

EXHIBIT A

The Detection and Determination
Of Chrysotile in USP Talc

Harry A. Rose

Abstract ☐ A procedure for the determination of chrysotile in talc has been developed. It depends on the adsorption of a sulfonphthalein dye by chrysotile but not by talc. The final measurement is a spectrophotometric determination of the dye left in solution after the adsorption step.

The wide use of talc as a dusting powder and as a diluent in capsule contents has caused concern about possible impurities in the talc and especially the possible presence of asbestos. Cralley et al. (1) found asbestos in a number of cosmetic talcs. Merliss (2) implicated asbestos in talc as a cause of stomach cancer in Japan.

Talc is a hydrated magnesium silicate which may ideally be represented as $Mg_3(OH)_2Si_4O_{10}$. It may be contaminated with other minerals such as quartz, dolomite, chlorite, and the various forms of asbestos. Of the asbestos minerals, chrysotile is currently of most physiological concern. Chrysotile is also a hydrated magnesium silicate which may ideally be represented as $Mg_6(OH)_8Si_4O_{10}$. The structure of both minerals is apparently made up of sheets of silicon and oxygen atoms interspersed with sheets of magnesium and oxygen atoms, the difference being in the added magnesium and oxygen in the chrysotile structure.

USP XVIII (3) is rather vague about the chemistry of talc and apparently would admit a talc containing some chlorite. The concern is for rather gross impurities such as excesses of pH or water-soluble iron. Thus, a rather substantial contamination of the talc with chrysotile could occur, and unless the product became gritty, no cause for rejection would appear.

The working solution was made by taking 20 ml. of the stock solution plus 40 ml. of 95% ethanol and diluting to 100 ml. with pH 4.2 acetate buffer. This working solution when diluted 10 ml. to 25 ml. with pH 4.2 acetate buffer should have an absorbance of .325 at 422 m μ .

The chrysotile was obtained from the Johns Manville Research Center and was used as received except for reduction in particle size to that of the talc being tested.

Procedure - Weigh three 0.2000 ± 0.0010 gram samples of the talc. To sample number two, add about 3 mg. of chrysotile and to sample number three about 6 mg. of chrysotile, both accurately weighed. To each sample add 10 ml. of 50% ethanol-water. Also, provide a 10-ml. sample of the 50% ethanol-water to serve as a blank. All samples and the blank are given an ultrasonic treatment¹ for two minutes at 70 watts of power. After the samples have cooled to room temperature, add 10 ml. of working dye solution to each sample and the blank. Mix and allow to stand for 30 minutes with occasional shaking. The samples and blank are then centrifuged followed by filtration through a 45 μ . millipore filter. A 10-ml. aliquot of each filtrate is diluted to 25 ml. with pH 4.2 acetate buffer.

¹Sonifier Cell Disrupter, Model W185D, from Heat Systems Ultrasonics, Inc. of Plainville, N.Y. The micro tip adapter was used.

From the assay in Figure 1 would indicate 1.1 mg. chrysotile in a 200-mg. sample, or 0.55%.

Eli Lilly and Company has been fortunate in being able to conduct a series of physiological and clinical tests for the purpose of determining the relative safety of the various preparations of the above mentioned drugs. These tests have all been conducted on the following

where $\mathbf{h}_i$ have independent $N(\mathbf{0}, \mathbf{I})$ and $\mathbf{h}_i^T \mathbf{h}_j = \delta_{ij}$.

(a) $\alpha_1, \alpha_2, \alpha_3, \alpha_4$ and α_5 are all simple roots
 (b) $\alpha_1, \alpha_2, \alpha_3, \alpha_4$ are simple roots and α_5 is not
 (c) $\alpha_1, \alpha_2, \alpha_3, \alpha_4$ are not simple roots and α_5 is
 (d) $\alpha_1, \alpha_2, \alpha_3, \alpha_4$ and α_5 are not simple roots

REFERENCES

- (1) L. J. Cralley, M. M. Key, D. H. Groth, W. S. Lainhart,
and R. M. Ligo, Amer. Ind. Hyg. Ass. J., 29, 350-354
(1968).
- (2) R. R. Merliss, Science, 173, 1141-1142 (1971).
- (3) The United States Pharmacopeia, 18th Revision,
Mack Publishing Co., Easton, Pa., p. 708.
- (4) A. L. Rickards, Anal. Chem., 44, 1872-1873 (1972).

ACKNOWLEDGMENTS AND ADDRESS

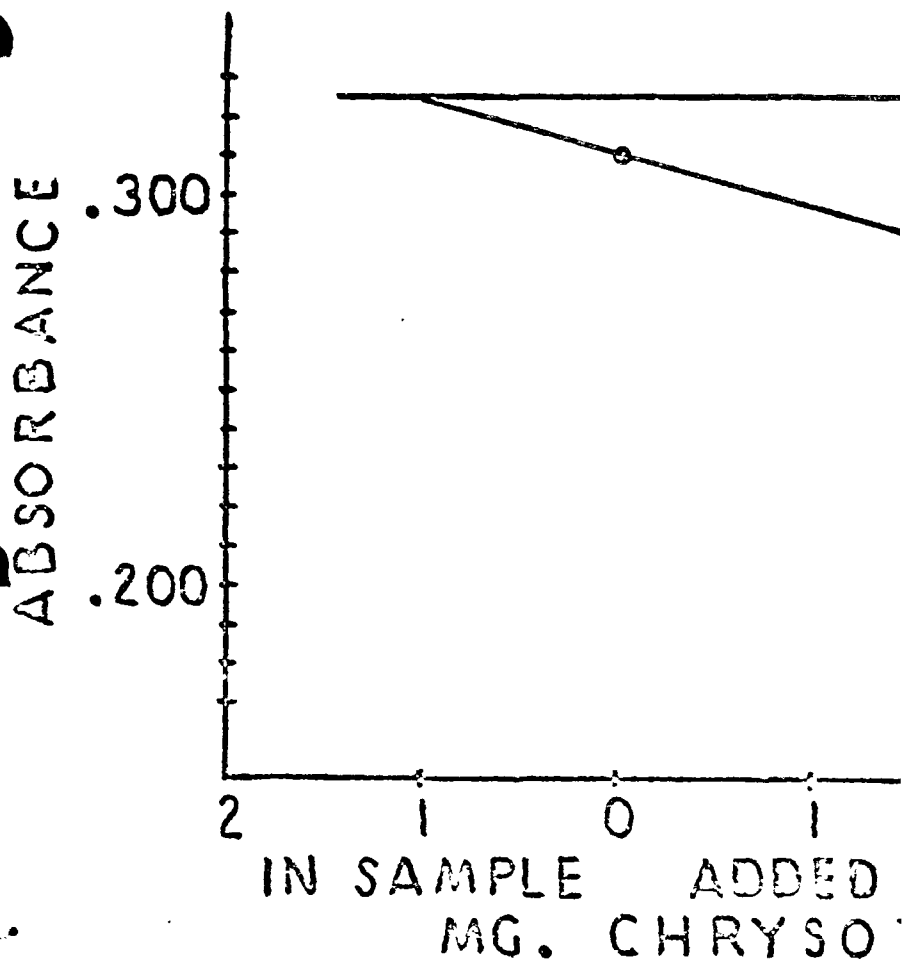
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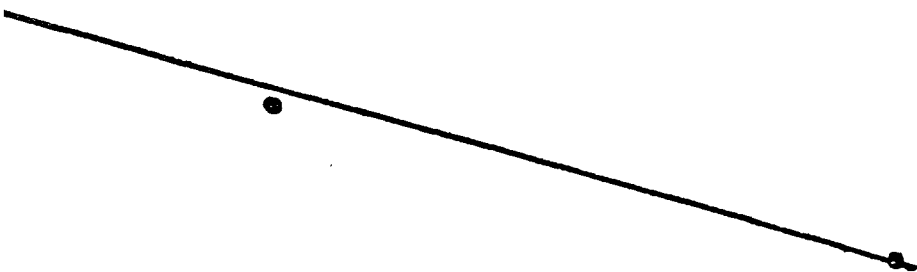
The author wishes to thank the Johns Manville Research Center and Dr. John M. Hayes of Indiana University for providing the samples of chrysotile.

Analytical Development Department, Eli Lilly and Company, Indianapolis, Indiana 46206.

2

Figure 1. Extrapolated graph of additions of chrysotile plotted against absorbance.





2 3 4 5 6

TO SAMPLE
TILE

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Comments Regarding Analytical Procedures for Asbestos Determination

We believe that the degree of polarization in the microscope should be defined. In our studies we employed a Leitz Ortho-Lux microscope which permits a continuous range of polarizations to be used in conjunction with the two refractive index fluids specified in the regulation. We found that the count of asbestos particles changed when the degree of polarization was changed in the microscope.

When the microscope is set at 400X with either refractive fluid, one experiences serious depth of field problems which make it difficult to determine axial ratios for a number of sizes of particles. It is particularly difficult to focus on large particles as when one portion of the particle is in focus the other part is out of focus and disappears. This in turn makes it difficult to determine the exact size of the particle since the whole particle is not in focus at any one time. A magnification of 100X would give a better depth of field yet this choice of magnification would also make the particle size selection process somewhat more difficult.

One of the significant problems that we encountered was the large number of counts obtained and the time employed making these counts using either refractive index fluid. Possibly a way to more easily perform counts and be able to determine sizes more accurately would be to use a device such as a hemacytometer, a microscope slide with a grid which is presently used to permit counting of blood cells in a specified volume and area.

In some of the talc we have been examining, we have found quite high levels of the chrysotile asbestos fibers and question the limit of not more than 100 fibers per milligram slide. Perhaps the data on which these limits have been set could be published in the Federal Register.

In summary, we found the analytical method as written to be ambiguous, time consuming and the apparently arbitrarily set limits to be somewhat tight. We feel the procedure could be run more easily at 100X magnification on a set amount of a dispersion at a set concentration delivered from a micropipette with the count being made in a given area, for example, on a hemacytometer.

Description of Modified Method to Revise Proposed Section 121.2006(c)(2)

Determine the N_z of the talc. Place 1 milligram of talc on a slide. Mix talc with refractive index liquid which has an N_d value most nearly equal to N_z of talc (liquid should be equal to or slightly less than N_z in talc). Spread particles evenly and place a cover glass (ca. 18 mm square) on the sample. Fibers counted by this method should meet the following criteria. (1) Length to width ratio of 3 or greater; (2) length of 5 μm or greater; (3) width of 5 μm or less. Count and record the number of asbestos fibers found in the 1 milligram sample as determined from a scan with a polarizing microscope at a magnification of approximately 400x. Chrysotile fibers will have indices less than the liquid in both extinction positions. Amphiboles will have indices greater than the liquid in both extinction positions. Check the extinction and sign of elongation for tentative identification. For specific identification of asbestos fibers, make additional mounts in appropriate refractive index liquids, and refer to the optical crystallographic data in the table. A count of not more than 1000 amphibole types of asbestos fibers and not more than 100 chrysotile asbestos fibers per milligram-slide constitutes the maximum limit for the presence of these asbestos fibers in talc. These limits assure a purity of talc at least 99.9 percent free of amphibole types of asbestos fibers and at least 99.99 percent free of chrysotile asbestos fibers.

If 100 or more chrysotile fibers are counted, the $2V$ of talc should be determined from the interference figure. If this value exceeds 10° there is a possibility that talc is being counted as chrysotile. In this case, the sample should be remeasured according to the above procedure in 1.574 refractive index liquid. Chrysotile fibers will have indices less than the liquid in both extinction positions.

Optical Data for Chlorites

Chlorites are 14Å layer-silicates with a wide range of chemical compositions and an equally wide range of optical properties. The hypothetical formula would be $\text{Mg}_6(\text{OH})_8\text{Si}_{10}\text{O}_{40}$. Aluminium replaces silicon and magnesium. Ferric and ferrous iron replace magnesium.

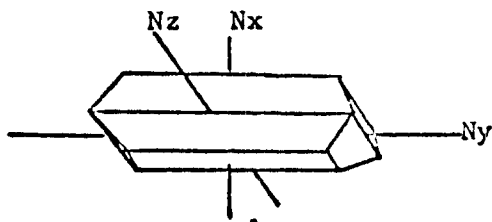
<u>Nx</u>	<u>Ny</u>	<u>Nz</u>	<u>Nx</u>	<u>Ny</u>	<u>Nz</u>
1.606	-	1.615	1.670	-	1.685
1.641	-	1.643	-	-	1.664
-	1.662	1.662	-	-	1.620
-	1.658	1.658	<1.63	-	>1.650
1.570	-	-	1.600	1.603	1.610
-	1.661	-	1.578	1.580	1.586
1.580	1.581	1.589	1.660	1.660	1.606
1.618	1.618	1.621	1.619	-	1.623
1.622	1.622	1.626	-	-	1.625
1.637	-	1.642	1.646	1.646	1.655
1.658	-	1.667	1.572	1.572	1.575
1.581	1.581	1.586	-	1.595	-
-	1.607	-	1.620	1.621	1.625

Extinction-parallel or inclined; elongation - positive or negative. Data from W.A. Deer, R.A. Howie and J. Zussman, 1965, Rock-Forming Minerals, Longmans, London.

Optical Data For the Epidote Minerals

The indices, birefringence, and optic angle vary rapidly with composition. There is a continuous series from $\text{Ca}_2\text{Al}_3(\text{OH})\text{Si}_3\text{O}_{12}$ (clinozoisite) to about 40 mol. % $\text{Ca}_2\text{Fe}_3(\text{OH})\text{Si}_3\text{O}_{12}$ (pistacite).

<u>Nx</u>	<u>Ny</u>	<u>Nz</u>
1.718	1.720	1.723
1.712	1.723	1.735
1.722	1.742	1.750
1.722	1.743	1.760
1.729	1.763	1.780
1.754	1.772	1.795
1.739	1.765	1.800
1.756	1.789	1.829



Epidote crystals have the Ny coinciding with the long direction, thus the needles will appear to have positive or negative elongation depending upon which side they are resting. They will have parallel extinction.

Data from Alexander N. Winchell and Horace Winchell, 1964, Elements of Optical Mineralogy, Part II, John Wiley & Sons, New York.

Optical Properties of Kaolinite and Chrysotile

Kaolinite

Kaolinite is a 7A layer-silicate with the formula $Al_4(OH)_8Si_4O_{10}$. The composition is subject to little variation but water adsorbed between the layers affects the optical properties.

<u>Nx</u>	<u>Ny</u>	<u>Nz</u>	<u>Extinction</u>	<u>Elongation</u>
1.560	1.565	1.566	Parallel	Positive
1.553-1.563	1.559-1.569	1.560-1.570	or Inclined	
*1.562	1.566	1.568	1-3°	
*1.553-1.565	1.559-1.569	1.560-1.570		
**1.553-1.563	--	1.560-1.570		
(more water)				
1.526		1.543		

Chrysotile

1.542	1.543	1.55	Parallel	Positive
***1.493	1.504	1.517		
***1.508	1.512	1.522		
***1.528-1.559	1.530-1.564	1.537-1.567		
***1.53-1.54		1.54-1.55		
***1.542		1.555		
***1.542	1.543 (calc.)	1.555		

<u>Nx</u>	<u>Ny</u>	<u>Nz</u>	<u>Extinction</u>	<u>Elongation</u>
***1.546	1.550	1.557		
***1.546	1.557	1.557		
***1.548	1.560	1.560		

Data from:

N. Winchell and Horace Winchell, (1964), Elements of Optical Mineralogy, John Wiley & Sons, Inc., New York.

*W.A. Deer, R.A. Howie, and J. Zussman, 1965, Rock-Forming Minerals, Longmans, London.

**Ralph E. Grim, 1968, Clay Mineralogy, McGraw-Hill Book Co., New York.

***Federal Register, Vol. 38, No. 188.

INVESTIGATION OF THE WINTERBORO TALC DEPOSITS,
TALLADEGA COUNTY, ALA.

by

Avery H. Reed, Jr. 1/

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1/ Mining engineer, Bureau of Mines, Tuscaloosa Branch.

Report of Investigations 4661

CHARACTER OF THE ORE

The talc is not homogeneous for any area nor for any sample. In general, the deposits consist of massive talc that contains varying amounts of red or yellow clay intimately mixed with it. An average section through the deposit shows, from the surface down, red and yellow clay, red and yellow clay with fragments of talc, talc with red or yellow clay, relatively pure talc, brown clay, and dolomite. These units are gradational, with no sharp contacts to distinguish them; the contact between talc with clay and relatively pure talc is especially irregular.

The talc is quite soft and is intensely fractured. None of it appears to be suitable for crayons or other uses that require strength. The talc from the south deposit is harder and less fractured than that from the north deposit.

The talc ranges in color from white and cream to yellow, gray, and blue. No appreciable amount of white talc is present, and an average sample from any large area grinds to a light cream color. The specific gravity of a representative sample of the north deposit was determined as 2.63, crushed and dried, by B. H. Clemmons, metallurgist, Southern Experiment Station, Tuscaloosa, Ala.

Few minerals other than talc and clay minerals are present. Occasional quartz stringers and limonite grains are found, especially near the edges of the deposits.

SAMPLING AND ANALYSIS

Overburden was fishtailed and carefully logged; when fragments of talc were found, coring was started immediately and continued through the talc section. Holes with low talc recovery were redrilled.

Cores that contained talc from holes that showed 5 feet or more of talc were carefully cleaned and analyzed for talc, Fe_2O_3 , Al_2O_3 , and CaO . Sample intervals from the cores were selected so as to determine the maximum amount of high-grade talc present in each core.

Talc cores from holes that showed less than 5 feet of talc or from isolated situations were not analyzed. The talc from these holes was generally low-grade and thoroughly mixed with clay.

Twenty-seven samples from 12 holes were assayed. Of the 75 holes drilled, 41 penetrated talc or talc fragments.

WORK DONE BY THE BUREAU OF MINES

The Bureau of Mines investigated the Winterboro talc deposits by drilling 75 holes totaling 3370.4 feet.

Holes were drilled within and around the two known deposits, and within the area between these deposits.

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1941

LETTER OF TRANSMITTAL

University, Alabama

March 25, 1941

Honorable Frank M. Dixon,

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Sir:

I have the honor to transmit herewith the manuscript of a report entitled "The Talc Deposits of Talladega County, Alabama" by Lynn McMurray of the Tennessee Valley Authority and Edgar Bowles of the Geological Survey of Alabama. It is requested that this be printed as Circular Number 16 of the Geological Survey of Alabama.

Respectfully,

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BENEFICIATION OF TALC ORE FROM TALLADEGA COUNTY

INTRODUCTION

This report deals with laboratory tests which were made on a talc ore from Talladega County, Alabama. These tests were in connection with an investigation of talc ores in the Tennessee Valley and nearby region in an attempt to prepare products which could be used in the ceramic, textile, paper, cosmetic, and other industries requiring a high grade talc. Initial investigations showed that only some of these ores were amenable to beneficiation methods. The beneficiation methods which proved most applicable were froth flotation and acid leaching. Many of the talc ores were found to contain appreciable percentages of serpentine and chlorite, which prevented them from becoming white on acid leaching. The acid leaching removes only the soluble iron from the ore. All of the talc ores, however, could be froth floated to a high purity, but only those which could be acid leached were suitable for refinement to high quality products.

As the Talladega County deposit could be acid leached, it appeared that a laboratory investigation toward the development of a suitable flowsheet would be well warranted.

CHARACTER OF THE ORE

Three samples, totaling 600 pounds, were taken from the deposit so that a reasonable accurate cross-section of the ore body was obtained. The mineralogical and chemical analyses of these samples, shown in Table I, indicate the rather uniform character of the ore body.

TABLE I

Chemical Analysis of Talc Ore from Talladega County, Alabama

Sample						Loss at
No.	MgO	SiO ₂	Fe ₂ O ₃	Al ₂ O ₃	CaO	900° C
1 —	31.25	61.74	1.60	0.50	0.22	4.84
2 —	29.12	60.78	2.12	1.98	0.42	5.41
			Fe ₂ O ₃ , Al ₂ O ₃ , CaO			
3 —	31.05	62.50		1.80		3.75

Mineralogical Analysis of Composite Samples Shown Above

Sample					
No.	Talc	Garnet	Quartz	Iron Oxide	Clay, etc.
Composite (1, 2, and 3)	93%	2%	2%	2%	1%

The talc as it occurs is surprisingly pure, but the presence of small amounts of garnet, quartz, and iron oxide prevents its use as a high grade talc product.

A physical study of the talc ore reveals that the garnet is liberated at 100 mesh and the quartz at a much coarser sizing. The iron occurs in streaks, pockets, and coating on the crude ore lumps. Grinding to 200 mesh is required to liberate this iron so that it will come in contact with the acid during leaching. As essentially all talc products require grinding to minus 200 mesh or less, this offers no additional treatment over that already necessary for marketable products. No serpentine or chlorite or dark colored minerals, other than garnet and iron oxide, occur in the ore.

BENEFICIATION TESTS

The froth flotation problem was the separation of the garnet from the talc. The quartz and appreciable amounts of the iron oxide could be easily depressed in the flotation cell. With any reagent combination used, a small amount of garnet contaminated the concentrates. In the laboratory garnet was removed by a magnetic separator, but the necessary fineness and dry condition are against such treatment in commercial practice. The garnet is