The Cosmetic, Toiletry and Fragrance Association, Inc.

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December 26, 1973

Hearing Clerk
Food & Drug Administration
Department of Health,
Education and Welfare
Room 6-86
5600 Fishers Lane
Rockville, MD 20852

Re: Proposed Order Method for Asbestos in Talc Published in the Federal Register (38 F.R., No. 188, pgs. 27076-27081) September 28, 1973

Dear Sir:

This letter and attachment is being submitted in response to the proposal published on September 28, 1973 (Federal Register, Vol. 38, No. 188, pages 27076-27081) in which a method is proposed for the determination of asbestos particles in food and drugs. The comments are being submitted on behalf of The Cosmetic, Toiletry and Fragrance Association, Inc., a national association representing manufacturers and packers of cosmetic products as well as the manufacturers and vendors of cosmetic product ingredients and supplies. Members of the Association manufacture approximately 85% of the cosmetic products distributed in the United States. While the Association is not directly affected by the Federal Register Proposal cited above, one of its scientific subcommittees, the CTFA Talc Subcommittee, has completed a critical review of the optical microscopic method published in this proposal. In the belief that this review is revelant for your consideration of this proposal, the report of the CTFA Talc Subcommittee, dated December 10, 1973. is attached as part of this submission.

As a result of round robin testing of five different types of talc, by members of the CTFA Talc Subcommittee, the subcommittee concluded that the proposed method does not provide a reliable means for the detection of asbestos in talc and that it results in both

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false-positive and false-negative findings. The procedure is also tedious and may consume as much time as one-half day per sample. The subcommittee has also reviewed several alternative methods to detect chrysotile and tremolite in talc including modifications of the optical microscopic method. As a result of its review the subcommittee feels confident that a feasible method can be developed, and recommends a collaborative effort between FDA and industry to develop such a method.

The questions concerning asbestos detection and the relationship of asbestos to human health are indeed complex ones. At a conference last month, sponsored by the National Institute of Environmental Health Sciences and the Environmental Protection Agency, three serious difficulties in determining the effects of asbestos on human health were presented:

1. "The term asbestos itself is misleading, for it encompasses a whole group of minerals that are distinct from each other in chemical composition, particle size, and probably biological effect.

2. Many of these particles are so small that detection is extremely difficult and time consuming, placing restraints on the scope of research that can be reasonably undertaken.

3. Perhaps the most serious difficulty in asbestos research, however, is the very long period between initial exposure and evidence of biological effects."(1)

Other points made at this Government sponsored meeting that merit consideration were:

1. Chrysotile fibers are too small to be detected by conventional optical microscopy.

2. Amphibole asbestos fibers are larger. But they also require sublight microscopes for careful examination and cannot be positively identified without additional microchemical or selective area diffraction analysis.

3. A question yet to be answered is the effect of low-level exposure to asbestos on the general population.

4. Dr. Ian Webster of the National Institute for Occupational Diseases in Johannesburg, Republic of South Africa, reported at the conference that very little ingested asbestos penetrates the walls of the stomach and colon and that almost all that does is of the smaller chrysotile type.

(1) Chemical & Engineering News, December 10, 1973, pages 18-19.

Similarly, studies with inhaled asbestos also show that the fiber is absorbed is predominately the chrysotile type.

5. Dr. William Eisenberg of the Food and Drug Administration was quoted as stating that "at present, analysis by polarized light microscopy is used to determine purity of food and drugs, even though this method probably misses many of the smaller and more easily absorbed asbestos fibers that may be present in these materials."

In light of the perplexing questions raised at this conference, the Association considers it premature for FDA to impose its proposed optical method and place a limit on asbestos in talc for food use.

The CTFA urges deferment of promulgation of the proposal until:

1. Determination of the standard deviation of the proposed compliance test method.

2. Evaluation of the validity of the assumption that a single milligram sample can be taken as statistically representative of any lot as well as the limit size of any lot so sampled.

3. A re-evaluation of the economic cost and practicality of the proposed Compliance Test Methods.

4. An intensive search is undertaken for an alternate procedure that is more reliable and more practical than the proposed test methods.

The Cosmetic, Toiletry and Fragrance Association, Inc., stands ready to assist the Food and Drug Administration in method development research as well as to provide assistance in other areas discussed above where as its scientific expertise may be of value.

Cordially,

Norman F. Estrin, Ph.D.
Vice President - Science

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Attachment

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REPORT OF CTFA TALC SUBCOMMITTEE ON METHOD TO DETECT CHRYSOTILE AND TREMOLITE IN TALC.

December 10, 1973

The Scientific Advisory Committee of the Cosmetic, Toiletry & Fragrance Association, 1625 Eye Street, N.W., Washington, D.C. 20006 at a meeting held on September 2, 1973, designated that a subcommittee be set up to study the optical microscopic method proposed by the Food and Drug Administration. This method was published in the Federal Register of September 28, 1973. The present membership of the CTFA Talc Subcommittee is shown on an attached sheet.

At the first meeting of the Subcommittee, it was agreed to submit several samples of talc to members who volunteered to apply the FDA proposed optical microscopic method. The following talc samples were distributed without identification - except for randomly applied and non-duplicated code numbers:

Italian Talc	
Montana Talc	
Montana Talc	Source I
Vermont Talc	Source II
Alabama Talc	
No. Carolina Talc	

In addition, a sample of Italian Talc spiked w/w with 1% chrysotile and 0.15% tremolite was sent to each participant. The participants were aware that the sample was spiked, but did not know the percentage of spiking.

The attached table summarizes all reports submitted:

Final Report

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Sample	No. of Fibers With R.I. Greater Than 1590	No. of Fibers With R.I. Less Than 1574	Status With Regard to Proposed FDA Method
Dr. John A. Reffner (U. of Conn.) for Avon Cont'd			
Montana-I	0	5,844	Fails chrysotile Passes tremolite
Montana-II	13	9,281	Fails chrysotile Passes tremolite
Alabama	26	15,125	Fails chrysotile Passes tremolite
Vermont	41	165	Fails chrysotile Passes tremolite
No. Carolina	14	11,852	Fails chrysotile Passes tremolite
Dr. Tryggve Baak of United Sierra			
Spiked	3,000	2,000	Fails
Italian	1,000	0	Passes
Montana-I	0	0	Passes
Montana-II	0	0	Passes
Alabama	0	0	Passes
Vermont	0	0	Passes
No. Carolina	500	0	Passes
(b) (4) for Whittaker C&D			
Italian	8,250	1,350	Fails chrysotile & tremol
Montana-I	18,000	450	Fails chrysotile & tremol
Montana-II	29,250	5,200	Fails chrysotile & tremol
Alabama	21,825	6,075	Fails chrysotile & tremol
Vermont	3,225	675	Fails chrysotile & tremol
No. Carolina	20,850	6,000	Fails chrysotile & tremol

Spiked sample was not run.

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Sample	No. of Fibers With R.I. Greater Than 1590	No. of Fibers With R.I. Less Than 1574	Status With Regard to Proposed FDA Method
Mrs. Lucy McCrone, McCrone Associates for Chesebrough			
Spiked	320	16	Passes
Italian	120	0	Passes
Montana- I	0	0	Passes
Alabama	0	0	Passes
Vermont	0	0	Passes
No.Carolina	0	0	Passes
Montana- II	0	0	Passes
Mr. Harold Stanley of Pfizer			
Italian	~100	>100	Fails Chrysotile Passes tremolite
Montana- I	~100	>100	Fails Chrysotile Passes tremolite
Montana- II	~100	>100	Fails Chrysotile Passes tremolite
Alabama	~100	>100	Fails Chrysotile Passes tremolite
Vermont	~100	>100	Fails Chrysotile Passes tremolite
No. Carolina	~100	>100	Fails Chrysotile Passes tremolite
Spiked	<1000	>100	Fails Chrysotile Passes tremolite
Mr. David Hamer of Johnson & Johnson			
Italian	0	0	Passes
Montana- I	1	0	Passes
Montana- II	25	0	Passes
Alabama	0	0	Passes
Vermont	0	0	Passes
No. Carolina	0	0	Passes
Dr. John A. Reffner (U. of Conn.) for Avon			
Spiked	632	12,930	Fails Chrysotile Passes Tremolite
Italian	220	1,114	Fails Chrysotile Passes Tremolite

Sample	No. of Fibers With R.I. Greater Than 1590	No. of Fibers With R.I. Less Than 1574	Status With Regard to Proposed FDA Method
	(b)(4)		for Kolmar (b)(4)
Italian	53	0	Passes
Montana-I	0	0	Passes
Montana-II	0	0	Passes
Alabama	0	0	Passes
Vermont	0	0	Passes
*No. Carolina	0	0	Passes
Spiked Sample	488	16	Passes

*Sample noted to contain some fiber bundles which are rolled up talc plus some non-fibrous tremolite

The following participants examined their samples but were unable conscientiously to count particles with confidence, therefore, did not report numbers:

Miss Marie Jones for Dr. G. Cohen - Bristol-Myers Products Research Labs.
Mr. Salvatore DiBianca - The Mennen Company
(b)(4) (b)(4), Research Center - for Kolmar Laboratories
Mr. John Facq - The Colgate Palmolive Company, Research Center

The table reveals strong inconsistency between results obtained by the different scientists applying the method to the same group of coded talc samples. This inconsistency is the result of problems encountered in the methodology.

1. The alpha refractive index of talc - one of the two indices exhibited by talc plates standing on edge - varies in value between 1.539 and 1.550[1]. This in combination with item 2, below, may easily result in the mis-classification of such plates as "fibrous, less than 1.574" and therefore chrysotile.

   Dr. Reffner of the University of Connecticut, in his report to Avon, admits that this factor is paramount - "counts for chrysotile are high since (talc) edges will often be mistaken for fibrous particles".

2. The immersion method for the determination of relative refractive index becomes unreliable when applied to extremely small (ca. 1 μm) particles. This is due in part to the fact that particles around 1 μm in width approach the limit of resolution of the human eye when both size and contrast are considered, especially when applying the Becke line technique prescribed. This will

2. cause eye fatigue and resulting errors. Thus, a fine talc shard or plate on edge may be easily mistaken for an asbestos fiber. This applies to both the chrysotile and amphibole portions of the test.

3. It is quite likely that chlorite - a mineral of varied composition commonly found in pharmaceutical grade talc - would be incorrectly identified as tremolite. Refractive indices for chlorite vary in the range 1.57-1.66[2].

4. The examination of a sample of one milligram dispersed on a single microscope slide presents the investigator with a preparation which is too dense for a petrographic study.

5. The method is laborious and time consuming. Dr. Reffner quotes an analysis time of about five hours per sample and at JOHNSON & JOHNSON the investigator (D. H. Hamer) estimated at least two or three hours.

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6. (b) (4) in an earlier letter to the FDA suggested that there were relatively few scientists in the country who could use the method effectively. Scientists at Bristol-Myers, The Mennen Company, Liberty Mutual and Colgate-Palmolive had great difficulty in following the method to conclusion.

7. The proposed FDA method implies that all fibrous particles in talc having optical properties similar to those of asbestos minerals are in fact asbestos. This is probably an unwarranted assumption.

REFERENCES:

1. Deer, W.A., Howie, R.A., and Zussman, J., Rock-Forming Minerals, Vol. 3, p. 121 (1962).

2. Ibid, p. 131.

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We have concluded that the method published in the Federal Register does not provide a truly reliable means for the detection of asbestos in talc. It results in both false-positive and false-negative findings. It is also tedious and may consume as much as one half day per sample.

The subcommittee urges that the Food and Drug Administration defer finalizing the proposed optical microscopic method and proceed into a Phase II program which would combine FDA and Industry in a strong effort to develop a truly reliable method for measuring chrysotile content in talc. We are confident that the detection and estimation of fibrous tremolite can also be done, if necessary, as a fringe benefit, at the same time.

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We estimate that a satisfactory method will take at least six months to a year to develop. We suggest a close liaison between FDA and industry in this all-out effort with updating reviews to take place as frequently as necessary.

Review of Alternate Methods

The CTFA Talc Subcommittee has reviewed several methods to detect chrysotile and tremolite in talc, including modifications of the optical microscopic method. These are listed with comments.

1. Optical Microscopic Method - may be used with some modification. Possibly better selection of R.I. liquids and reduction of sample size per slide.

2. X-ray Step Scanning - A good method for detecting tremolite if we could accept about 0.2% as the threshold of detection. It does not distinguish fibrous from non-fibrous tremolite. The simultaneous detection of chlorite makes method impractical for chrysotile. $50M 1 lab

3. X-Ray Step Scanning + Optical Microscopy - Acceptable as in #2 above but the optical method continues to present the dilemma in reliable identification of chrysotile. However, this does not rule out a major revision of the optical method to do the chrysotile identification and counting.

4. X-Ray Scanning - The problem of chlorite interference in the detection of chrysotile is present in all x-ray procedures thus far available. It is reliable for the detection of 1% tremolite (both fibrous and non-fibrous).

5. Differential Thermal Analysis - This procedure is capable of detecting chrysotile at the 1% level, however, it will not detect tremolite. $20! 45K

6. Scanning Electron Microscopy - This procedure is not capable of identifying asbestos. Even with energy dispersive analysis, completely satisfactory identification is not possible.

7. Transmission Electron Microscopy + Electron Diffraction - This appears to offer the best, most reliable method and is probably capable of detecting chrysotile and tremolite (fibrous), both at a level of 0.1%. It is estimated that an installation would cost about $130M +, and is obviously prohibitive for the small manufacturer who uses talc. The amount of talc sample examined by this procedure is miniscule.

Summary

The CTFA Talc Subcommittee has completed its review of the Optical Microscopic Method for the Estimation of Chrysotile and Fibrous Tremolite in Talc, which appeared in the Federal Register, vol. 38 (No. 188),(p. 27076, September 28, 1973). It recommends postponement of the finalization of the proposed regulation on talc. In addition, a collaborative effort between FDA & industry to resolve a satisfactory method of estimating chrysotile and tremolite in talc, is recommended, with periodic liaison reviews to monitor the project status. A task force of industry experts has been designated to pursue alternate methods. We invite FDA to participate in collaboration with the task force.

George W. Sandland
Chairman CTFA Talc Subcommittee

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