

Title: It is Important to Distinguish between Asbestos Fibers and Non-asbestiform Elongated Mineral Particles during Analysis of Talc-containing Consumer Products

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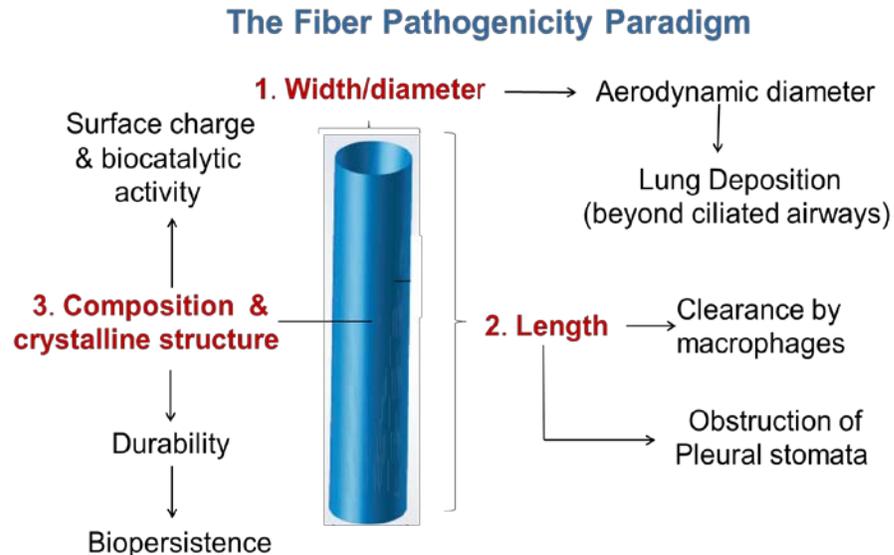
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Comment Category, Docket # FDA-2020-N-0025: **Terminology Use** concerning Asbestos and Other Elongated Mineral Particles in the Analysis of Talc-containing Consumer products

Reference Source: “Preliminary Recommendations on Testing Methods for Asbestos in Talc and Consumer products containing Talc”. Quotes:

- “Lack of consensus concerning what should be called “asbestos”.....”
- “Because both types of elongate minerals are suspected of having biological activity with similar pathological outcomes, the distinction is irrelevant.”
- “Covered minerals include chrysotile (but not other serpentine minerals) and members of the amphibole group (inclusive; not restricted to the five amphiboles used commercially)”.

Statement #1: The Fiber Pathogenicity Paradigm (FPP) distinguishes between the effect of long biopersistent asbestos fibers, capable of reaching the site of pleural pathology, and elongate mineral particles (including non-asbestiform amphiboles) that lack similar disease-causing features



Adopted from Donaldson 2011

- The FPP is a widely used disease construct for explaining the causation of mesothelioma by asbestos fibers
- The FPP recognizes the importance of asbestos fiber length, diameter, composition and crystalline structure in the impact on pleural injury. Obstruction of lymphatic drainage pores in the parietal pleural triggers chronic inflammation as a precursor to the events leading to carcinogenesis
- Although non-asbestiform amphiboles may occasionally (but less frequently) attain similar length and diameter characteristics as pathogenic asbestos fibers, non-asbestiform amphiboles do not exhibit the durability and biopersistence of asbestos fibers
- Studies with biopersistent, size-controlled engineered nanomaterials (e.g., nano wires) confirm the tenets of the FPP

Implication: Talc testing methods that are being considered for assessment of asbestos contamination should separately report asbestos fibers and non-asbestiform amphiboles since they do not exhibit the same pathogenicity features

Statement #2: It is not definite, in light of cellular and animal experimentation studies, to state that asbestos fibers and non-asbestiform amphiboles have similar pathological outcomes and that the distinction is irrelevant. The tenets of the fiber pathogenicity paradigm applies to the cellular and animal experimentation.

Cellular Studies

- Fiber and EMP length, diameter, composition, crystalline structure and surface properties determine biological responses in mesothelial cells and macrophages
- Mechanistic cellular studies show differences in the toxicological profiling of asbestos fibers versus non-asbestos cleavage fragments and talc in biological assays that report cell viability, cell death, proliferation, oxidative stress responses, gene expression profiling and signal transduction pathways

Animal Studies

- Demonstrate the importance of fiber length, diameter and retention, as per the FPP
- Intra-pleural and intra-peritoneal administration demonstrate the lack of carcinogenic potential of non-asbestos amphiboles in support of the FPP
- Inhalation carcinogenicity studies in mice, rats and hamsters do not show evidence of carcinogenicity for non-asbestos talc

Implication: There is evidence that the pathogenic potential of asbestos fibers differ from non-asbestiform EMPs in animal carcinogenesis and cellular studies, refuting the claim that the distinction between these materials is irrelevant.

Statement #3: Occupational and therapeutic talc exposures in humans do not show increased risk of mesothelioma, even when admixed with non-asbestiform EMP contaminants

- The tenets of the FPP have been confirmed in human asbestos studies and have been used to develop safer fibrous vitreous products for consumer use through tuning of fiber length, diameter and biopersistence properties
- Epidemiology studies in talc miners and millers fail to demonstrate an increased risk of mesothelioma, even in the presence of non-asbestiform cleavage fragments
- Long-term follow-up studies of talc pleurodesis patients failed to show evidence of mesothelioma, even upon installation of gram quantities of FDA-approved talc products into the pleural cavity.
- Occupational exposure studies, looking at hairdressers who are frequently exposed to talc products, have not shown an increased risk of mesothelioma

Statement #4: By establishing rigorous talc-testing guidelines, it should be feasible through the use of modern characterization techniques (e.g., TEM assisted by SAED and XPS) to distinguish asbestiform from non-asbestiform amphiboles. This will preclude changing terminology to achieve consensus.

- FDA has not previously used the NIOSH definition of “covered” materials, which groups non-asbestiform amphiboles under the term “asbestos”. This is incongruent with the mineralogical definitions of asbestos and how OSHA uses the asbestos definition to perform regulatory oversight.
- NIOSH’s Bulletin 62 was released in 2011 to “remove confusion” about the inclusion of covered materials (in 1990). The bulletin recognizes that the earlier inclusion of non-asbestiform amphiboles in fiber counting was based on inconclusive science and epidemiology. OSHA also made their decision on the basis of epidemiologic studies that were either inconclusive or revealed no adverse health effects from non-asbestos minerals.
- Bulletin 62 discusses the “platform for fiber pathogenicity”, which remains valid today and is supported by more recent research on high aspect ratio nanomaterials (which allow better control over test material properties than the heterogeneous makeup of asbestos fibers and non-asbestiform EMPs).
- The implementation of rigorous test methods and criteria to assess, without bias, which mineral contaminants are present talc, will allow each mineral element to be identified on its own merit rather than adopting confusing terminology for which there is no conclusive evidence.