United States Department of the Interior

U.S. GEOLOGICAL SURVEY
Reston, Virginia 20192

In Reply Refer To:
Mail Stop 983

November 20, 2000

Dr. Mary S. Wolfe
Executive Secretary
NTP Board of Scientific Counselors
P.O. Box 12233, A3-07
Research Triangle Park, NC 27709

Re: National Toxicological Program (NTP) Board of Scientific Counselors Report on Carcinogens (RoC) Subcommittee meeting, December 13-15, 2000 in Washington, DC

Dear Dr. Wolfe:

The NTP Board of Scientific Counselors RoC Subcommittee will meet in Washington, DC on December 13-15 to review the listing of asbestiform talc and nonasbestiform talc as a carcinogen in the *10th Report on Carcinogens* to Congress under the Public Health Service Act. Solicitation of public and written comments were made in the draft of a Federal Register notice dated October 6, 2000.

As you are well aware, the decision to classify talc as a carcinogen is not a trivial matter. While the public has to be protected from unknowingly using harmful materials, consideration has to be given to the impact of such a decision. The Committee must ensure that it gives full consideration to *all* available evidence when making its decision. The following comments are addressed to the December 2000 draft Report on Carcinogens Background Document for Talc, Asbestiform and Nonasbestiform, that is available on the National Toxicology Program WEB site.

I found the discussions of the health effects of exposure interesting although the conclusions drawn in the various sections of the draft background document could use fuller explanations. The reason is best exemplified in Section 3.1, occupational exposure to talc. The section presents the results of epidemiological studies that found various degrees of association between exposure and cancer, some positive and some negative. However, the review in sections 3.2.1 and 3.1.2 and the summary paragraphs in section 3.1.3 contained caveats and warnings about problems with all of the studies. Despite this, the working group concluded that results "suggest a moderate increase in lung cancer mortality....including the rubber and paper industries." This conclusion does not seem consistent with the discussion. Even more puzzling was the inclusion

of the rubber and paper industries as supporting evidence because it is noted on page 21 that particulates in those four studies were poorly characterized, exposure levels were unknown, and other carcinogenic agents were present.

Another example is in section 3.2 where ovarian cancer is discussed. The working group concluded in Section 3.2.6, page 28, that there was a 30% to 60% increased cancer risk of ovarian cancer associated with genital exposure to talc based on cases studies with odds ratios in the 1.3 to 2.5 range. However, large confidence intervals associated with these odds ratios (table 3-3), coupled with caveats concerning risk factors discussed throughout section 3.2, suggest that there could be a good deal of uncertainty in these calculated odds ratios. A more complete explanation could possibly explain this discrepancy.

The working group also indicated that it reviewed *all* significant research conducted since the International Agency for Research on Cancer report in 1987. However, I was surprised to see no mention of the conference on talc that was sponsored by the International Society of Regulatory Toxicology and Pharmacology and the U.S. Food and Drug Administration (Talc: Consumer Uses and Health Perspectives, National Institutes of Health, Bethesda, MD, January 31-February 1, 1994). This was a major conference on the health risks posed by talc. No mention also is made of the special issue of Comments on Toxicology (v. 6, no. *5*, 1998, p. 307-366) on talc. The ISRTP/FDA conference and the special issue both offered important insights into the health risk posed by talc and would have been highly germane to your discussion of carcinogenicity.

Another concern is the surprisingly large amount of the background document devoted to health effects of exposure to asbestos. Asbestos is a known carcinogen. Talc containing asbestos would be a suspected carcinogen because of its asbestos content. However, the discussion of asbestos carcinogenicity is not appropriate for "nonasbestiform talc." My concern is that the inclusion of discussions of asbestos may be misconstrued as implying that talc is similarly carcinogenic. Evidence of this occurs in section 3.2.1, page 24 where it states that "talc was suspected of being a risk factor for ovarian cancer based on its mineralogical and chemical similarity to asbestos, possible contamination of talc by asbestos ..." This is followed by a discussion of asbestos exposure and ovarian cancer. I do not know the context in which this statement was originally used by Rohl et al., but it undoubtedly did not imply that talc could be treated the same as asbestos. Also in section 3.2.1, it is states that talc is suspected as a risk factor for ovarian cancer because of presence granulomas. However, the bulk of the supporting evidence in that same paragraph focuses on asbestos rather than talc. The same is true in section 5.2, pages 58-63, where, lacking data on talc, the genotoxic effects of asbestos are presented and in section 6.2, pages 69-72, where research on asbestos predominates.

More obvious is the statement in section 3.3, page 28. Here the working group indicated that information on asbestiform fibers is limited mainly to occupational settings. However, the working group went on to say that "because of the widespread contamination of talc and commercial talc products with asbestiform minerals, it must be assumed that talc without further specification of mineralogy or morphology may contain asbestos fibers. The weight of the evidence thus indicates that it would be prudent to regard such undifferentiated talc materials as carcinogenic." This does not follow. It is difficult to understand how the lack of mineral

characterization can be misconstrued to indicate a carcinogenic nature for any mineral or mineral product.

It was encouraging to see Wylie et al. (section 6.2.3, pages 69-70) inject correct mineralogical characterization and nomenclature into health studies with their work comparing the cytotoxic effects of a fibrous talc to those of asbestos. This is important because it properly recognizes that although talc can be fibrous if it has altered from a fibrous mineral, it is not asbestos and its effect on the cellular system is not the same as asbestos. The point being that when asbestiform talc is mentioned in the background documentation, it is not always clear whether the researchers are discussing fibrous talc, talc/amphibole intergrowths (where the crystal structures of talc and amphibole are intermingled within a single grain), or talc that is contaminated with asbestos. Based on the large percentage of the background document dedicated to discussions of the health risk posed by asbestos, it must be assumed that the working group was focusing on talc contaminated with asbestos. However, accurate mineral characterization such as that by Wylie et al. would eliminate the identification problem and allow health researchers to more accurately determine the health effects of exposure to talc particulates.

In summary, generalizations about the definition and mineralogy of talc are not appropriate, particularly when an entire industry's future hinges upon the decision of the subcommittee. While many health scientists would rather not address the mineralogy which, admittedly, can be quite complex and out of their realm of expertise, it is essential that they do so if there is going to be a fair (or even a useful) evaluation of the health risk posed by minerals.

The importance of the working group's final decision cannot be stressed enough. The talc industry is relatively large, with 900,000 metric tons valued at $100 million sold annually. The industry employees about 680 people. With its use in thousands of commercial and consumer products, any actions regarding talc will have a significant ripple effect on other industries. If the evidence warrants classifying talc as a carcinogen, then the actions are justifiable. If the evidence is not definitive, however, discretion must be exercised. The working group must also keep in mind that any labeling of talc as a carcinogen is not an end in itself. Committee decisions are used to activate portions of many laws, such as the Occupational Safety and Health Administration's Hazard Communications Standard, the Mine Safety and Health Administration's Hazard Communication Standard (to be enacted shortly), or the State of California's Proposition 16.

Thank you again for this opportunity to comment on this issue.

Robert L. Virta

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