DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Sanford A. Miller, Ph.D.
Director, Bureau of Foods, HFF-1

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Taylor M. Quinn
Associate Director for Compliance, HFF-300

Status Report On Talc

Attached is a report that summarizes the current state of our knowledge concerning talc contaminated with asbestos. This update was requested by Dr. Armand Casola of the Bureau of Drugs.

Asbestos fibers inhaled in large amounts have been determined to cause cancer. Talc, used as a component of baby powder and other cosmetics, has not been shown to cause the health effects associated with the inhalation of asbestos. Additionally, aside from the noted increase in gastrointestinal cancer associated with occupational exposure to asbestos, there is no evidence that the ingestion of small amounts of asbestos found in food and water poses any health risk to man.

The last agency action concerning talc and asbestos restricted the utilization of asbestos filters in the manufacture of parenteral drugs and parenteral drug ingredients. Additionally, it delayed the finalization of the establishment of good manufacturing practice limitations for talc used in foods and drugs pending the development of adequate methodology for the determination of asbestos in talc and foods, and the resolution of the questions concerning the ingestion of asbestos.

Several recent studies indicate that talc itself does not present a hazard when inhaled. There are several ongoing asbestos feeding studies and an inhalation study on talc that have been designed to address these questions. Additionally, progress is being made in the development of analytical methodology for the separation and determination of asbestos in foods, drugs and talc. Further action awaits the outcome of these studies.

The problem areas that need resolution prior to any further agency action with regard to talc include:

(1) The contribution of the concentration, fiber geometry and chemical composition of the fibers to the production of disease in relation to both the inhalation and ingestion of asbestos must be defined.

(2) The potential for the production of cancer and other diseases by the ingestion of asbestos must be determined.

(4) The levels of occurrence of asbestos in foods above background levels must be determined.

(5) Problems of separation of asbestos from the food matrix must be resolved.

Attachment

(b) (5)

INTRODUCTION

Talc is GRAS for use in food-packaging materials, in dietary supplements and in chewing gum, is a prior-sanctioned food ingredient for use in coating polished rice, is allowed for use as an antisticking agent in forms used in molding various food shapes, and is regulated for use as a pigment and colorant under several indirect food additive regulations. Talc, however, has been shown to be contaminated with asbestos.

Documented evidence reveals that airborne asbestos fibers are related to human disease, specifically pulmonary fibrosis, carcinoma, and pleural mesothelioma. Quantification of health risks associated with specific airborne concentrations, fiber dimensions and chemical composition of the fibers, however, is inexact. The problem of estimating the magnitude of this risk to human health is further complicated by the 20-to-40-year latency period between exposure and the appearance of disease.

Additionally, the inhalation effects of asbestos raise questions about the ingestion of talc contaminated with asbestos. Because of the ubiquitous nature of asbestos, the known health hazard from inhalation exposure, and the possible hazard from ingestion, it is necessary to reduce exposure to this contaminant wherever possible. The following is an update of the steps taken by the Bureau of Foods towards the development of a regulatory policy regarding talc contaminated with asbestos.

BACKGROUND

Regulatory Status

FOOD - On September 23, 1973, the FDA proposed to restrict the utilization of asbestos filters in the manufacture of parenteral drugs and parenteral drug ingredients and to establish good manufacturing practice limitations for asbestos-contaminated talc used directly as a food or drug ingredient, or in food and drug packaging materials, within certain analytical restrictions. The finalization of this proposal in regard to talc had to be delayed (40FR11865) pending the development of a suitable method for determining the presence of asbestos in talc. However, the restriction on the use of asbestos filters in drug preparation was finalized.

At the present time, talc is generally recognized as safe under §182.70 as a substance migrating to food from cotton and cotton fabrics used in dry food packaging, and under §182.90 as a substance migrating to food from paper and paperboard products. Talc is a prior-sanctioned food ingredient for use in coating polished rice. FDA opinion letters to trade associations have stated general recognition of safety of talc for use in dietary supplements and in chewing gum when the talc meets the specifications of the U.S. Pharmacopoeia. Talc is also cleared for use as a pigment and colorant under §§175.300, 175.380, 175.390, 176.170, 177.1210, 177.1350, and 177.1460. Another opinion letter allowed for the use of talc as an antisticking agent in forms used in molding various food shapes.

COSMETICS - There are no regulations concerning the use of talc as an ingredient in cosmetic products.

Under current law the burden of proof that a cosmetic may be harmful in that it contains a harmful substance rests with FDA. FDA must have data or other information demonstrating that a product contains a poisonous or deleterious substance that is harmful under customary conditions of use before any action can be taken either to restrict or prohibit the use of an ingredient or product.

Summary of Health Effects

INHALATION - Asbestos fibers are known to cause cancer when inhaled in large amounts. Occupational exposures to asbestos have been found to induce asbestosis and mesothelioma of the pleura and peritoneum as well as cancer of the lung, esophagus, and stomach, after latent periods of 20 to 40 years. From FDA's standpoint, the major inhalation problem of exposure is that due to fibrous asbestos-contaminated cosmetic talc (baby powder).

INGESTION - Because of the recognition of disease problems associated with occupational exposures to asbestos, questions were raised about the ingestion of this material as a contaminant of talc. To date, there are no satisfactory answers to these questions.

UPDATE OF INFORMATION

Toxicological Studies

Completed studies - Inhalation

(1) - Inhalation of Talc Baby Powder by Hamsters. Wehner, A.R., Zwicker, G.M., Cannon, W.C., Watson, C.R., and Carlton, W.W. Fd. Cosmet. Toxicol. 15:121, 1977.

The talc used was cosmetic-grade with no asbestos fibers found; exposure to talc aerosol had no effect on body weight, survival, or type, incidence or degree of histopathological change in exposed compared to sham-exposed controls.

(2) - Pulmonary Deposition, Translocation and Clearance of Inhaled Neutron-Activated Talc in Hamsters. Wehner, A.P., Wilkerson, C.L., Cannon, W.C., Buschbom, R.L., and Tanner, T.M. Fd. Cosmet. Toxicol. 15:213, 1977.

Study was conducted to determine pulmonary deposition, translocation and clearance of inhaled talc in 10-week-old hamsters receiving a single 2-hour nose-only exposure to neutron-activated talc. From 20 to 80 mg talc (6-8% of inhaled quantity) was deposited in the alveoli. The biological half-life of the talc deposited in the alveoli was 7-10 days. Alveolar clearance was essentially complete 4 months after exposure. No translocation of talc to liver, kidneys, ovaries or other parts of the body was found. Several hundred micrograms of talc were found in the faecal samples.

(3) - Talc Dusting Studies. Pooley, F.

Talc dusting experiments have been performed to estimate the level of exposure to infants during applications. (See Attachment A).

Completed studies - Ingestion

A number of animal studies have been performed both to determine whether asbestos fibers can penetrate the gut and to determine if any pathological effects occur upon ingestion of asbestos. There appears to be conflicting evidence as to whether, upon ingestion in food and water, asbestos fibers can penetrate the gut of animals. No experimental evidence has been developed to date in which gut tumors in animals have been produced upon the ingestion of even large amounts of asbestos.

(1) - The Short-Term Effects of Chronic Asbestos Ingestion in Rats. Bolton, R.E. and Davis, J.M.G. Ann. occup. Hyg. 19:121, 1976.

Rats fed a diet supplemented with an asbestos (Chrysotile A, Crocidolite, and Amosite) margarine formulation for periods of up to 1 year were examined for short-term clearance and evidence of penetration of, or damage to, the gut mucosa; no evidence of asbestos retention within gut lumen, and no sign of cell penetration or damage to the intestinal mucosa.

(2) - A Preliminary Study of Biochemical Changes in the Rat Small Intestine Following Long-Term Ingestion of Chrysotile Asbestos. Jacobs, R., Dodgson, K.S., Richards, R.J., Br. J. exp. Path. 58:541, 1977.

Rats fed chrysotile asbestos for 10 months (0.5-50 mg/day) in crushed pellet diet or margarine; changes are reported in DNA, RNA, protein and brush border enzymes in small intestine mucosa lining cells and gut lumen; intracellular levels of RNA, DNA and protein remained unchanged, but significant alterations, consistent with a mineral-induced cytotoxicity, were found in the lumen level of DNA (↑) and RNA (↓) in the treated rats; most intracellular enzyme levels were consistently, but not significantly, elevated in animals maintained on diets containing asbestos, while the activities within the lumen were significantly higher than those found in normal animals.

(3) - Effects of Ingested Chrysotile on DNA Synthesis in the Gastro-intestinal Tract and Liver of the Rat. Amacher, D.E., Alarif, A, Epstein, S.S. Environ. Hlth. Perspect. 9:319, 1974.

Male rats gavaged with chrysotile suspensions in normal saline (5, 100, 500 mg/kg) were sacrificed in 2 weeks; a dose-response study indicated that 2 weeks after a 5 mg/kg dose, DNA synthesis was increased in small intestine and colon, and reduced in liver; synthesis was reduced in small intestine 2 weeks after 500 mg/kg dose; following 100 mg/kg, a transient increase in DNA synthesis was noted in stomach and small intestine at 1 and 7 days, respectively, and increased in colon from 28-63 days; data suggest that asbestos penetrates gastrointestinal mucosa and influences regulation of DNA synthesis in GI tract.

(4) - Public Health Aspects of Asbestos Fibers in Drinking Water. Cooper, R.C., Cooper, W.C. AM. Water Works Assoc. J. 70:338, 1978.

A review of several health-related aspects of the presence of asbestos fibers in drinking water. Concludes that, at present, there is no concrete evidence that asbestos ingested via drinking water causes disease in man.

(5) - Animal Experiments with Talc. Wagner, J.C., Berry, G., Cooke, T.J., Hill, R.J., Pooley, F.D., and Skidmore, J.W. In Inhaled Particles and Vapours, IV. ed. Walter, W.C., New York, Pergamon (in press).

Rats were fed 100 mg per day of UICC Canadian chrysotile prepared in milk powder on a five-day per week schedule for a total of 100 days of ingestion. The mean survival for the experimental rats was 619 days as compared to the controls (641 days). One gastric leiomyosarcoma was observed in the chrysotile group. No tumors of this type were found to occur in the controls.

(6) - Gibel, W., Lohs, K., Horn, K.H., Wildner, G.P., and Hoffman, F. Tierexperimentelle untersuchungen uber eine Kanzerogene wirkung von asbestifilter - material nach oraler aufnahme. Arch. Geschwulstforsch 46:437, 1976.

Rats were fed 50 mg/kg body weight per day of asbestos filter material added as a water suspension which contained approximately 52% chrysotile. The study reported a statistically significant ($p < 0.01$) increase in the incidence of malignant tumors in experimental rats as compared to controls. The average survival time for experimental rats was 441 days as compared to 702 days in untreated controls.

Ongoing studies - Inhalation

An ongoing study (Lovelace Foundation) on the inhalation of pure talc by hamsters is nearing completion and the results are expected to be submitted to FDA in the near future. To date, all findings are negative.

Ongoing studies - Ingestion

The effects of ingested asbestos are currently being investigated by the National Institute of Environmental Health Sciences. Newborn rats and hamsters are receiving 1% asbestos by gavage until weaning when they will be put on diets containing 1% asbestos until death. Additionally, lifetime feeding studies in rats and hamsters are being conducted to determine the toxicity of ingested asbestos with and without dimethylhydrazine. Complete histopathological evaluations will be performed at termination of exposure in all of these studies. These studies are scheduled for completion in 1979. (Attachment B)

Analytical Methodology

The FDA currently has a contract with Structure Probe, Inc., of West Chester, PA to develop analytical methodology for the determination of asbestos in foods, drugs, and talc. Successful preliminary methods have been developed for wine and beer, while good progress has been made on methods for catsup and mayonnaise. The methods being developed use the scanning electron microscope with energy dispersive X-ray fluorescence capability as the determination instrumentation for any asbestos separated from the samples of interest. (See Attachment C). For analytical methodology relative to cosmetic talc, see Attachment D.

Cosmetic Talc Surveillance Program

The Bureau of Foods has a modest surveillance program under which it monitors the asbestos fiber content of retail units of cosmetic talcum powder products. To date, it has not found any grossly contaminated products.

GRAS Review of Talc

The FDA is conducting a comprehensive study of direct human food ingredients classified as generally recognized as safe (GRAS) or subject to a prior sanction. Under this review, the safety of talc is being re-evaluated. This compound was the subject of a search of the scientific literature from 1920 to the present, and is being evaluated by the FDA with the aid of the Select Committee on GRAS Substances of the Life Sciences Research Office, Federation of American Societies for Experimental Biology (FASEB). In 1974, the FAO/WHO Committee set no limit, within good manufacturing practice, for the acceptable daily intake of talc pending the development of a satisfactory method for estimating asbestos-like particles in talc. The Select Committee tentatively concluded that there is no evidence in the available information on asbestos-free talc that demonstrates or suggests reasonable grounds to suspect a hazard to the public when used at levels that are now current or that might reasonably be expected in the future (see Attachment E.)

The uses of talc considered by the Select Committee include use in paper and paperboard packaging materials, in cotton and cotton fabrics used in dry food packaging, as a coating for rice, in chewing gum base, and as a filler in cross-linked polyester resins for use on food contact surfaces.

PROBLEM AREAS

Toxicology

(1) The contribution of the fiber concentration, fiber geometry and chemical composition of the fibers to the production of disease in relation to both the inhalation and ingestion of asbestos must be defined.

(2) The potential for the production of cancer and other diseases by the ingestion of asbestos must be determined.

Methodology

(1) There must be a refinement in the existing methodology for the determination of asbestos in foods and talc.

(2) The levels of occurrence of asbestos in foods above background levels must be determined.

(3) Problems of separation of asbestos from the food matrix must be resolved. (It is anticipated that methods suitable for use by FDA for most food types will be developed by the end of the current contract in July 1979).

CONCLUSION

Studies have been instituted to determine the health effects of the inhalation of talc and the ingestion of asbestos, and to develop adequate analytical methodology for the determination of asbestos in foods and cosmetics. To date, there is no evidence to suggest a health hazard from the ingestion of asbestos or the inhalation of talc. In addition, the analytical methodology has not been developed and refined to a point where very small amounts of asbestos contaminating talc could be detected. Therefore, until these issues have been resolved, no further action is contemplated.