring clarification.

As indicated in the attached memorandum, we are expecting to hear from you
or other U.S. representatives, on this matter by the end of April 1974.

If you have any questions on the substance of the information, or if you
need additional time to undertake this work, please let your written response
directly to me.

Sincerely yours,

(cc) [redacted] [redacted]
CMA [redacted]
Division [redacted] Policy & Initiative
Bureau of [redacted]

Enclosure

cc: HPT-300
HPT-330
HPT-335
CHfile:pah:4-3-74

Memorandum of Conference
February 27, 1974

Between: Corbin L. Hill, Review Branch, DTCA/HFF
William V. ... , Microanalytical Branch, DT/HFF
Albert Voltz, ... and Additives Branch, DCP/HFF

and Richard Carter, Johns-Manville
Richard Lamar, Johns-Manville
Jim Leinweber, Johns-Manville

Subject: Migration Data, ... by Johns-Manville, in Contexts of
December 21, 1973, on ... to IR Proposal of September 28, 1973,
(38 F.R. 27076).

Dr. Hill requested this meeting to seek clarification of numerous questions arising from PDA review of the subject comments. The questions requiring clarification, represent consolidated questions of the above PDA personnel. The questions and clarification requested of the above Johns-Manville personnel were:

1. PDA personnel need data relationships of fiber counts observed versus food contact area or box area, etc..
2. We want a comparison of transmission electron microscopy (TEM) and radiochemical method sensitivities. ... should be done on samples of similar origin and should indicate ... findings by TEM to assure proper functioning of this instrument.
 - a) Standardized TEM with known tremolite tale.
 - b) Do TEM analysis on 10 or 19 cps food samples, if possible.
3. Recovery and validation data should be generated for the entire analysis at low levels of spiking.
4. J-M should keep all reserve samples and ... from non-destructive tests. PDA may have to check our method ... used by J-M.
5. We would like to see detailed data for the ... abrasion test, similar to the 19 cps data. J-M will repeat the test of ... to evaluate by TEM.
6. We want a sample X-ray diffraction calculation to demonstrate the percent talc in papers (Morton salt sample as an example).
7. What is the Valley abrasion test? This question was answered satisfactorily.
8. Why is there a decrease in residue values in the 6-12 hour interval

on Table IVA, p. 11, and Table I of appendix I.

9. Recovery and validation data should be generated for the J-M heat sampler test.

10. All tests reported in these comments were on papers containing approximately 10% talc as a for pitch control. What about highly defibrated papers containing higher levels of talc? J-M agreed to test some of these papers also.

11. FDA concern was expressed for the data on the salt blank in Appendix 1, p. 12, Table 1. If salt blank contains approximately 1% fillers, why are none observed in analyzed samples using this blank?

12. Data expressed as "possible trace" should be more explicit.

Mr. Carter asked how long IPA could give Johns-Manville to work on these problems, submit further data, and clarify these questions? Dr. Miles said that he thought other evaluations would take approximately two months. He would therefore want J-M additional data about the end of April. J-M responded that these expectations were reasonable, and Mr. Carter agreed to prepare J-M's memorandum of this meeting, indicating their understanding of FDA questions asked.

Respectfully submitted,

Corbin I. Miles, Ph.D.
GRAS Review Branch

cc: WFT-200
WFT-330
WFT-335
CIMiles:pah:4-3-74

GRAS Review Branch, HFF-735

February 26, 1974

Attn: Dr. C. Miles

Organic and Additives Chemistry Branch, HFF-122

Johns-Manville Letter 12/21/73 and Data on Asbestos in Talc.

In our evaluation of the migration of asbestos from talc used in paper making we have reviewed several Johns-Manville (J-M) submissions.

The first J-M data (4/22/73 and accompanying details) was covered in our 12/25/73 memo. This evaluated their migration studies for aqueous and fatty foods by liquid-phase machine transfer tests and heat packaging. There were a number of questions raised in our 12/25/73 review since this testing did not follow our standard extraction testing for soluble migrants.

J-M is allowed to carry out migration testing for more definitive informative migration data for the following reasons:

1. "Coated papers" packaging applications are mostly devoted to dry foods which should therefore result in abrasive action on the paper.
2. Any wet or moist food packaging applications are generally on highly calendered papers and are of short time periods.

Based on the above reasoning our consideration of the talc-asbestos migration potential would rank the J-M's evaluations in the following order of significance:

- a. Testing of actual packaged foods (salt, macaroni, dry milk, rice, and corn flakes).
- b. Results of packaged salt shipping tests.
- c. Laboratory "scuff" packaging tests.
- d. Heat packaging tests.

These abrasion test results were supplied in the 12/21/74
dental reports of Dr. [redacted] and Dr. [redacted]. The purpose
of the test was to determine the evaluation of the talc-
based abrasives as reported by Dr. [redacted] (Lisenberg-
Smith) in their 1/17/74 report.

In our 2/21/74 meeting with Dr. Lisenberg we summarized the
above questions and asked the above reports which
representatives of the [redacted] representatives at the forth-
coming 2/27/74 meeting.

A. Holtz

D/D Unit:
[redacted]

CC:
HFF-139
HFF-140
HFF-141
HFF-142
HFF-143
HFF-144

Holtzman 2/26/74

March 12, 1974

Richard Carter
Director, Consumer Relations
Johns-Manville Products Corp.
Greenwood Plaza
Denver, Colorado 80217

Dear Mr. Carter:

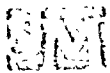
We have your letter of March 22, 1974, addressed to the Hearing Clerk
concerning upon the proposal for a color additive in Food and Drugs
published in the FEDERAL REGISTER of September 28, 1973 (38 F.R. 27076).

We appreciate your comments and will consider them along with others
received in preparing a recommendation for final action in this matter.

Sincerely yours,

Carlton L. Miles, Ph.D.
CMS Review Branch
Division of Food and Color Additives
Bureau of Foods

cc: HEF-300
HEF-330
HEF-335
Comment File
CEfiles:dbb:3-12-74



Johns-Manville
Products Corporation

Greenwood Plaza
Denver, Colorado 80217
(303) 770-1000

December 21, 1973

CERTIFIED MAIL
RETURN RECEIPT
REQUESTED

Hearing Clerk
Food and Drug Administration
Room 6-86
5600 Fischers Lane
Rockville, Maryland 20852

Dear Sir:

I am responding in behalf of Johns-Manville Products Corporation ("J-M") to the Food and Drug Administration's (FDA) Notice of Proposed Rule Making relating to asbestos particles in food and drugs, as published in the Federal Register on September 28, 1973 (hereinafter referred to as the "Proposal").

The Proposal indicates that interested persons may, on or before December 27, 1973, file with the Hearing Clerk, written comments regarding the petition from the Center for Science in the Public Interest and the Environmental Defense Fund and the Proposal.

Desert Minerals, Inc., an affiliate of Johns-Manville Products Corporation, is a major producer of crude and processed talc, a substantial portion of which is sold for use in the manufacture of food and drug packaging materials.

On April 20, 1973, J-M forwarded to FDA a letter with attachments containing comments to proposed regulations covering the use of talc in food and food packaging material, as published by FDA in the Federal Register on August 12, 1972.

It is requested that those comments be incorporated as part of the record with respect to the Proposal. The Proposal, as it relates to the use of talc, differs importantly from the earlier FDA proposal in that FDA is now additionally proposing a restriction on the use of talc containing asbestos fibers in "any drug, drug ingredient, or drug packaging material."

packaging applications. United States paper manufacturers import significant quantities of pulp from Canadian and Scandinavian producers for consumers in the U. S. Packaging materials and packaged foods and drugs are imported from many areas of the world. Thus, the Proposal adversely affects the entire worldwide pulp, paper and packaging industries. Therefore, limitations on the use of talc cannot practically be restricted to only food and drug packaging materials.

It should be noted that the only form of asbestos found in J-M talc is tremolite. J-M "CYCLO-SORB", which is used for pitch control contains 2% to 5% tremolite by volume and J-M "CYCLO-FIL", which is used for high brightness filling, contains 20% to 30% tremolite by volume. Some highly tremolitic talcs, such as those from upper New York State (which contain as much as 60% to 70% tremolite and some traces of chrysotile) are too abrasive for use in the manufacture of pulp and paper. The Valley Abrasion loss with these products is well over 100 mg. Any talc addition which results in a Valley Abrasion loss over 20 mg. is impractical to use. These highly tremolitic talcs, with possible traces of chrysotile, have been tried and rejected for use in the paper industry.

Use of commercial talc in the manufacture of pulp and paper in substantial amounts was begun approximately 15 years ago and its use has increased enormously during the period. As used in these processes, talc becomes an integral part of the pulp and paper formulation. As such, the talc becomes locked into place in the paper. Talc is never dusted dry on the surface of the paper.

Use of Talc for Pitch Control

In the 1950's, a study undertaken as to the fundamental properties of talc, and particularly its surface characteristics, showed that the mineral talc is virtually unique among mineral substances in that it is strongly hydrophobic and organophilic. It is capable of adsorbing various kinds of organic, fatty, or resinous materials in the presence of large volumes of water. When added to a latex, it will selectively adsorb and rob the latex of its stabilizer system causing the latex to gel. Latex stabilizers are generally either anionic or nonionic surface active agents. These are fairly high molecular weight compounds with a hydrophobic end and a hydrophilic structure at the other end of the compound.

industry based largely on fishing, has recently required mills to close up their water systems and to limit the use of surface active agents. The use of talc for control of pitch is the only feasible alternative.

When talc is used for pitch control in the pulp mill, colloidal pitch particles are adsorbed onto the surface of the talc. The talc holds the pitch in a finely dispersed and innocuous state preventing agglomeration and deposition on the machinery. The talc with its adsorbed pitch remains locked in the pulp or paper. The pitch itself aids in binding the talc into the paper.

The use of talc for pitch control has grown very rapidly worldwide. Talc is now used in most pulp and paper mills throughout the United States, Canada, Western Europe, Scandinavia, Japan, and in all other major pulp and paper producing areas, solving a problem that had plagued the paper industry for years. No other product works as well under such a variety of conditions and at the same time, solves major stream pollution problems associated with paper production. Pitch control is now the major use on certain grades of talc.

The rate of talc addition for pitch control will vary with the severity of the problem, the type of pulping (Kraft or sulfite), the kind of wood, the age of the wood, time of year, water temperature, pH, etc. In the pulp mill, talc is added just ahead of that processing step where the pitch first begins to appear. Under these conditions, the talc is present to adsorb the pitch as it is released. If the talc is added later, after the pitch has started to agglomerate, it is not as effective and higher rates of addition are needed for control. Normal rates of addition in the pulp will vary from as low as 0.25 per cent to 1.5 percent, although additions of up to 5 percent are infrequently encountered.

Talc introduced in the pulp mill is carried over into the paper mill as an integral constituent of the pulp. As the pulp is further refined in the paper mill, more pitch is released and additional talc must be added for control. Here the pitch is in a more agglomerated form requiring higher rates of talc addition. Paper mill addition rates are normally between 0.50 percent and 2.0 percent.

Use of Talc as a Functional Filler

Talc is also used in the paper industry as a functional filler. In this use, talc is added in the paper mill to increase the brightness and opacity of the paper. It also makes the paper smoother, more amenable to calendering, and more receptive to high fidelity color printing. As with the pitch control use, talc for filling is beat up with the pulp and becomes locked in as an integral part of the sheet of paper along with the cellulose fiber, resin size, clay, titanium dioxide ("TiO₂") and all of the other parts of the furnish.

In this use, talc can and is being used to replace a portion or all of the TiO₂ in some papers. Although heavier loadings of talc are needed to develop the same opacity as TiO₂. This application is becoming more important as TiO₂ is in critically short supply.

For high brightness filling applications, up to 15 percent loading might be used. Normal rates of addition would range between 5 and 10 percent of talc based in the weight of dry paper pulp. In all cases, the talc is incorporated wet into the cellulose fiber matrix. High brightness opaque papers containing talc filler are generally a high-grade paper typically used as stationary, memo, bond ledger, offset, duplicating and publication paper. The use of such high-grade paper in food or drug packaging would be most unusual due to the relatively high cost. Talc is infrequently used as a filler in food and drug packaging materials, as brightness and opacity is not of primary concern in these paper applications.

Use of Talc in Recycling Paper

Of increasing importance is the use of talc in the deinking process for recycling of paper. In this application, talc selectively adsorbs the oil and resin which serves as the vehicle or binder for printing ink and other residual organics. The ink is then flushed from the waste stock leaving the residual organics bound to the talc in the waste stock. The talc also controls the agglomeration and deposition of latex binder and impurities found in the waste paper.

Waste stock containing talc is then added in varying degrees to pulp for production of finished paper. The percentage

of waste paper which may be used in recycled paper is increased dependent upon the effectiveness of the deinking process. Thus, the use of talc permits a much greater use of a wider variety of waste paper in the furnish. The increased cost and shortage of pulp, as well as ecological considerations, dictate the increased use of waste paper, necessitating greater use of talc for that purpose. Surface active agents, while useful for these purposes, are less effective than talc and have adverse ecological impacts as indicated above.

Use of Talc as a Direct Food or Drug Additive

The vital use of talc in the manufacture of pulp and paper should be contrasted with its use as a direct additive in food and drugs (such as dusting chewing gum and as a tableting aid). In these latter applications, talc does not serve a vital and valuable function, adequate substitutes for talc are readily available and a restriction on the use of talc as a direct additive would have little if no adverse economic consequences on the U. S. talc industry or the food and drug industries. However, as was noted in J-M's April 20, 1973 comments and as is indicated hereinafter, the use of talc containing tremolite, even as a direct food or drug additive, poses no real health hazards from ingestion.

2. TREMOLITE DOES NOT MIGRATE FROM PACKAGING MATERIALS TO FOOD OR DRUG CONTENTS

Studies performed by J-M and independent consultants and reported on in J-M's prior comments conclusively demonstrated that any tremolite contained in talc used in food packaging materials does not migrate to the food. As a result of the raw meat wrapping and sandwiching freezing tests reported in our earlier comments, no tremolite migration at all was detected.

As a result of J-M's discussions with FDA, J-M conducted further migration studies to determine whether or not the possible abrasive action of dry food substances or drugs would result in the migration of tremolite fibers from packaging paper containing tremolitic talc. In designing a migration test capable of producing scientifically valid results, J-M consulted with Mr. Allen Spiher, Chief, GRAS Review Branch, and Mr. G. Higgenbottom of FDA, who provided certain test guidelines.

The initial study of dry food abrasion requested by FDA is set forth in Report No. E414-2 from the Johns-Manville Research & Engineering Center, a copy of which is attached hereto as Exhibit I and referred to as the "scuff test."

The "scuff test" was designed to determine the extent to which tremolite fibers contained in talc used in the manufacture of paper for food and drug packaging applications might be expected to migrate into food or drugs with which it would come in contact. The test conditions used were arrived at after considerable discussions with FDA. At the suggestion of FDA, salt was used as the medium for the scuff test, since its sharp edged cubic crystals would act as a more abrasive material than any other dry food substance or drug. The test was "artificial" in that it was designed in an attempt to duplicate, in a laboratory, the conditions present during actual commercial shipment of food and drugs. The test consisted of lining glass containers with paper manufactured with tremolitic talc, partially filling the containers with salt (NaCl) and vibrating the containers for a period of 24 hours on a shaker tester.

As Exhibit I indicates, the scuff test established that migration of tremolite did not occur in the absence of partial destruction of the paper itself. When partial destruction of the integrity of the paper occurred, the resulting migration had the composition of the paper insofar as could be measured, indicating that tremolite does not "dust out" or selectively migrate from the paper.

At a frequency of 10 cycles per second (a frequency equivalent to that of a freight train having a flat spot on one pair of its wheels, traveling almost 60 miles per hour) no evidence of paper breakdown was detectable and no tremolite migration whatsoever could be detected. Only when vibration was increased to 19 cycles per second did substantial breakdown of the paper occur after 24 hours, with resulting migration of all components of the paper.

Additional testing was performed to determine if during commercial shipment of food and drugs, the vibration and movement actually encountered results in abrasion sufficient to cause the partial breakdown of the integrity of the paper packaging materials.

The second migration study performed is contained in Report No. E414-6 from the Johns-Manville Research & Engineering

Center, a copy of which is attached hereto as Exhibit II.

The test consisted of lining containers with tremolitic talc containing paper (identical to that used in the test described in Exhibit I) and shipping these containers which were partially filled with salt by commercial truck from Denver, Colorado to Manville, New Jersey and back (a round trip of approximately 72 hours and 4,000 miles of travel). The shipment of these test containers of salt resulted in no breakdown in the integrity of the paper and no migration into the salt of tremolite or any other ingredient of the paper.

In addition to the salt shipping test, a variety of dry foods packaged in paper containing tremolitic talc were purchased at a local supermarket and examined to determine whether migration of tremolite had occurred. This study established that tremolite contained in talc used in food packaging does not migrate to any dry food substances during normal commercial shipment and handling. The food purchased at a local supermarket showed no evidence of tremolite migration. This was so even though foods were chosen which were likely to have been shipped long distances and were likely to be abrasive, such as corn flakes, macaroni and salt.

On the basis of studies reported in Exhibit II, J-M has concluded that actual commercial shipping and handling conditions of packaged dry foods does not cause sufficient abrasion to the containers to result in the breakdown of the integrity of the paper or migration of tremolite. The latter tests (Exhibit II) establish that the conditions existing in the scuff test (Exhibit I) are indeed much more severe than actual commercial shipping and handling conditions.

In Exhibits I and II, results are reported to the reliable levels of identification by optical (petrographic) microscopy and weight determinations and with the additional use of transmission electron microscopy in Exhibit II.

The shipped salt samples and the purchased food materials were first examined by petrographic methods as recommended in the Proposal. Over 100 fields of view were examined for each sample, with considerable effort exerted to identify the possible presence of talc or tremolite.

In addition to the petrographic examinations, the samples were also examined by transmission electron microscopy. Each entire sample was scanned in its entirety for suspicious particles and fields were chosen at random for specific counts.

However, even following these stringent analytical procedures, the presence of tremolite could not be detected.

It is evident to J-M as a result of the studies reported herein, that actual conditions of commercial transportation do not create a severe enough environment for paper breakdown to occur, and the migration of tremolite from paper containing tremolitic talc used in food and drug packaging applications does not occur.

3. NO EVIDENCE EXISTS OF A HEALTH HAZARD ASSOCIATED WITH THE INGESTION OF TREMOLITE

In J-M's comments dated April 20, 1973, it was stated that there is no evidence whatsoever to indicate that the ingestion of tremolite constitutes a health hazard. Tremolite cannot properly be considered as a "poisonous or deleterious substance" as contemplated in in section 402(a)(1) of the Food, Drug and Cosmetic Act. The studies which have suggested that the ingestion of asbestos fibers may be carcinogenic are based on substantial occupational exposures to other asbestos minerals, and not to tremolite.

In the animal ingestion and injection studies and human epidemiological studies of talc workers, cited in J-M's April 20, 1973 comments, no excess incidence of gastrointestinal cancers have been reported. Animal studies involving tremolitic talc have been conducted by Dr. William E. Smith, Health Research Institute, Fairleigh Dickinson University, Madison, New Jersey and by F. Pott and Friedrichs in West Germany, both of which studies were reported by Dr. Wright in Exhibit F to J-M's April 20, 1973 comments.

Pott and Friedrichs introduced tremolitic talc directly into the mesothelial spaces, which failed to produce mesotheliomas, a finding in contrast to the production of mesotheliomas using other forms of asbestos. (1)

Dr. William E. Smith has both fed chrysotile and amosite asbestos to hamsters and has administered tremolitic talc by

intrapleural injection to hamsters. A summary of Dr. Smith's findings is attached hereto as Exhibit III.⁽²⁾ Dr. Smith's findings are as follows:

"In 45 hamsters maintained throughout their lives on diets containing 1% of the chrysotile or amosite varieties of asbestos, we found no gastric carcinomas and no tumors in the gastrointestinal tract except for a neoplasm in the mesentery of the colon. We are unable to relate that lesion to the treatment, since ashing has revealed no asbestos fibers in it.

We have now completed an experiment in which the hamster intrapleural method was used to test for carcinogenicity of a sample of talc containing asbestos. For this work, we have obtained samples of commercial talcs from Whittaker, Clark & Daniels, Inc., New York City ... X-ray diffraction analysis revealed the presence of major amounts of tremolite asbestos and talc and a minor amount of a serpentine mineral (antigorite).

Each of 50 hamsters were given right intrapleural injection of 25 mg of this sample suspended in 0.5 ml saline. The animals were followed for their life spans. No tumors attributable to the treatment were found."

In a meeting on December 7, 1973, with Dr. Virgil Wodicka and Dr. Albert C. Kolbye of FDA, a copy of Dr. Smith's Terminal Progress Report: Grant No. 3R01-EC-00226-0451 entitled "Mesothelioma in Relation to Asbestos" was delivered to them. Among other studies, this contained his finding that long fiber tremolite injected directly into the pleura space of hamsters did not produce mesotheliomas, whereas other kinds of asbestos used in similar amounts did produce these tumors. A copy of Dr. Smith's Terminal Progress Report is attached hereto as Exhibit IV.

J-M's comments of April 20, 1973, cited the study by Dr. Morris Kleinfeld of talc miners and millers exposed to talc containing extremely high concentrations of tremolite.⁽³⁾ In this study, Dr. Kleinfeld concluded that there was no significant difference between the observed and the expected mortality from carcinoma of the gastrointestinal tract and peritoneum among these talc workers. Also included as Exhibit G to J-M's April 20, 1973 comments

was a copy of a letter from Dr. Kleinfeld dated January 24, 1973, reporting the results of his follow-up study of these talc miners and millers. Dr. Kleinfeld concluded in his follow-up study that "With regard to cancer of the gastrointestinal tract and peritoneum among the talc workers, we did not find any significant differences between the observed and expected values in the overall and specific age groups studied".

This follow-up study has not yet been published, although Dr. Kleinfeld has advised us it has been accepted for publication. In view of this fact, and the importance of Dr. Kleinfeld's work, J-M has obtained from Dr. Klenfeld a paper which he presented at the Metal and Non-Metallic Mine Health and Safety Symposium on Talc Dust Hazards sponsored by the Bureau of Mines and held in Washington, D. C. on May 8, 1973. A copy of this paper is attached hereto as Exhibit V, and summarizes both his earlier study and the follow-up study.

It should be noted that at the recently held EPA-NIEHS Joint Symposium on the Biological Effects of Ingestion of Asbestos, Dr. William F. Smith mentioned his animal feeding experiments, in which he fed quantities of asbestos to hamsters with no resulting gastrointestinal cancers. After reporting on his animal studies, he then posed the following question to all those in attendance at the Symposium: "Was there anyone who has conducted animal experiments where asbestos fibers had been ingested (including inhalation studies) and observed any evidence of gastrointestinal cancers?" There was no response received from anyone in attendance at the Symposium and no evidence was introduced at that Symposium to indicate that any animal ingestion studies involving asbestos had resulted in the development of gastrointestinal cancers.

It should also be noted that to the extent that tremolitic talc has been used in dusting chewing gum and in preparations of oral medicines, the public has participated in a large scale ingestion study over a lifetime. If one thinks of ingestion of tremolite at this level as being hazardous with respect to causing mesothelioma, why is this such a rare tumor, occurring at a rate of 1 to 1.5 per million population annually in the public at large? This sort of exposure dates back to the beginning of the century. The ingestion of fibrous tremolite in this manner would exceed any possible potential from the use of packaging ma-

terial containing tremolitic talc for food and drug packaging applications.

Evidence offered by FDA in its earlier proposed regulation on talc (August 12, 1972), to support the proposition that ingestion of tremolitic talc is hazardous, is limited to an article by Dr. R. R. Merliss in Science (September 17, 1971), in which Dr. Merliss attempts to show a causal relationship between the use of talc-polished rice and the high incidence of gastric cancer in Japan. The data used for this purpose is spurious, to say the least. Dr. Merliss, himself, now doubts his conclusion as is indicated in his recently published article entitled "Talc-Coated Rice," Life and Health, March 1973. A copy of this paper is attached hereto as Exhibit VI.

No medical-scientific evidence was offered by FDA in the latest Proposal (September 28, 1973) to prove that the ingestion of asbestos, and particularly tremolite, is injurious to health. As a matter of fact, the studies cited by FDA in the Proposal indicates that ingestion is not injurious, based on the animal studies reported.

No one in the medical scientific community has concluded that asbestos, when ingested, is carcinogenic. Even in those studies where there is some suspicion that ingestion of asbestos may result in a higher incidence of gastrointestinal cancer, this suspicion arises only in cases involving individuals most highly exposed to asbestos in occupational settings, and the asbestos being forms other than tremolite.

The Center for Science in the Public Interest and the Environmental Defense Fund in their petition submitted to FDA, do not introduce any evidence whatsoever tending to either incriminate tremolite or to prove that tremolite will migrate from packaging materials. The studies cited by these two groups in their petition relate to insulation workers most heavily exposed to asbestos in occupational settings for prolonged periods of time. As indicated in J-M's earlier comments, these studies may not be validly related to tremolite. One cannot assume that all forms of asbestos will react biologically in the same way and one must also recognize that there is a dose-risk relationship with respect to exposure to asbestos. Even in those studies of individuals occupationally exposed to asbestos, there is a substantial dose tolerated by occupationally

exposed individuals before evidence of any possible excess cancer experience develops. These two groups in their petition fail to cite any studies relating to the effect of ingestion of tremolite. Such studies are conspicuously absent from the petition.

4. THE FDA PROPOSED TEST METHOD IS NOT WORKABLE

In its Proposal, FDA has proposed a test method for determining the presence of asbestos fibers in food-grade talc. The Johns-Manville Research Center believes the test to be unworkable on both practical and technical grounds. This belief has been confirmed by independent consultants. Attached hereto as Exhibit VII is a test method which is a modification of the one proposed by FDA and which, in the opinion of J-M, is a more suitable method for determining the presence of asbestos fibers in food-grade talc.

However, it should be noted that J-M's talc does not meet the FDA proposed test method, nor the one proposed herein, and the talc of most other talc producers falls in the same category unless the limits of detectable tremolite are increased substantially.

Conclusion

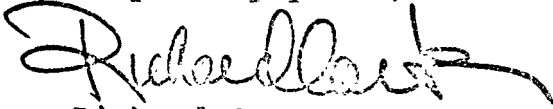
In conclusion, we have attempted to respond in our comments dated April 20, 1973 and in this document to the issues raised by FDA in its proposals published on August 12, 1972 and September 28, 1973, with respect to the use of talc containing asbestos in food and drug packaging materials.

J-M believes that the use of talc is essential in the manufacture of pulp and paper and is ecologically and economically desirable. Tremolite does not migrate from tremolitic talc containing paper packaging materials to the food or drug contents during commercial handling and shipping. There is no credible evidence indicating a health hazard due to the ingestion of tremolite and there is conclusive evidence that the ingestion of tremolite by humans and animals and the injection of tremolite into the pleura space of animals does not result in an increased incidence of gastrointestinal cancer or mesothelioma.

It is submitted that on the basis of all known facts, adoption of the Proposal would constitute an arbitrary and capricious action totally in conflict with the best scien-

tific evidence and needlessly destructive of the domestic talc industry and disruptive of the world-wide pulp and paper manufacturing industry. As there is no justification for imposing any restriction on the use of talc containing tremolite in food and drug packaging applications, it is urged in the public interest, that, no cause being shown for its adoption, the Proposal severely restricting the use of tremolitic talc in food and drug packaging material, be withdrawn.

Very truly yours,

A handwritten signature in dark ink, appearing to read "Richard Carter", with a stylized flourish extending to the right.

Richard Carter
Director, Government Relations
Johns-Manville Products Corporation

REFERENCES

- (1) Pott, F. and Friedrichs, (1972), "Tumors in Rats After Intraperitoneal Injection of Fibrous Dusts" (German). Naturwissenschaften 59: 318.
- (2) Smith, William E. (May 1973) "Asbestos, Talc and Nitrites in Relation to Gastric Cancer" American Industrial Hygiene Association Journal, May: 227-228.
- (3) Kleinfeld, M., et al (1967), "Mortality among Talc Miners and Millers in New York State", Archives of Environmental Health 14:663-667.

Title: PRELIMINARY STUDIES OF FOOD CONTAMINATION
BY CONTACT WITH PAPER

SUMMARY

A study was undertaken to determine the extent to which the tremolite fibers contained in talc used in the manufacture of paper for food and drug packaging applications might be expected to "migrate" into food or drugs with which it would come in contact.

For these studies, a test method and procedure were worked out which established that the migration of tremolite contained in talc used in food packaging paper occurs only after partial destruction of the paper after being in contact with food. Without some destruction of the integrity of the paper, no migration of tremolite occurs.

When partial destruction of the integrity of the paper occurred, the resulting migration had the composition of the paper insofar as could be measured. Partial destruction of the integrity of the paper and migration of the component elements of the paper occurred both with talc-containing and non-talc containing papers. In those paper samples containing tremolitic talc, the residue in the food also contained a similar proportion of talc and tremolite fiber. Since talc usually constitutes one percent or less of the total paper, talc migration is so low as to be barely measurable and tremolite fiber levels could be three orders of magnitude less.

The test conditions used here were arrived at by discussions with the Food and Drug Administration.

Additional testing must be undertaken to determine whether or not the test conditions used herein actually, in fact, duplicate the conditions and what takes place when food is shipped commercially, so as to determine whether in commercial shipping the partial destruction of the integrity of food packaging paper occurs.

Contents: Summary, Discussion, Conclusions, Recommendations, and Appendix I, II, and III.

Reported by:

R. J. Zazenski
R. J. Zazenski

G. R. Bell
G. R. Bell

kjm

DISCUSSION

Introduction

FDA on September 28, 1973, published a Notice of Proposed Rule Making which would restrict the use of talc in food, drugs, and food and drug packaging materials. The proposed rule would preclude all such uses for talc, if the talc contained more than specified numbers of chrysotile and tremolite fibers.

Talc is widely used as a pitch control agent in the initial manufacture of paper pulp from wood, and also in the actual manufacturing of paper. Talc so used, becomes an integral part of finished paper produced from this pulp. The finished paper, which may also contain various other special purpose fillers and pigments such as clay, whiting, and TiO_2 , etc., is used for the full spectrum of paper applications, including food and drug packaging.

This study was undertaken to determine the extent to which the tremolite fibers contained in talc used in the manufacture of paper for food and drug packaging applications might be expected to "migrate" into food or drugs to which it would come in contact.

Tremolite Migration (or Scuffing) Studies

Basis

Migration as used here is appropriate only in the sense of overall determination of loss of paper fiber, talc and other fillers tightly held in a homogeneous sheet of paper. None of the types of paper commonly used for food contact applications has loose surface fibers or powdery material which will come loose on simple contact, hence the term "migration" as used in that sense does not apply.

Mechanical action or "scuffing" of some sort is required to dislodge talc or other filler materials, and incidentally, cellulose paper fibers, from finished paper. With direction from FDA, a test method was devised which does scuff or abrade material from a paper sheet simulating the action a cylindrical table salt carton might receive during commercial shipment for an extended period of time. For simplicity, this is referred to as the Scuff Test in this report. A description of the directions from FDA for a test method is set forth in Exhibit I attached hereto.

Paper Samples

Ten samples of paper made for various food packaging applications were obtained from trade sources. Four of these were brown kraft, two with tremolitic talc and two without; four were white locker and counter papers, again two with tremolitic talc and two without; and two waxed papers purported to have talc. A more complete listing is given in Appendix I, Tables I and II.

Confirmation of Talc Content

Since migration of tremolite from food packaging paper to food products in contact with such paper is the thrust of this study, positive identification of the presence or absence of tremolitic talc is important. Talc per se can be positively identified by both its characteristic X-ray diffraction (XRD) patterns and petrographic microscope examination. However, attempts to positively identify the talc in any of the paper samples as received proved unsuccessful by either of these methods; and, it was not until the paper samples were low-temperature (400°C) ashed that talc was detected and identified by these methods. Both the Longview Paper Company and Brown Company have advised us that their sole source of supply for talc is Johns-Manville. Both companies' purchases of talc are restricted to J-M "CYCLO-SORB", a grade of talc containing approximately five (5%) percent tremolite by weight. The actual talc concentrations of the paper samples, as determined by X-ray diffraction, are located in Table II.

Scuff Test

The philosophy behind the "Scuff Test" was to attempt to simulate actual shipping and handling conditions of food-containing packages. It is assumed that during shipping, particularly rail shipping, the most severe and prolonged shaking or vibrating of the packages will be incurred. During this time, it is possible that the vibrating contents could have an abrasive effect on their containers, thus possibly causing some of the package interior to be scuffed off and mixed with the contents. Therefore, a test that could simulate these conditions would permit examination of the material scuffed off and determination of what, if any, materials (i.e., cellulose, talc, tremolite, etc.) have been dislodged from the paper fiber.

J-M was directed by FDA to use salt as the medium for the "Scuff Test" since its sharp edged cubic crystals would act as a more abrasive material than any other dry food substance or drug. (See Exhibit 1) Paper containers were simulated by lining the inside of 8 ounce squat glass jars with test paper. Vibration settings on a shake tester were set at its maximum amplitude of 1/16-inch (1/8-inch full excursion) and minimum frequency of 8 cycles per second. It was soon found though, that these conditions did not produce any visible vibration of the salt. The contents simply rode up and down with the jars. It was not until the frequency was raised to approximately 15 cps that visible movement was in evidence. This fact aroused some question as to how much, if any, prolonged shaking actually does occur to packaged foods during transport. It was calculated that a freightcar, having a flat spot on one pair of wheels, traveling at 40 mph would only vibrate with a frequency in the range of 6.8-7.5 cps; and at 60 mph, 10.2-11.2 cps, depending on wheel diameter. However, it was decided to run the initial test at severe enough conditions to cause detectable movement of the salt so that microscopic analysis of the salt would be meaningful.



However, one must recognize that it is possible that the salt and glass jar were moving at different frequencies which were not apparent to the eye, and it is conceivable that the frequency rate of 10 cps may more nearly duplicate vibration and possible scuffing during commercial shipment. If this is so, based on the data from the 10 cps test, no degradation would be anticipated under actual shipping conditions.

A fourth test was then initiated to determine at what rate the scuffing occurred at the higher frequency of 19 cps. Again, sample RS 73242-2 was selected for observation because of its performance in Test 2. Samples were removed from the vibrator at 2, 4, 6, 12, 24, 48, and 72 hours. Duplicate samples were run for the 2, 4, and 6-hour tests in order to serve as a check for the minute amount of residue expected. It must be emphasized that these results only reflect the scuffing characteristics of this particular paper sample and may not be representative of the other papers. This sample demonstrated that the rate at which the integrity of the paper is broken down is linearly related to time, up to 48 hours. The quantitative results are located in Appendix I, Table IVA and a plot of the paper residue weight versus time is represented in Appendix III, Figure 1.

Microscopic and petrographic examination of the residues revealed that the residue contained all of the components that the original paper contained and so far as can be determined optically, in the same proportions. This leads to the conclusion that the material scuffed off and recovered as residue was due to the partial destruction of the integrity of the paper lining itself, and cannot be attributed simply to the migration of any select materials such as talc, cellulose, fillers, etc., out of the paper.

This conclusion is supported by the fact that approximately the same amount of material was recovered from scuffed papers which did not contain tremolitic talc as those which did.

Comments on Test Procedure

Although only limited testing has thus far been performed, it is apparent that attempts to quantify test results at these exceedingly low levels of concentration is difficult. It is equally difficult to generate reproduceable results. A case in point involves the use of technical grade salt which has a maximum insoluble impurities limit of 0.005 percent. In using 200 grams of salt, it is possible to have between 0-10 milligrams of unwanted impurities contaminate the residue deposit from each test. When it is considered that only a few milligrams of abraded residue is recovered at the conditions the test was run, it is obvious that a deviation or error of well over 100 percent is possible. But let it be emphasized that although a weight difference was found in some samples run at identical conditions, this had no effect on the relative proportions of materials identified microscopically.

CONCLUSIONS

Inspection of the results obtained from the Scuff Tests lead to the following conclusions:

1. At a frequency of 10 cps or a frequency equivalent to that of a freight train having a flat spot on its wheels traveling almost 60 mph, no evidence of paper breakdown was detectable when the samples were run for 24 hours, and no migration at all was detected.
2. As reported before, visible movement of the salt relative to the movement of the jar was not in evidence until approximately 16 cps.
3. Paper breakdown due to the abrasive action of the salt is detectable when run at a frequency of 19 cps and 1/8-inch full excursion for extended periods of time. But let it be emphasized that this frequency was settled upon only to ensure visible salt movement within the container, and at the time this frequency was selected, there was no reason to believe that such a high frequency rate was necessary to duplicate the vibration and movement that actually occurs during the commercial shipment of food or drugs. It is, therefore, very possible that the frequency rate of 19 cps resulted in test conditions far more stringent than those which occur in actuality during commercial shipment.
4. In all cases, the material scuffed off and recovered as residue was due to the partial destruction of the paper lining itself, and is not due to the selective migration of individual materials such as cellulose, talc, tremolite, etc., out of the paper. The examined residues were identified to contain all the materials of the original paper sample in the same proportions, as best as can be determined optically.
5. Although only limited testing has thus far been performed, it is apparent that attempts to quantify test results at these exceedingly low levels of concentration is difficult. It is equally difficult to generate reproduceable results.

RECOMMENDATIONS

It is recommended that:

1. A determination must be made as to whether the test conditions described herein do, in fact, duplicate conditions during actual commercial shipment of food and drugs.



2. It is essential to perform additional testing to determine if during commercial shipment of food and drugs, the vibration and movement encountered is sufficient to result in the partial breakdown of the paper packaging. This is necessary as the tests described herein indicate that there is no migration of tremolite or any of the ingredients of the paper unless there is a partial breakdown of the integrity of the paper itself. This test has not established whether paper breakdown actually occurs under commercial conditions.

APPENDIX I
Table 1DESCRIPTION OF PAPER SAMPLES TESTED

Identification No.	Source	Description
RS 73242-1	Longview Paper Company	Brown kraft paper reportedly containing 6.7-pound CYCLO-SORB per 1000-pound pulp.
RS 73242-2	Longview Paper Company	Ditto except containing 10.2-pound CYCLO-SORB per 1000-pound pulp.
RS 73242-3	Longview Paper Company	Ditto except no talc.
RS 73242-4	Brown Company	40-pound MG bleached bag stock coated with 5-pound clay latex, used for cookie bags. Talc content not stated.
RS 73242-5	Brown Company	30-pound white DOK, wide food wrap use. Talc content not stated.
RS 73242-6	Brown Company	25-pound Royal white waxing (this sample not waxed). Wide food contact uses (cookies, sugar, etc.). Talc content not stated.
PS 73242-7	Brown Company	36 1/2-pound Spec. white locker waxed one side. ("Wax" not apparent). Used for freezer locker paper. Talc content not stated.
RS 73242-8	Longview Paper Company	30-pound No. 801 wrapping paper. No talc.
RS 73248-6	Brown Company	31-pound Royal white food wrap paper (waxed). Talc content not stated.
RS 73248-7	Brown Company	Printed and waxed paper for wrapping butter. Talc content not stated.

APPENDIX I
Table II

TALC IDENTIFICATION OF PAPER SAMPLES BY X-RAY DETERMINATION*

Sample	Source Reported Talc Content	% Talc Determined By X-Ray Diffraction
RS 73242-1	0.67 percent	0.35%
RS 73242-2	1.02 percent	1.0 %
RS 73242-3	None	**
RS 73242-4	Unknown	0.05%
RS 73242-5	Unknown	**
RS 73242-6	1-1.5 percent	0.60%
RS 73242-7	1-1.5 percent	0.25%
RS 73242-8	None	**
RS 73248-6	Unknown	**
RS 73248-7	Unknown	**

* Paper was ashed for X-ray determination.

** Below detectable limits.

APPENDIX I
Table IIIAQUANTITATIVE RESULTS OF SCUFF TEST RUN AT 19 CPS - 24 HOURS

Sample	Residue Due To Scuffed Paper (gms)	Loss per sq in of Paper (gms/sq in)	Loss per sq cm of Paper (gms/sq cm)
RS 73242-1	0.00151	0.83×10^{-4}	1.28×10^{-5}
RS 73242-2	0.00444	2.44×10^{-4}	3.78×10^{-5}
RS 73242-3	0.00148	0.81×10^{-4}	1.26×10^{-5}
RS 73242-4	0.00356	1.95×10^{-4}	3.03×10^{-5}
RS 73242-5	0.00133	0.73×10^{-4}	1.13×10^{-5}
RS 73242-6	0.00353	1.94×10^{-4}	3.01×10^{-5}
RS 73242-7	0.00508	2.79×10^{-4}	4.32×10^{-5}
RS 73242-8	0.00293	1.61×10^{-4}	2.48×10^{-5}
RS 73248-6	0.00685	3.76×10^{-4}	5.82×10^{-5}
RS 73242-7	0.00798	4.38×10^{-4}	6.79×10^{-5}

APPENDIX I
Table IIIBAPPROXIMATE NUMBER OF TALC PARTICLES PER 35 MM
DIAMETER RESIDUE ON MILLICORE MEMBRANE BY PETROGRAPHY
AT 500X - RESIDUES FROM 19 CPS - 24 HOUR TEST

Sample	Actual Talc Content of Paper	Number of Talc Particles	Number of Chrysotile Fibers	Number of Tremolite Fibers
3242-1	0.35%	29,000 ²	0	668
3242-2	1.0 %	52,500 ²	0	2,002
3242-3	**	2,500	0	0
3242-4	0.03%	7,500	0	668
3242-5	**	Present ³	0	0
3242-6	0.60%	35,000	0	2,804
3242-7	0.25%	50,000	0	2,937
3242-8	**	10,000	0	0
3248-6 ¹	**	Too waxy to read	-	-
3248-7 ¹	**	Too waxy to read	-	-

Below detectable limits.

Predominant constituent appears to be minute blebs of crystalline wax ranging from 0.5 to 5 microns in size. Very small percentage of carbonate and cellulose-type fiber.

The average size of these talc platelets is approximately 1 micron x 1 micron x 1/2 micron. Using this average particle size and a density of 2.8 gms/cm³ for talc, 29,000 particles would weigh approximately 2×10^{-5} mg, and 52,500 particles would weigh approximately 3.7×10^{-5} mg.

Profuse amount of doubly terminated minute acicular crystals (2 to 10 microns in length) which are anisotropic, but unidentified. These acicular crystals are not retained after ashing.

Blanks were examined to try to establish background level of talc. CELITE 3248-7 (-alt-washed water) was studied in some detail by employing 20 fields low at 500X. Minute particles of carbonate-like material predominate and may constitute as much as one million particles per 35 mm diameter residue. Certain platelets of talc platelets were detected on these blanks for no discernible reason, except possibly due to contamination. The calculated results for the residue are:

No. of talc particles	- 3,000 (platelets, few short)
No. of chrysotile fibers	- 0
No. of tremolite fibers	- 0
Cellulose-like fibers	- trace

APPENDIX I
Table IVA

SCUFF RATE OF SAMPLE RS 73242-2
(Determined Over a Cycle of 72 Hours)

Time	Total Filter Residue	Average Insoluble Salt Residue**	Residue Due to Paper Abrasion
2 hours	0.00236 gms *	0.00216 gms	0.00020 gms
4 hours	0.00242 gms *	0.00216 gms	0.00026 gms
6 hours	0.00445 gms *	0.00216 gms	0.00229 gms
12 hours	0.00266 gms	0.00216 gms	0.0005 gms
24 hours	0.00300 gms	0.00216 gms	0.00084 gms
48 hours	0.00359 gms	0.00216 gms	0.00143 gms
72 hours	0.00364 gms	0.00216 gms	0.00148 gms

* Average residue

** Average from 7 salt blanks

APPENDIX I
Table IVB

CELLULOSE AND TALC ON MILLIPORE FROM 19 CPS FREQUENCY
SERIES RS 73242-2 BROWN PAPER

Time	Estimated No. of Cellulose Fibers Per Membrane	Estimated No. of Talc Particles Per Membrane
0 - Salt Blank	400	700 ²
2 hours	600	2,000 ²
4 hours	1,100	5,000 ²
6 hours	2,500	12,000 ²
12 hours	>3,000 ¹	17,000 ³
24 hours	>3,000 ¹	38,000 ³
48 hours	>3,000 ¹	68,000 ²
72 hours	>3,000 ¹	75,000 ³

1. The cellulose fiber population was tremendous on these membranes. Their inter-twining and matting made counting extremely difficult. By extrapolating, their count could easily reach as high as 20,000 per membrane. V. E. Wolkodoff
2. Based on ash
3. Based on dissolved millipore membrane

APPENDIX II

SCUFF TEST

A. Equipment

1. L.A.B. type RVH vibration test stand or equivalent.
2. Millipore filtration apparatus, 0.45 and 0.80 micron filters (vacuum filtration).
3. Fisher Magnetic Stirrer.
4. 8 ounce flint glass, squat form wide mouth bottles.
5. Several 1500 ml beakers (carefully cleaned).
6. Mettler Balance or equivalent.

B. Reagents

1. Distilled water
2. Sodium chloride, CP
3. Test paper

C. Test Method

1. Cut selected test paper to the dimensions of 2 5/16-inch x 8 1/2-inch. Curl the paper and place it inside a clean, dirt and fiber free 1/2 pint jar. Line the paper on the inside surface (there will be a slight overlap); mark this overlap with a few pencil dots; remove the paper and tape the outside of the overlap; then re-insert inside the jar.
2. Weigh out 200 gm of the salt and place it in the lined jar. Cap the jar.
3. Place on vibrator which has been set to run at 19 cps, 1/16-inch amplitude, (1/8-inch full excursion), for 24 hours.
4. After 24 hours of running, remove jar(s) from vibrator. Any run should also be accompanied by a control blank of a jar simply filled with 200 gms of salt.
5. Filter some distilled water through 0.45 micron millipore filters. Approximately 1500 ml will be needed for each sample. Also, use this filtered water to rinse out all containers and equipment with which the sample liquid will come in contact. It is important to keep all equipment dust and fiber free.

SCUFF TEST (Cont'd)

6. Empty the salt from the test jars into 900 ml (0.45 micron filtered) of water which is being stirred by a magnetic stirrer. Remove the test paper lining and tap it over the beaker in order to remove any salt clinging to it. Then use an additional 100 ml of filtered water to rinse the jar and cap. Pour this into the beaker also. Allow the mixture to stir approximately 5 minutes in order to dissolve all the salt.
7. Preweigh two 0.2 micron millipore filters for each sample. When the salt is dissolved, pour the liquid through the filter apparatus in which both filters are present, one directly on top of the other, (the bottom filter is a control). Use an additional 200 ml of filtered water to rinse out the beaker and pour this through the filter. (A wash bottle provides the most effective method of rinsing.) Then use an additional 300 ml of filtered water to wash the filters. This will help wash away any minute salt particles that are clinging to the filters. When washing is completed, let both filters dry completely.
8. When the filters are dry, weigh them. These samples are now available for microscopic examination.

D. Calculations

1. (For 1 Sample)

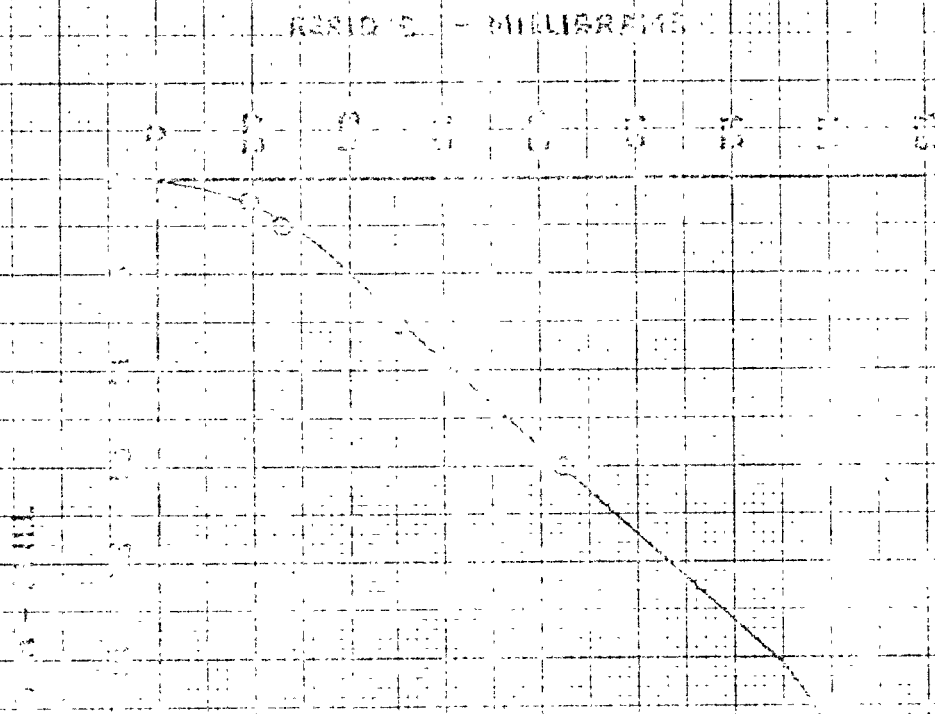
Filter No. 1 (Before)	= X gms
Filter No. 1 (After)	= $\frac{X + (\text{residue}) \text{ gms}}{(\text{Residue}) \text{ gms}}$
Filter No. 1A (Before) = Y gms	
Filter No. 1A (After)	= $\frac{Y \pm Z \text{ gms}}{(Z) \text{ gms}}$

Filter No. 1A acts as a control. It might change in weight by the amount of (Z) gms. This might very well be an increase in weight if all the salt was not washed out of the filters. But whatever weight is found in No. 1A, it must be subtracted from the apparent residue weight, because approximately the same change in weight will occur to the top filter as did to the control filter.

2. (Residue) gms - ($\pm Z$) gms = Actual Residue (gms)

3. The actual residue contains both the residue from the paper and the salt, so the actual weight of paper scuffed off equals:

$$\frac{[\text{Actual Residue (gms)}] - [\text{Actual Residue (gms) from Salt Blank}]}{\text{Weight of Scuffed Material}} =$$



[100] Johns-Manville

Internal Correspondence

To: R. S. Lamar - R&D Ctr

Date: August 28, 1973

From: V. E. Wolkodoff - R&D Ctr

Copies:

Subject: FILLER MIGRATION FROM FOOD WRAP PAPERS

On Tuesday, August 28, 1973, I spoke to Mr. G. Higgenbottom of the FDA in Washington, D.C. He and Mr. A. Spiher had discussed possible methods which could be used to determine the amount of filler migration from a food wrap paper to the foodstuff contained therein. It is necessary to devise a suitable method, since there is no standard method in existence. The lack of an approved method was determined by Mr. A. Bolts, Packaging Chemist for the FDA. The method they suggest is as follows:

1. Construct a small container from the paper in question and partially fill with ordinary salt (NaCl). We agreed that reagent grade salt would be used since it would not contain the insoluble additives normally used in table salt.
2. Shake or tumble the salt-filled container for 24 hours. The intensity of shaking was not specified, but they will accept anything we feel is reasonable.
3. Remove the salt from the container and dissolve in a suitable quantity of water.
4. Filter the salt solution through a Millipore membrane (0.8 um pore diameter), and examine for "asbestos" fibers by the normal (NIOSH) methods.

In addition to the above, the FDA would also like to have a determination of the limit of detection. This would be determined by adding known increments of "asbestos" or "asbestos"-containing talc to salt and following the same analytical procedure.

V. E. Wolkodoff

V. E. Wolkodoff

jmw

Title: LACK OF FOOD CONTAMINATION BY CONTACT
WITH PAPER DUE TO SHIPPING

SUMMARY

The purpose of this study was first, to determine the severity of the effects of transportation on the contents of food and drug packages and second, to determine the relevance of using an artificial test to simulate the effects of actual shipping conditions. Specifically, the study was to determine whether actual shipping would cause sufficient abrasion to the containers to cause migration of part of the paper into the contents of food packages.

This study established that tremolite contained in talc used in food paper packaging does not migrate to any food substances during normal commercial shipment and handling.

Test containers of salt lined with tremolitic talc-containing paper shipped by truck from Denver to New Jersey and back caused no breakdown in the integrity of the paper and no migration of the tremolite or any other ingredient of the paper. Additionally, food packaged in tremolitic talc-containing paper purchased at a local supermarket showed no evidence of tremolite migration due to paper breakdown. This was so even though foods were chosen which were likely to have been shipped long distances and were likely to be abrasive.

It was established by the data reported in Report No. E414-2 that migration of tremolite from food packaging paper to food can only occur if some partial breakdown of the paper occurs. Migration does not occur unless the integrity of the paper is at least partially destroyed and then all of the components of the paper will migrate (be released) in the same proportion as they exist in the paper (no selective migration). This conclusion was verified by the "Scuff Test" reported in Report No. E414-2, which was questioned as possibly being more severe than actual commercial shipping conditions.

This present report establishes that the conditions established in the "Scuff Test" are indeed much more severe than actual commercial shipping conditions. Actual shipping conditions result in no migration, at least to reliable levels of identification by transmission electron microscopy, optical (petrographic) microscopy, and weight determinations.

Contents: Summary, Discussion, Conclusions, Recommendations, and Appendix.

Reported by

R. J. Zazenski
R. J. Zazenski

Reported by

J. R. Bell
J. R. Bell

DISCUSSION

Introduction

Initial studies on tremolite migration from paper manufactured with tremolitic talc established that migration will only occur with partial destruction of the integrity of the paper which is in contact with the food. Without some destruction of the paper, no measurable migration occurs, i.e., there is no selective migration initiated by the abnormally severe "shaking" or "scuffing" of the packages' contents. To simulate this action, an artificial "Scuff Test" was employed which deliberately caused paper destruction. This enabled us to analyze the mechanism of migration.

The purpose of the present study was to determine the relevance of this artificial test to actual shipping conditions, as well as evaluate the severity of actual transportation. To accomplish this, specially prepared containers were sent by REA truck from Denver to Manville, New Jersey and back to Denver, a round trip of approximately 72 hours and 4,000 miles of constant truck travel. In addition, actual food commodities were purchased at a supermarket for the purpose of analyzing them for possible tremolite migration.

Actually Shipped "Controlled" Samples

Four paper lined, salt containing jars were sent by truck on their 72-hour journey. These lined jars were prepared in identical fashion to the test jars used in the artificial "Scuff Test". Four different test papers were employed, each specifically chosen because it contained tremolitic talc (they ranged from 0.25-1.0 percent talc). Two hundred grams of technical grade salt served as the food medium in each of the lined jars. Evaluation of the salt samples after shipment consisted of: (1) determining the weight of the abraded material from the paper, if any, (2) inspection for cellulose fibers, talc, tremolite, and chrysotile, by petrographic analysis, and (3) inspection for talc and asbestiform materials by Transmission Electron Microscopy (TEM). These analyses were conducted in the same fashion as were the samples that were tested by the artificial "Scuff Test" reported in Report No. E414-2, with the exception of additional analyses by TEM in the present test after no migration was detected by petrographic analysis.

In examining these samples, an effort was made to concentrate on the detection of the presence of talc since the previous studies showed no selective migration. Therefore, it can be presumed that if no talc is detected in the residue, then there would be no tremolite (on a weight basis, there should be 95 unit weights of talc for every 1 unit weight of tremolite in this particular talc). This technique was used as conservative means of

detecting the presence or absence of tremolite. To serve as check, thorough scanning was made for tremolite, even though its presence might be beyond the levels of detection with practically insignificant amounts of paper breakdown.

The overall analyses indicated that no migration was found. Thus, the actual shipping route of 72 hours of constant road travel did not create conditions severe enough to cause appreciable destruction of the paper liners. Petrographic analysis of all four test samples revealed only a possible trace of talc and no evidence of the presence of any chrysotile or tremolite fibers due to migration.

Upon comparing these results to the artificial "Scuff Test" that was run for only 24 hours, it is evident that the artificial test causes conditions which are overwhelmingly more severe than actual commercial transportation. As an example, the results of one particular paper sample that was run in both the artificial and actual tests are compared in this tabulation.

Comparison of Artificial and Actual Shipping Test Results
Petrographic Evaluation
Paper Sample RS 73212 2

	Number of Talc Particles	Number of Chrysotile Fibers	Number of Tremolite Fibers	Duration
Artificial Test	52,500	0	2,002	24 hours
Actual Test	possible trace	not detected	not detected	72 hours

In addition to examining the shipped salt samples by petrographic methods, they were also examined by TEM (8000X). The fields were selected at random after considerable scanning specifically looking for talc and tremolite. Thirteen plates were made in those cases where scanning indicated the possible presence of talc or tremolite. The results from examination of these 13 plates showed the possibility of only one talc particle and also the possibility of only one tremolite fiber. In addition, no fibers of any kind longer than 5 microns could be detected. Tables 1 and 2 in the Appendix have the complete examination results in tabular form.

This complete and thorough analysis of these shipped samples establishes that normal transportation does not create a severe enough environment to even allow salt (which is one of the most abrasive food materials packaged) to cause appreciable destruction of its containers. Thus, under actual commercial conditions, migration of tremolitic talc caused by paper breakdown due to shipping and handling is highly unlikely.

Evaluation of Food Products

Five food items were purchased at a local supermarket for the purpose of analyzing them for the presence of tremolitic talc in the paper packaging and the possibility of any migration from those papers. Items that had been transported the longest distances as well as those foods that would be particularly abrasive were specifically chosen. The food items selected were macaroni, rice, salt, corn flakes, and dry, non-fat milk.

The petrographic analysis of these food items indicated absolutely no migration of tremolite fibers. The food containers were analyzed by X-ray diffraction, and petrographic methods to identify if the paper packaging contained talc and tremolite. Table 3 reports the results of these analyses. Petrographic examination revealed no talc in four of the five contents, with only the possibility of a trace in the Morton's Salt. Examination of the Morton's Salt was extremely difficult because one of its additives, sodium silico aluminate (a crystalline material still present after ashing), interfered with the optical examination. Subsequent examination showed no tremolite or chrysotile fibers present in any of these foods. These results are located in Table 4 in the Appendix.

TEM examination of the ashed food samples also revealed no tremolite fibers. Several small chrysotile and talc particles were detected, but all were sub-optical in size. Each ashed food item underwent a thorough examination of at least 20 fields by the TEM, each field 80 microns square. These results are located in Table 5.

CONCLUSIONS

1. Analysis of salt test samples which endured approximately 3 days of constant road travel showed no evidence of appreciable breakdown in the integrity of the paper liners and no migration of tremolite fibers, although the test papers were known to contain tremolitic talc in the range of 0.25 to 1.0 percent.
2. Analysis of actual food commodities purchased at a supermarket also showed no evidence of appreciable breakdown in the integrity of the packaging paper and absolutely no migration of tremolite fibers, even though three of the paper containers were known to contain tremolitic talc.
3. These studies support the conclusion arrived at in Report No. E414-2: Regardless of the composition of the paper (container), migration will not occur unless severe enough conditions cause the container's contents to scuff and abrade the inside lining enough to cause paper breakdown.

4. It seems evident that actual conditions of transportation do not create a severe enough environment for paper breakdown to occur; thus, migration from paper is highly unlikely.
5. The artificial Scuff Test, as used in Report No. E414-2, was found to be appreciably more severe than actual commercial shipping conditions.

RECOMMENDATIONS

1. It is recommended that an artificial Scuff Test should not be used to simulate actual transportation for food packaging migration studies because it produces results not comparable to actual commercial shipment.

APPENDIX
Table 1

RESULTS OF PETROGRAPHIC EXAMINATION OF
RESIDUES FROM SHIPPED TEST SAMPLES⁵

Sample No.	Actual Talc Content of Paper ¹ (percent)	Talc Particles Per Membrane ²	Chrysotile Per Membrane	Tremolite Per Membrane
RS 73242-1	0.35%	possible trace	not detected	possible trace ⁴
RS 73242-2	1.0 %	possible trace	not detected	not detected
RS 73242-6	0.60%	possible trace	not detected	not detected
RS 73242-7	0.25%	possible trace	not detected	not detected

1. Talc content determined by X ray diffraction.

2. The entire contents of the test samples were dissolved in filtered water and filtered through a 0.8 micron membrane. Therefore, only insoluble impurities present in the contents were collected on the membrane.

3. Three fibers present ranging in length from 300 to 480 microns, but have to be considered as outside contamination, as talc is commercially ground so fine as to prohibit the presence of chrysotile fibers of such a length.

4. Based on the total examination of one 10 mm field, only one tremolite fiber was detected. This could have resulted from contamination from unknown source.

5. These analyses were based on the examination of at least 100 fields of view per sample at 500X magnification.

Possible Trace should be divided into 2 terms:

Possible - optical properties indicate the presence of a particulate mineral, possibly talc.

Trace - if there, the above is present in a trace amount.

APPENDIX
Table 2EXAMINATION OF SHIPPED TEST SAMPLE RESIDUES
BY TRANSMISSION ELECTRON MICROSCOPY

8000X - TEM			
Sample No.	Plate Number	Talc	Tremolite
RS 73242-1	2216A	0	None
	2216B	0	None
	2216C	0	None
	2216D	0	None
RS 73242-2	2217A	0	None
	2217B	0	1 possible, 5 micron long
	2217C	0	None
RS 73242-6	2218A	0	None
	2218B	0	None
	2218C	possibly 1	None
RS 73242-7	2219A	0	None
	2219B	0	None
	2219C	0	None

1. Samples ashed at 800^oF for 16 hours.
2. Entire samples were scanned looking specifically for talc and tremolite.
3. Fields were selected at random.
4. No fibers of any kind detected longer than 5 microns.

Examination performed by V. E. Wolkodoff

APPENDIX
Table 3

PETROGRAPHIC EXAMINATION OF ASHED FOOD CONTAINERS
Optical Examination for Chrysotile and Tremolite at 500X

<u>Sample</u>	<u>Chrysotile</u>	<u>Tremolite</u>
4385-35-1	ND	present
4385-35-2	ND	ND
4385-35-4	ND	ND
4385-35-5	ND	present
4385-35-8	ND	present

APPENDIX
Table 4

ASHED FOOD MATERIALS EXAMINED PETROGRAPHICALLY
FOR TALC AND AMBESTIFORM MINERALS

Commodity	% Talc in Container	% of Total Package Contents Examined	Presence of Tremolite in Container ²	Talc Detected in Food Contents	Tremolite and Chrysotile in Food Contents
Macaroni	0.23%	31.67%	Positively Identified	Not Detected	Not Detected
Dry non-fat milk	0.84%	23.14%	Not Detected	Results Inconclusive	Not Detected
Quick Rice	0.25%	10.77%	Not Detected	Not Detected	Not Detected
Corn Flakes	0.05%	6.41%	Positively Identified	Not Detected	Not Detected
Morton's Salt ¹	1.26%	13.55%	Positively Identified	Possible Trace	Not Detected

1. 85 g dissolved on millipore membrane before ashing.

2. Examined by petrographic analysis. Conclusions based on at least 100 fields of view.

NOTE: All food materials ashed at 800°F in air atmosphere for 7 days. To remove all carbonaceous material, except for Morton's salt, a higher temperature may be required, but optical properties would change.

Comments from Petrographer: The ash from dry milk was extremely difficult to read and the results are inconclusive. An extremely small amount of the crystalline materials in ashed Morton's Salt has been identified as talc and the percentage is officially listed as a possible trace.

Examination performed by V. E. Wolkodoff.

APPENDIX
Table 5

TRANSMISSION ELECTRON MICROSCOPY EXAMINATION OF FOOD CONTENTS
(ASHED)

Sample No.	Description	% of Total Package Contents Examined	TEM Plate No.	Talc	Chrysotile	Tremolite
4385-35-1F	Macaroni Ash	31.67%	224A	ND	2 < 1 micron	ND
			B	ND	ND	ND
			C	ND	ND	ND
4385-35-2F	Dry Milk Ash	23.14%	225A	ND	ND	ND
			B	ND	ND	ND
			C	ND	ND	ND
4385-35-4F	Ashed Rice	10.77%	226A	ND	2, one > 1 micron	ND
			B	ND	1 clump	ND
			C	2 particles	1 < 1 micron	ND
4385-35-5F	Ashed Corn Flakes	6.41%	227A	ND	ND	ND
			B	ND	ND	ND
			C	ND	ND	ND
4385-35-8F	Morton Salt Ash	13.55%	228A	1 particle	ND	ND
			B	1 particle	ND	ND
			C	ND	ND	ND

Industrial Hygiene Summary Reports

This Journal welcomes brief comments derived from daily activities which may be useful to other members of the profession. Address your communications to: Richard F. Scherberger, Health and Safety Laboratory, Building 320, Kodak Park Works, Eastman Kodak Company, Rochester, New York 14650.

Asbestos, Talc and Nitrites in Relation to Gastric Cancer

Recently, Meriliss¹ suggested that the high incidence of gastric cancer in Japan may be associated with treatment of rice with talc in Japan. He noted that some commercial "talc" contain asbestos, which he proposed as an etiologic agent in gastric cancer. Meriliss cited a report of a small excess of gastric cancer in a group of insulation workers exposed to dusts containing asbestos and a larger excess of pulmonary carcinomas and pleural mesotheliomas in miners who appear to have had mixed exposures to asbestos and talc. He noted that some geologic deposits of talc are associated with tremolite, anthophyllite and chrysotile varieties of asbestos, accounting for the presence of fibrous particles of asbestos together with platy particles of talc in some commercial preparations of "talc."

Our group has carried out tests for carcinogenicity of various preparations of asbestos through experiments with animals. The present paper summarizes some results and reports a new experiment with a preparation of talc containing asbestos. A possible alternative mechanism involving nitrites in gastric carcinogenesis is discussed.

In 45 hamsters maintained throughout their lives on diets containing 1% of the chrysotile or amosite varieties of asbestos, we found no gastric carcinomas and no tu-

mors in the gastrointestinal tract except for a neoplasm in the mesentery of the colon.² We are unable to relate that lesion to the treatment, since ashing has revealed no asbestos fibers in it.

After intrapleural injection of 25 mg chrysotile or amosite into hamsters, we reported tumors diagnosed as pleural mesotheliomas.² Eight to 10 such tumors were found in each of 3 groups of 50 hamsters treated at this dose level.¹

We have now completed an experiment in which the hamster-intrapleural method was used to test for carcinogenicity of a sample of talc containing asbestos. For this work, we obtained samples of commercial talcs from Whittaker, Clark & Daniels, Inc., New York City. A sample of cosmetic talcum powder grade was seen by microscopic examination to be composed of platy particles typical of the mineral, talc (hydrous magnesium silicate). Another sample of a grade used for some industrial purposes ("#13 Talc") was found to be a mixture of platy and fibrous particles. X-ray diffraction analysis revealed the presence of major amounts of tremolite asbestos and talc and a minor amount of a serpentine mineral (antigorite).

Each of 50 hamsters were given right intrapleural injection of 25 mg of this sample suspended in 0.5 ml saline. The animals were followed for their life spans. No tumors attributable to the treatment were found. Granulomatous lesions were com-

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mon on pleural surfaces, but these lesions tended to be small and focal in contrast to larger and more fibrotic lesions induced in hamsters by chrysotile or amosite.

The negative results of this test for carcinogenicity of a talc containing asbestos, and our earlier test on feeding asbestos to hamsters, do not offer support to the view that asbestos-containing talc contributes to the incidence of gastric cancer in Japan.

Although death rates reported for gastric cancer are notably high in Japan in comparison to other countries, the highest reported rate comes from Chile.⁴ Studies of gastric cancer in Chile have been reported from our laboratory with an hypothesis that high rates for esophageal and gastric cancer may be due to conversion of nitrates to nitrites by soil bacteria with subsequent synthesis of nitrosamine carcinogens in plants used as food or through interaction in the stomach with secondary amines in food.²

Chile has the world's largest known geologic deposits of nitrates, which are used as fertilizers. Nitrosamine has been reported in wheat plants and wheat grains.⁶ Nitrosamines can form through interaction of nitrites with secondary or tertiary amines in the stomach, and have been shown to induce esophageal and gastric cancers in rats.^{7,8} High concentrations of secondary amines have been reported from Japan in dried fish.⁹

The situation invites attention to a potential role of the nitrogen cycle in environmental carcinogenesis. A source for direct ingestion of nitrites by human populations

arises from use of nitrites as food additives. Other potential factors in gastric carcinogenesis have been recently reviewed by Haenszel *et al.*¹⁰ who found no support for the talc-asbestos hypothesis on epidemiologic grounds.

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William E. Smith, M.D.
Health Research Institute
Fairleigh Dickinson University
Madison, N.J. 07940

As described in the preceding section, the dissections were performed which were complete except for the head. Gross observations were recorded. Thoracic cavities were fixed in formalin as were pertinent lesions found elsewhere. Microscopic sections were cut and stained with hematoxylin and eosin. For recording and summarization of data, we designed and used a punch card for individual maneuvers as illustrated in Fig. 1.

[illegible]

Fig. 1. Punch card used to record findings on individual
monsters.

At necropsy, the prospector entered identification and date of death of the individual animal on this card, placed the number of days in experiment, presence or absence of pleural adhesions, character of adhesions

local or diffuse), presence or absence of deposits, pleural plaques, cardiac thrombi, other pathology. Gross findings in the thorax were then sketched on diagrams shown in the center of the card. Histopathologic findings were subsequently entered in the spaces provided to the right of the double line with special reference to diagnosis of any tumors, as characteristics of pleural adhesions, presence or absence of mineral particles, ferruginous bodies or other pathology. Where additional descriptions of gross or microscopic pathology were warranted, these were entered on a separate blank card.

All animals in these experiments have been examined at necropsy except for rare cannibalized individuals. Histopathologic studies have now been made on tissues saved from all animals except for rare autolyzed individuals. All tumors diagnosed as mesothelioma have been confirmed microscopically. No tumors suggesting mesothelioma in the gross were in animals where autolysis precluded histopathologic study. Tumors listed in this report as mesothelioma resembled those illustrated and described in our previous work with intrapleural injection of chrysotile and amosite into hamsters. (Smith, W.E., T. Miller, R.M. Elsaszer and D.D. Hubert. Tests for Carcinogenicity of Asbestos, *Annals N Y Acad Sci* 132 (Part 1):466-483, 1955), (Smith, W.E., T. Miller, J. Chung, and D.D. Schloffer. Mesothelioma in Hamsters Following

in pleural injection of 100 mg. of chrysotile (Group 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) findings from the present experiments are summarized in Table 1.

Tumors listed in Table 1 under the heading "Mesothelioma" were with few exceptions large masses in the pleural space. They compressed but rarely invaded the lungs. Microscopically, they were composed of elongated or rounded cells that appeared malignant. Under a separate heading of "Lymphoid Tumors", Table 1 lists lymphomas, lymphosarcomas or reticulum cell sarcomas that were found in occasional animals of the various groups. These "Lymphoid Tumors" occurred in mediastinal or mesenteric nodes, sometimes with neoplastic features. Injection site sarcomas, also listed separately in Table 1, were tumors found subcutaneously on the chest wall in the area where intrapleural injection had been made. Mineral particles of the test samples were usually seen in microscopic sections of injection site sarcomas.

From yields of tumors designated as mesotheliomas in Table 1, information emerged on the following points:

1. The yield of mesotheliomas in response to 3 dose levels of chrysotile (Groups 2, 7, 8), 2 dose levels of amosite (Groups 9, 10) and 2 dose levels of crocidolite (Groups 18, 19) is dose related, hence

These should be confirmed by appropriate
experiments in experimental animals. Chrysotile asbestos with
chromophyllite (Cron, 1955), appear less carcino-
genic than crocidolite.

2. Closely comparable yields of mesotheliomas
resulted from soft (Group 1) and harsh (Group 2)
chrysotile fibers prepared from Arizona ores, and
from the same soft fibers heated to reduce their
content of molecular water to the level of harsh
fibers (Group 3). The tumors arose more rapidly
in response to native harsh fibers (Table 2).
Studies of pleural adhesions revealed that harsh
chrysotile induced thicker and denser scars than
soft chrysotile. Although heat treatment of soft
chrysotile gave no appreciable enhancement of
carcinogenicity, it did enhance fibrogenicity (3).

3. At the highest dose level tested (25mg), 3
samples of chrysotile with mean fiber lengths between
32 and 39 microns yielded 8, 9 and 10 mesothelioma-
bearing animals (Groups 1,2,3). When fiber lengths
of these chrysotiles were reduced to an extent
where the large majority of fibers were less than
5 microns in length, fibrogenicity was reduced and
carcinogenicity was eliminated (Groups 4,5,6).