SUMMARY MINUTES OF THE OTC PANEL ON
ANTIPERSPIRANT DRUG PRODUCTS

Twelfth Meeting
July 9 and 10, 1975

Parklawn Building
5600 Fishers Lane, Rockville, MD 20852

PANEL MEMBERS

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CTFA REPRESENTATIVES

G. Hildick-Smith, M.D. - Director, Medical Affairs, Johnson & Johnson
F. Pooley, Ph.D. - Department of Mineral Exploitation, University College Cardiff, Wales, U.K.
F. R. Rolle, Ph.D. - Assistant Manager of Analytical Research, Johnson & Johnson
G. Lord, D.V.M., Ph.D. - Director, Johnson & Johnson Research Foundation
A. Wenner, D.M.D. - Biology Department Battelle Pacific Northwest Laboratories
R. Wulf, Ph.D. - Assistant Research Director, Carter Products Research, Carter Wallace, Inc.
W. E. Smith, M.D. - Director, Health Research Institute, Fairleigh Dickinson University

Decisions reported herein are provisional in nature and may be modified or revised in subsequent meetings of the Panel or in their final complete report to the Commissioner.

Whenever there is a lack of unanimity on any given point, the vote will be given. Regulations do not permit voting by the Liaison Members, Consultants, or FDA Staff Members.

Adopted August 15 1975

Lee Goldman for

Chairman
E. William Rosenberg, M.D.

SUMMARY MINUTES

The OTC Antiperspirant Panel met in the Parklawn Building on July 9 and 10, 1975. Drs. Shefter and Clayton were unable to attend the meeting.

Open Session:

An extensive open session was held to discuss the identification and toxicity of talc. Talc and starch are used in the formulation of aerosolized antiperspirants. The Cosmetic Toiletries, Frangrance Association made an industry presentation. Dr. Albert Miller of Mount Sinai Hospital was present as an expert invited by the Panel to discuss the presentation made by the industry group and to discuss his own work as part of a group at Mount Sinai doing research in Environmental Health and Safety.

CTFA Presentation

Dr. Gavin Hildick-Smith of Johnson and Johnson served as coordinator for the presentation and introduced the speakers. He told the Panel that the subject is complex and hoped that the presentation would better help them to understand the distinctions in the types of talc used in cosmetic products.

Dr. Pooley's Presentation

Dr. Pooley was present as an expert consultant to the CTFA group. He is from the Deptartment of Mineral Exploitation, University College, Cardiff, Wales, U.K. He spoke on the mineralogy of talc. He listed some of the minerals found in talc, expecially the asbestos minerals, which are the point of concern for the Panel.

There are two groups of asbestos minerals: 1) The serpentine group and 2) The amphibole group. The serpentine group contain a mineral called chrysotile and the amphibole group contains minerals such as crocidolite, amosite, anthophyllite, tremolite, and actinolite. Talc powder refers to an industrially used material which contains from 40 to 95 percent by weight of talc mineral. The talc mineral itself is sheet silicate. In pure talc there is 31.7 percent magnesium oxide, 63.5 percent silicon dioxide and 4.8 percent water, by weight.

Dr. Pooley described the formation of talc and pointed out that often there are intrusions of other minerals into the talc site. The minerological composition of talc, including the mineral fibrous (asbestiform) and non-fibrous (non-

asbestiform), depends on the geological formations present at the source of the talc. Cosmetic grade talc (platy talc) normally contains 90 percent talc with the contaminates being carbonate and chlorite minerals.

Dr. Miller questioned Dr. Pooley about the asbestiform content of the cosmetic talc that he had analyzed. Dr. Pooley said that he had found no chrysotile in about 40 samples from different sources. There was detectible amounts of tremolite in a few samples.

Dr. Miller commented that he believed analysis on the finished product rather than the talc at the source would provide more information about possible risk to the consumer.

Some questions concerning the adequacy of types of analysis of talc components were deferred until after Dr. Rolle's presentation.

Dr. Rolle's Presentation

Dr. Rolle of Johnson and Johnson reiterated some points about content of talc to distinguish industrial and cosmetic

talc. Because of allegations that talc contained asbestos, a CTFA task force was formed on the methodology for identifying asbestos in talc. The committee decided that the method for determining fibrous and non-fibrous content must be specified, have definable detection limits and must be reproducible with criteria for pass or fail for a sample.

A critical element is the definition of a fiber. Dr. Rolle read the definition of the Department of Labor, Occupational Safety and Health Administration as: "must appear to be fibrous rather than crystals or slivers, the maximum diameter of a fiber to be counted is 3 microns, the minimum length of a fiber to be counted is 30 microns, the length to width ratio is 5 or more to one."

After examining procedures such as scanning electron microscopy, infra-red and optical microscopy, the Task force selected x-ray diffraction with a detection limit of 0.5 percent. If amphibole particles are present, the fibrous material is examined by optical microscopy and dispersion staining. If it is detected as a fibrous amphibole, the talc fails.

The Task force selected differential thermal analysis (DTA) as the procedure for identifying chrysotile.

Dr. Miller commented on Dr. Rolle's talk. He said that the medical profession and the consumer are interested not only in chrysolite but in any amphibole fraction. He felt that x-ray diffraction was a less sensitive method than scanning electron microscopy. Dr. Miller quoted a standard for asbestos in industrial sources from the Western Health Industrial Conference. This source stated that no level of asbestos minerals should be developed as a standard when considering carcinogenic effects. If this goal were accepted, the goal would be no asbestiform particles.

Dr. Rolle in commenting on the mineral contamination of talc said that it is incorporated as an integral part, deep in the lattice structure of the talc and in that position is inert and does not come out.

Presentation by Dr. Hildick-Smith

The long and widespread use of talc in cosmetic products was reviewed. In the publications concerning talc there is

frequently no description of the type of talc used and it is therefore difficult to assess the activity of cosmetic grade talc. Published articles relate to three areas:

1. Industrial health. Reports of miners health after prolonged exposure to high levels of mineral, often containing asbestos.
2. Accidental suffocation. Pulmonary insult occuring often as a result of spilling large amounts of powder on the the face of an infant or child.
3. Misuse or excessive exposure. Reports of individuals who have overused products.

Talc has been shown not to be an allergen. In in vitro tissue culture studies, various mineral dusts produced a fibroblastic response while cosmetic talc produced no change. In a study of pulmonary macrophage function, no attenuation in function was noted with cosmetic talc.

Presentation by Dr. Wehner

Dr. Wehner is with the Batelle Pacific Northwest Laboratories. He described an animal study in hamsters with talc in which the exposed animals were allowed to live out

their life span. Hamsters were exposed for 30 days to simulate the talc exposure of human infants since this period would correspond to the infant life of the hamster. Another group was exposed for 300 days which was considered equivalent in the hamster to the life span of a woman through her child-bearing years. The hamster was chosen because it was shown to be an appropriate animal for testing potential carcinogens. No adverse effects from the talc were found in the treated animals. Both test and control animals showed these random pathological effects on necropsy.

Dr. Wehner was asked about concentration procedures in order to increase the detection limit of asbestiform particles.

Presentation by Dr. Wulf

Dr. Wulf of Carter Products described inhalation tests with a product made by them containing talc, Light Powder Arrid Antiperspirant. The product contains 0.75 percent Italian talc. A 90-day subacute aerosol inhalation test in rats was performed in which animals were exposed to a 30-second burst follow by 15-minute exposure to the resulting

aerosol for 5 day/week for 13 weeks (130 exposures). No adverse effects were seen in control or test animals. A second similar test was run in monkeys with the exposure concentration estimated as 10 times higher than in the rat study. Lung function studies were performed on the monkeys. No adverse effects attributable to the product were noted.

Dr. Miller noted that from the history of delay of the onset of adverse pulmonary function effects in industrial workers, it would be unlikely to see function changes in monkeys in 90 days.

Presentation by Dr. Smith

Dr. A. E. Smith of Health Research Institute of Farleigh Dickinson University described feeding studies in hamsters. He gave hamsters asbestiform minerals in their feed. Varying incidence of tumors (mesotheliomas) were observed in animals at 25 and 10 mg with the four major forms of asbestiform minerals. Different minerals showed effects at varying dose levels. Dr. Smith found no tumors in animals dosed with tremolite talc. The talc used in the

test was industrial talc. When the chrysotile was reduced to submicroscopic particles and tested in the hamsters, no turmors were found.

Presentation by Dr. Hildick-Smith

Dr. Hildick-Smith described a study designed to examine talc mine workers to determine if their cause of death is different from a similar control population. Deaths for all types of carcinogenesis, overall deaths and respiratory diseases were compared. Respiratory disease deaths were increased among miners. This study was performed by Professor Rubino, of Italy, and presented at the meeting of the American Occupational Medical Association, Turin Italy, Oct. 7, 1974.

Dr. Miller pointed out some problems in epidemiologic studies when this type of worker population is selected. He felt that the death certificate might not be a reliable source of information on the cause of death because they would be a poor source of such information in this setting and would, in the time period studied, be unreliable.

Dr. Hildick-Smith summarized the conclusions which can be drawn from the information presented by the CTFA Group.

Presentation by Dr. Miller

Dr. Miller of Mount Sinai Hospital discussed his own work and his view of the earlier presentations. He described his interest in the content of talc and the epidemiology of any disease caused by it. Dr. Miller questioned the distinction between cosmetic and industrial talc as it is now made. He thought that perhaps this did not necessarily apply to the cosmetic talcs in wide use in the past as far as analysis of asbestos content. Dr. Miller quoted work by Dr. Arthur Langer of Mount Sinai Hospital in which he analyzed 50 commerical cosmetic powders by various methods including electron microscopy. He did find several powders with up to 30 percent quartz. One powder showed 30 percent anthophyllite and tremolite, which are asbestiform fibers. He emphasized that he thought it was important to analyze the product from the shelf rather than at the source in the mine. Dr. Miller quoted a study by Schepers and Durkan in the Archives of Industrial Health (12:182-197, 1955), in which inflamatory response was found in animals insufflated with true talc. He described another study by Kleinfeld et al. (Environmental Research 6:132-143) at the New York Department of Health in which changes in pulmonary function

were seen in workers exposed to both fibrous and granular talc. The exact means of differentiation of the talc was not detailed. Dr. Miller referred to several cases where pneumoconiosis or other lung effects were reported in patients who had excessive exposures to talc in work situations or with overuse.

The difficulties in identifying fibrous particles by some of the methods used in the references cited by Dr. Miller were discussed following Dr. Miller's summary.

Closed Sessions:

Discussion of Toxicity of Talc in Aerosolized Antiperspirants

The Panel reviewed the presentations by CTFA and Dr. Miller. The Panel urged that further work be undertaken to set limits for asbestiform fibers and to reduce the limit of detection to as low as possible from the presently accepted 0.5 percent. The Panel accepted that there is virtually no risk from asbestos in aerosolized talc in the amounts found in antiperspirants if the material is determined to

be cosmetic talc free of asbestiform fibers, determined by the CTFA procedure. This procedure should pertain until more sensitive analytical techniques are available. They concluded that the use of talc in antiperspirants constituted only a small portion of the potential problem with talc in the environment in view of the much larger experience accompanying the use of baby powders. They felt this exposure to talc would not constitute a hazard. The Panel did not consider the safety of talc in products other than antiperspirants.

Efficacy Discussion:

The Panel made a general plan of work still remaining to be done.

One large portion of the review still remaining is the review of effectiveness testing procedures.

The necessity for tests, type of tests and the procedures for interpreting them were discussed.

Some Panel members thought that most test results showed a reduction of perspiration fell in a range between 20

and 40 percent based on the OTC submissions. The type of test to be run and the subsequent use of the results in making comparative labeling claims were discussed.

The difficulties in testing the effectiveness of active ingredients when they are influenced by formulation in products was discussed.

Mr. Pinco of the OTC staff discussed the scope of the regulations which apply to review of the ingredients rather than products. The Panel discussed the problem of attempting to determine the efficacy of antiperspirants without testing them in product form. No final decisions were made but general ideas of Panel members concerning effectiveness were expressed and reviewed.

The differences in the results obtained in hot room testing and in in-use testing and the possible ways of interpreting them were outlined. The use of a highly selected population in one case was contrasted to the use situation in the wide-ranging population who use the product daily.

The possibility of developing a test with specifications and criteria for interpretation which would determine whether a specific product met a minimum effectiveness level was raised.

The Panel agreed to request through their industry liaison member that industry present their various procedures for testing and analysis of the test results at the next Panel meeting. Some of the pertinent details to be discussed are the degree of reduction in hot room tests and its relation to effectiveness, type of analysis of results, number of subjects, controls, use-tests, and label claims. The idea that antiperspirants may not be effective at all will be raised.

The August meeting to discuss effectiveness is scheduled for August 14 - 15, 1975 and a meeting is scheduled for September 18 - 19, 1975 at the Parklawn Building.

Prepared by:

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Executive Secretary