

Item	Recommendation	Response	Changes to Roadmap
	<p>Recommendation 1 - Clarify the Vision and Rationale NIOSH should revise the <i>Roadmap</i> to clearly state the overarching vision and rationale for the research program</p>		
1	<p>The overarching vision should point toward research that will differentiate effects from exposure to a range of elongate mineral particles and help determine the influence of size, shape, and other physical and chemical characteristics of these particles on human health. This research would identify which elongate mineral particles, or what characteristics of those particles, should be included in recommendations to protect the public and workers from hazardous occupational and environmental exposures.</p>	<p>NIOSH agrees that the overarching vision and rationale for the research program should be clearly stated. Although the overarching vision was presented in Section 2.5 of the draft <i>Roadmap</i> [Section 3.7 of draft <i>Roadmap</i> (V4)], the <i>Roadmap</i> would be improved by bringing this forward in the document and elaborating on this vision. In fact, NIOSH finds that the Committee has stated the vision quite well.</p>	<p>A new <i>Introduction</i> section, inserted at the beginning of the draft <i>Roadmap</i> (V4), describes the overarching rationale and vision for the <i>Roadmap</i> and future research.</p>
2	<p>The rationale for the <i>Roadmap</i> should clearly articulate the influence that ongoing and future research can have on improving public and occupational health.</p>	<p>NIOSH agrees that the rationale for the research program should be clearly stated. The rationale was presented in various sections throughout the draft <i>Roadmap</i>, but would be communicated more clearly by synthesizing it early in the document.</p>	<p>A new <i>Introduction</i> section, inserted at the beginning of the draft <i>Roadmap</i> (V4), describes the overarching rationale and vision for the <i>Roadmap</i> and future research.</p>
3	<p>A clearer vision and purpose would help strengthen the goals that the research is intended to support. The research should be prioritized as to the hazard and exposure.</p>	<p>NIOSH agrees that a prioritization of the research will be important, to the extent that it is possible at this time. However, the early surveillance and research results may point to different priority needs, and the research programs will need to be evaluated and refocused on an on-going basis.</p>	<p>A general prioritization scheme is now included in Section 4.3 of the draft <i>Roadmap</i> (V4).</p>
	<p>Recommendation 2 - Include Key Components</p>		
4	<p>NIOSH should ensure that four key components are included or refined in</p>	<p>Responses to the first two of the four components are addressed in a new <i>Introduction</i> section added to the</p>	<p>A new <i>Introduction</i> section, inserted at the beginning of the</p>

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	<p>the Roadmap: (1) vision, (2) rationale, (3) goals, and (4) framework</p>	<p>Roadmap (see above responses). With respect to (3) goals and (4) framework, the Roadmap presents broadly written goals that fit the intended strategy for the Roadmap. The Roadmap is intended to identify the key issues and provide a general approach to the research needed to address the key issues. A second phase is envisioned and described in the Path Forward. In this second phase, the research program (including specific aims and projects) will be developed in detail by multi-disciplinary study groups with representatives from a variety of organizations.</p>	<p>draft Roadmap (V4), describes the overarching rationale and vision for the Roadmap and future research. The goals and framework have not been substantially modified.</p>
<p>5</p>	<p>Recommendation 3- Improve Terminology NIOSH should revise its Roadmap with careful attention to consistency in the use of nomenclature and terminology. The goal is that authoritative terminology should permeate research and regulatory efforts, specifically:</p> <p>For research purposes, the term <i>elongate mineral particles</i> is useful for encompassing a broad category of mineral particles of a certain dimension and aspect ratio; more specific mineralogical terminology would be needed for regulatory purposes;</p>	<p>To minimize confusion with the term <i>fiber</i> as used by the mineralogical community, NIOSH used the term <i>elongate mineral particles</i> as a replacement for the term <i>fiber</i> as traditionally used by the health community. NIOSH agrees with the Committee that the term <i>elongate mineral particles</i> prevents confusion about the nature of the particles and is useful for encompassing a broad category of mineral particles of specified dimensions and aspect ratios. NIOSH also agrees with the Committee that the term <i>elongate mineral particle</i> is not a rigorous mineralogical term and that its use should be limited. Because the health community has often used the term <i>fiber</i> without clear descriptions of the particles to which it is applied, its use should be continued when describing previously published research. However, NIOSH believes that, until more mineralogically-precise recommendations are developed, the term <i>elongate mineral particles</i> should be used in the clarified 1990</p>	<p>In the draft Roadmap (V4), <i>elongate mineral particle</i> has been replaced with <i>elongate mineral particle</i>. In addition, careful attention has been paid to any remaining uses of the term <i>fiber(s)</i> in the Roadmap. Wherever possible and appropriate to do so, those remaining instances have been replaced with more precise terminology, including <i>elongate mineral particle(s)</i>.</p>

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6	<p>Revisions should be made to the <i>Roadmap</i> glossary using accepted mineralogical terminology or nomenclature from the current American Geological Institute's <i>Glossary of Geology</i> or other standard texts; citations should be provided for each definition; nonstandard terms should be removed from the glossary and the main text; and</p>	<p>recommendaion and as a limited-use generic term going forward.</p> <p>NIOSH agrees that research efforts in this area have been hampered by the use of non-standard terminology and definitions, thus making it difficult to comprehend some studies and compare across others. NIOSH believes that there is no current reference standard for terminology and definitions that is complete and unambiguous. NIOSH supports the development of standard terminology and definitions which are acceptable to the majority of scientists. NIOSH further supports the dissemination of standard terminology and definitions to the community of non-scientists and would encourage their usage by this community.</p>	<p>To describe the need for development of standard and unambiguous terminology, a new section (2.3) has been added to the draft <i>Roadmap</i> (V4). This new content is also identified as a priority effort of the greater scientific community that should precede, or at least be concurrent with, further research efforts. In addition, wording has been included to reinforce the need for such standardized terminology to be adopted and used by all scientists working in this field and stakeholder communities. The Glossary has been reorganized, and a new table with mineralogical definitions from a variety of sources is provided.</p>
7	<p>Terminology used in sections referring to epidemiology and toxicology should also use definitions from current standard texts and be included in the glossary with citations.</p>	<p>NIOSH agrees that nomenclature and terminology should be used consistently and that authoritative terminology, when available, should permeate research and regulatory language. However, the definitions of the terminology used in published studies cited in the <i>Roadmap</i> are not always clear, and providing a standard definition in the Glossary would not clarify those uses.</p>	<p>NIOSH has identified inhalational terms used in the <i>Roadmap</i> that are pertinent to epidemiology and toxicology and provides definitions in the <i>Glossary</i>. These definitions apply to descriptions in the <i>Roadmap</i> of research to be conducted. NIOSH cannot vouch for the definitions used in the various cited papers.</p>

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8	<p>NIOSH should revise the Roadmap to give greater attention to the mineralogical foundations of the proposed research. Discussions of mineralogy in the Roadmap should be strengthened by incorporating current understanding in this field using accepted terminology and by proposing research on the fundamental mineralogical properties relevant to toxicology, epidemiology, and exposure assessment. Specifically, mineralogical research is needed on physical and chemical properties, biopersistence, and mineral source characterization, including the development of standard sets of tests and methodologies.</p>	<p>NIOSH agrees that the minerals encountered in occupational settings and those intended to be studied in toxicological and epidemiological studies should be characterized to the extent possible. NIOSH, as a health and safety agency, does not believe that it is the appropriate agency to lead the development of a research agenda on fundamental mineralogical properties. However, NIOSH recognizes the need for this type of research. NIOSH calls on the relevant agencies and institutions to develop a mineralogical research agenda that complements the goals of the <i>Roadmap</i>. This effort should be accomplished with input from relevant health agencies and institutions.</p>	<p>The draft <i>Roadmap</i> (V4) has been revised to give greater attention to the mineralogical foundations of the proposed research. A discussion of the need to harmonize and standardize definitions among the relevant disciplines involved in research on EMPs has been added in section 2.3 of the draft <i>Roadmap</i> (V4).</p>
9	<p>NIOSH should work with other federal agencies and organizations to develop a repository of well-characterized and standardized reference minerals for use in research.</p>	<p>NIOSH agrees that a repository of well-characterized and standardized reference minerals for use in research is critical to the success of the recommended research programs. For this reason, a recommendation to develop such a repository was presented and discussed in the draft <i>Roadmap</i> on p. 64, as the second paragraph under Section 2.1 <i>Strategic Research Goals and Objectives</i>. More details on the contents of the repository were provided on p. 89, and more details on the use of the repository were described on p. 51. By placing these discussions in several locations, the importance NIOSH</p>	<p>To bring greater attention in the <i>Roadmap</i> to this important piece of research infrastructure, it has been given its own section (3.3) near the front of the <i>Framework for Research</i>; details provided in other locations in the previous draft <i>Roadmap</i> have been consolidated in this section.</p>

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		placed on the repository and its central role in the research framework may not have been apparent.	
	Recommendation 6 - Emphasize Interdisciplinary Efforts		
10	<p>NIOSH should revise the <i>Roadmap</i> to emphasize the need for collaboration and integration of research among the mineralogical, toxicological, epidemiological, and exposure assessment disciplines.</p>	<p>NIOSH agrees with the Committee on the importance of having an interdisciplinary approach to the conduct of research on asbestos and other elongate mineral particles. Collaboration among various scientific disciplines is critical for ensuring the appropriate integration of research that can be used in developing public health policies. NIOSH stated in the <i>Foreword</i> and <i>Section 3</i> of the draft <i>Roadmap</i> the importance of having a robust public-private sector partnership comprised of labor, industry, academia, and other interested parties to help focus the scope of research, enhance extramural research, and assist in the development and dissemination of research results. Also, NIOSH indicated the need for an interdisciplinary approach in planning and accomplishing the research in several locations within the draft <i>Roadmap</i>. By placing these discussions in several locations, the importance NIOSH placed on it and the central role of a multi-disciplinary effort in the research framework may not have been apparent.</p>	<p>To bring greater attention in the <i>Roadmap</i> to the need for an interdisciplinary approach to accomplish the research conducted within the framework, it is reorganized into a new section (3.2) in the draft <i>Roadmap (V4)</i> and emphasized where appropriate throughout the document.</p>
	Recommendation 7 - Develop a Systematic Strategy for the Toxicological Assessment of Elongate Mineral Particles		
11	<p>Characterizing the chemical and physical properties of the elongate mineral particles beginning with petrographic analysis and proceeding through X-ray diffraction, transmission and scanning electron microscopy, and other techniques; and</p>	<p>NIOSH should revise the <i>Roadmap</i> to describe a systematic tiered strategy for characterizing and testing the relative toxicities of elongate mineral particles and/or their mixtures. The strategy should include the following:</p> <p>"Petrographic analysis" refers to multiple methodologies used to characterize minerals. X-ray diffraction (XRD) is often considered one of these methods, as are optical polarized microscopy, X-ray fluorescence (XRF), and electron microprobe.</p>	<p>Section 2.8 of the draft <i>Roadmap (V4)</i> has been revised to include a discussion of petrographic analysis as it applies to characterization of chemical and physicochemical properties of EMPs.</p>

<p>[Item]</p>	<p>[Recommendation]</p> <p>Using tiered panels of <i>in vitro</i> and <i>in vivo</i> assays of increasing complexity to identify and characterize biological responses and categorize the potential hazards.</p>	<p>[Response]</p> <p>NIOSH agrees that a systematic, tiered strategy for testing the relative toxicities of elongate mineral particles and/or mixtures is appropriate for inclusion in the <i>Roadmap</i>. For tiered testing of fibrous particles, the strategy developed by the ILSI Risk Science Institute Working Group, supported by EPA, and published in 2005, is an appropriate starting point. However, this scheme should be periodically reviewed and revised as needed by the multi-disciplinary expert study groups formed as described in the <i>Path Forward</i> section of the <i>Roadmap</i>. Also, the specific tests and methods will need to be identified by the expert study groups.</p>	<p>[Changes to Roadmap]</p> <p>The draft <i>Roadmap (V4)</i> now includes a modification of the published ILSI scheme in Section 3.4.</p>
<p>12</p>	<p>Recommendation 8 - Emphasize Additional Research Areas</p> <p>NIOSH should revise the <i>Roadmap</i> to include an emphasis on the following:</p> <p>Incorporating petrographic analysis and developing new exposure assessment tools using electron microscopy methods that are mineralogically and toxicologically relevant and that minimize reliance on phase contrast microscopy methods;</p>	<p>NIOSH believes that there is a role to be played by any relevant analytical technique in assessing exposures. Research into improving measurement methods is therefore encouraged. However, an International Standard (ISO) already exists for fiber counting using scanning electron microscopy, and it is noted that the method has not widely replaced optical microscope methods in most countries for various reasons including: traceability of measurements to existing regulatory risk assessments; field portability; and cost. NIOSH finds these reasons compelling and thus feels there is a basis for maintaining, and possibly improving, optical microscope methods, in addition to supporting further research into other techniques, including electron microscopy. Petrographic analysis, by its very nature, cannot be applied directly to samples of airborne EMPs, though could provide insight into the nature of airborne EMP exposures in situations where the source of the</p>	<p>Section 2.8 of the draft <i>Roadmap (V4)</i> has been revised to highlight the complementary areas of applicability of optical and electron microscopy in counting of EMPs and thus the importance of continuing a research effort in both methodologies.</p>
<p>13</p>	<p></p>	<p></p>	<p></p>

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14	<p>Toxicological mechanisms of action of a range of well-characterized elongate mineral particles with attention to early biomarkers of human health effects;</p>	<p>EMPs is understood and where bulk samples of the source rock are available.</p> <p>NIOSH agrees that additional emphasis in the <i>Roadmap</i> on the toxicological mechanisms of action with attention to potential development of early biomarkers of human health effects is appropriate.</p>	<p>The draft <i>Roadmap (V4)</i> includes a new outline of a toxicological testing scheme to develop a mechanistic understanding of EMP toxicity, with the aim of developing <i>in vivo</i> biomarkers of effect in humans in Section 3.4.3.</p>
15	<p>Additional opportunities for epidemiological research including studies of Libby, Montana worker and resident populations, as well as cohorts exposed to elongate mineral particles in other countries.</p>	<p>NIOSH agrees that the <i>Roadmap</i> should provide additional details concerning epidemiological research on workers and residents exposed to Libby amphiboles and additional emphasis on cohorts exposed to EMPs in other countries.</p>	<p>Section 2.6.1.2 of the draft <i>Roadmap (V4)</i> has been revised to include a brief description of a cluster of mesothelioma deaths in Italy attributed to an asbestiform amphibole mineral, as well as new content describing ongoing research on workers and community residents exposed to Libby amphiboles. The draft <i>Roadmap</i> has also been revised with the addition of a new section, 2.6.2, which includes brief descriptions of epidemiologic studies of erionite, which have been conducted mainly in Turkey. Section 3.5.3 now includes a new paragraph citing several studies of environmental exposures to asbestos conducted in other countries where potential opportunities for further research</p>

Item	Recommendation	Response	Changes to Roadmap on non-occupational exposures may exist.
16	<p>Statistical methods for addressing analytic variability and determining the relationships between mineralogical and exposure variables and health outcomes.</p>	<p>NIOSH has reviewed the comments regarding analytical variability and believes they fall into two categories, comments regarding inter-sampler comparisons and comments regarding fiber-counting. For inter-sampler comparisons, NIOSH prefers to support the use of expanded uncertainty as detailed in the ISO Guide to Uncertainty in Measurement (GUM). For fiber-counting, mixed-model analysis of a Poisson distribution has previously been considered for PCM fiber count data, although with different statistical techniques [Miller 1984]. As specific research programs are developed and study results are produced, the optimal data analyses for specific purposes can be identified and used.</p>	<p>No Revisions.</p>

References

Miller BG [1984]. A statistical method for analysis of membrane filter samples of airborne fibre. Ann Occup Hyg 28:217-227.