

## Monticello Conference report

The Monticello Conference on Elongated Mineral Particles (EMP) was held from the 16<sup>th</sup> to 20 October 2017 in Charlottesville, Virginia. The conference attendance was by invitation only and limited to 60 people. The attendees were selected based on a review of scientific literature to identify those who are performing or have performed research related to EMPs. The conference chairs also solicited attendee recommendations from governmental agencies both in the US and internationally. (A list of attendees is included below)

The conference proceedings were published as a special issue of the journal Toxicology and Applied Pharmacology (TAAP), vol 361, 2018.

The conference scientific program consisted of 5 sessions:

- 1) Defining EMPs,
- 2) Effects and Mechanisms,
- 3) Human Exposure, Effects, and Risks,
- 4) Rapporteur Reports and General Discussion, and
- 5) Future Research.

The sessions are described below along with the points of consensus of Monticello attendees that were reported in the TAAP publications. The TAAP volume dedicated to the conference also included individual publications from the speakers. A list of these is included at the end.

**The following points were of interest:**

- **The term EMP does not alone imply elevated risk for an asbestos related disease.**
- **The terms “fibrous” and “asbestos” are not synonymous.**  
**Asbestos is fibrous, but all fibrous minerals are not asbestos.**
- **An EPA panel that was discussed, after reviewing the extensive literature, concluded, by consensus, that chrysotile asbestos fibers are far less likely to cause disease than the major commercial amphiboles, amosite and crocidolite, by a factor of at least two orders of magnitude.**
- **The panelists also agreed that the available data suggest that the risk for fibers less than 5 µm in length is very low and could be zero” and that “...for mesothelioma, the panelists supported the use of different relative carcinogenic potencies for the different fiber types.**
- **Agency for Toxic Substances Disease Research (ATSDR), part of the Centers for Disease Control, concluded by consensus that “there is a strong weight of evidence that asbestos [fibers] shorter than 5 µm are unlikely to cause cancer in humans.**
- **For EMPs that are long and durable, decreasing widths result in increasing carcinogenic potential.**
- **EMPs with length less than 5 microns present insignificant risk for EMP-related cancer.**
- **Sufficiently high and prolonged inhalation exposures to some respirable EMPs, notably including amphibole asbestos fibers, can increase risk of inflammation-mediated diseases**

including malignant mesothelioma, pleural diseases, fibrosis, and lung cancer (note: chrysotile was not mentioned).

- It is now accepted that the biological effects fibers may produce in lung tissue once deposited are closely related to their concentration but more critically to their variation in length and diameter.
  - Thresholds exist for excess disease risk from the inhalation of EMPs. Subthreshold exposures do not result in human disease development.
  - The scientific community needs to be disease specific when discussing the potential health impacts of EMPs. For example, mesothelioma, lung cancer, pleural diseases, and asbestosis may be caused by exposures that vary by specific fiber populations.
  - Quantitative assessment of biopersistence should be standardized.
  - It would be useful to collate, expand, and evaluate the data regarding the tremolite associated with Canadian chrysotile (versus tremolite found elsewhere). This information would inform our understanding of the carcinogenic potential of EMP.
- 

## 1) Defining EMPs:

Moderator: Ann Wylie

Rapporteurs: C. Barlow, R.P. Nolan, A. Rogers

Papers were given by Drs. Oberdoester, Erskine, Roggli, Pooley, Asgharian, Van Orden and Chatfield.

Seven papers on elongate mineral particles (EMPs) were presented in Session I. These papers explored the geologic identification and characterization of EMPs in the air and the lung with an emphasis on the factors important for potential health effects.

The term elongated mineral particles was defined by the group as:

- The use of aspect ratio alone should be avoided in EMP characterization.
- **The term EMP does not alone imply elevated risk for an asbestos related disease.**
- **The terms “fibrous” and “asbestos” are not synonymous.**  
**Asbestos is fibrous, but all fibrous minerals are not asbestos.**

Chrysotile & short fibers: There was discussion of the conclusions of panels from the EPA and ATSDR as follows:

**“An EPA panel, after reviewing the extensive literature, concluded, by consensus, that chrysotile asbestos fibers are far less likely to cause disease than the major commercial amphiboles, amosite and crocidolite, by a factor of at least two orders of magnitude (see US EPA, Report on the Peer Consultation Workshop to Discuss a Proposed Protocol to Assess Asbestos-Related Risk, May 30, 2003). “The panelists also agreed that the available data suggest that the risk for fibers less than 5 µm in**

length is very low and could be zero” and that “...for mesothelioma, the panelists supported the use of different relative carcinogenic potencies for the different fiber types. The panelists unanimously agreed that the available epidemiology studies provide compelling evidence that the carcinogenic potency of amphibole asbestos is two orders of magnitude greater than that for chrysotile fibers”. Similarly, a panel of the **Agency for Toxic Substances Disease Research (ATSDR), part of the Centers for Disease Control, concluded by consensus that “there is a strong weight of evidence that asbestos [fibers] shorter than 5 µm are unlikely to cause cancer in humans.”** ATSDR, Report on the Expert Panel on Health Effects of Asbestos and Synthetic Vitreous Fibers: The Influence of Fiber Length, Mar. 17, 2003, available at <http://www.atsdr.cdc.gov/HAC/asbestospanel/asbestostoc.html>(last accessed October 19, 2017).” (TAAP, 361 (2018) 47-49).

## **2) Effects and Mechanisms,**

Moderator: R. McClellan

Rapporteurs: E.J. Chatfield, M. Finkelstein, V. Roggli

Session II involved a discussion and analysis of effects of elongated mineral particles (EMP) and their mechanisms of action. There were six presentations by Günter Oberdörster, Brooke Mossman, David Bernstein and Rick Rogers, Agnes Kane, Uschi Graham, and Alessandro Gualtieri.

Based on the presentations and discussions in the effects and mechanisms section the following points were agreed upon:

- There was broad consensus that what happens at the lung level is based on a population of fibers getting to the deep part of the lung and not based on one EMP interacting with one lung cell.
- **For EMPs that are long and durable, decreasing widths result in increasing carcinogenic potential.**
- **EMPs with length less than 5 microns present insignificant risk for EMP-related cancer.**
- Sufficiently high and prolonged inhalation exposures to some respirable EMPs, **notably including amphibole asbestos fibers, can increase risk of inflammation-mediated diseases including malignant mesothelioma, pleural diseases, fibrosis, and lung cancer.** Chronic inflammation sustained by ongoing activation of the NLRP3 inflammasome plays a crucial causal role, enabling immune cells to produce the potent proinflammatory cytokines IL-1 $\beta$  and IL-18, consistent with the previous understanding that had identified upregulation of reactive oxygen species (ROS) as playing a central role in creating and maintaining a pro-inflammatory environment in these diseases and others.
- The physical characterization of retained EMPs from the lungs is extremely important in providing information regarding the etiology of the disease they may produce. **It is now accepted that the biological effects fibers may produce in lung tissue once deposited are closely related to their concentration but more critically to their variation in length and diameter.** In order to assess the disease risk of exposure to EMPs, it is necessary to accurately describe their lengths and diameter distribution. Microscopic examination of lung burden and respirable airborne dust samples EMPs are therefore among the most important investigations

necessary to assess the risks of exposure to EMPs and provide an understanding of the manner in which they can produce a disease response.

### **3) Human Exposure, Effects, and Risks**

Moderator: Graham Gibbs

Rapporteurs: D.W. Berman, P. Hibbs, M. Lippmann

Session III was designed to address EXPOSURE, EFFECTS, and RISKS of EMPs.

It comprised 13 presentations. 10 of these were devoted to 15-minute reviews of historic and important studies of human inhalation exposures and/or health-related responses to a variety of EMPs (including those composed of talc, RCF, and taconite) based on lung burden and epidemiological studies by Bruce Case, Paolo Boffetta, Alan Rogers, Jeffrey Mandel, Mark Utell, John Kelse, David Garabrant, Bian Liu, and Gary Marsh & Christy Barlow and Michele Carbone.

- **Thresholds exist for excess disease risk from the inhalation of EMPs. Subthreshold exposures do not result in human disease development.**
- **The scientific community needs to be disease specific when discussing the potential health impacts of EMPs. For example, mesothelioma, lung cancer, pleural diseases, and asbestosis may be caused by exposures that vary by specific fiber populations.** Research needs to focus specifically on individual diseases rather than assuming a certain exposure type could or could not lead to excess risk of developing any of the malignant and non-malignant diseases.
- Recent evidence was presented that did not provide support to the hypothesis that exposure to cosmetic talc is associated with development of pleural mesothelioma.
- Exposure to non-asbestiform EMPs found in R.T. Vanderbilt (RTV) talc do not produce the high prevalence and severity of pneumoconiosis observed in workers exposed to amphibole asbestos EMP (fibers). The lesser toxicity of RTV EMPs is also supported by the mortality, animal and cell studies of this talc, though controversy persists with respect to human mesothelioma.
- There is no published evidence that exposure to cleavage fragments cause asbestos-like diseases.
- There is sufficient evidence that BAP1 mutations leads to a higher propensity for humans to develop mesothelioma.

### **4) Future Research**

Moderator: David Weill

Rapporteurs: Gunter Oberdorster, Brooke Mossman, Robert Glenn

A number of recommendations for future research were discussed and presented in the TAAP meeting publication. These include:

- The establishment of a protocol for characterization of aerodynamic impact of various diameters in those EMPs greater than 5 microns in length would be useful to the community.
- **Quantitative assessment of biopersistence should be standardized.**
- **It would be useful to collate, expand, and evaluate the data regarding the tremolite associated with Canadian chrysotile (versus tremolite found elsewhere). This information would inform our understanding of the carcinogenic potential of EMP.**
- In addition numerical modeling of EMP characteristics and fiber potential toxicity index are proposed.
- Nanotechnology is an emerging industry based on commercialization of materials with future applications predicted in energy and catalysis, microelectronics, CO<sub>2</sub> capture, environmental sensing and remediation, and nanomedicine. Carbon nanotubes are one-dimensional fibrous nanomaterials that physically resemble asbestos fibers. Toxicologic studies in rodents demonstrated that some types of carbon nanotubes can induce mesothelioma, and the World Health Organization evaluated long, rigid multiwall carbon nanotubes as possibly carcinogenic for humans in 2014. The nanotube studies have identified width, length, and biopersistence of high aspect ratio fibrous nanomaterials as critical determinants of lung disease, including mesothelioma. **Based on recent theoretical modeling studies, a fourth factor, mechanical stiffness, will be considered as predictive of potential carcinogenicity.**



## Conference Attendee List:

We would like to thank the speakers, participants, moderators and rapporteurs who joined us in Charlottesville, VA for the Monticello Conference.

Bahman Mark Kelly Christy D. Wayne David Paolo	Asgharian Bailey Bailey Barlow Berman Bernstein Boffetta	Applied Research Associates, Principal Scientist Asbestos TEM Labs, President Kelly Bailey Consulting, LLC GZA, Associate Principal, Manager of Toxicology Aeolus, Inc. Consultant in Toxicology, Owner Mount Sinai School of Medicine, Associate Director of Population Sciences of The Tisch Cancer Institute and Chief of the Division of Cancer Prevention and Control University of Hawaii Cancer Center, Director, Thoracic Oncology McGill University, Department of Epidemiology, Biostatistics and Occupational Health, and Associate Member, McGill School of Environment Chatfield Technical Consulting, LTD., President Cox Associates, Consultant United States Department of Labor, Physical Scientist National Stone, Sand & Gravel Association, VP for Occupational & Environmental Health Policy University of Sherbrooke, Faculty of Science, Professor Kleinfelder, Principal Geologist Murry Finkelstein and Associates, Epidemiologist Cardno ChemRisk, Principal Health Scientist EpidStat Institute, President Safety Health Environment International Consultants Corp. President. Glenn Consulting Group Topasol LLC, President The University of Modena and Reggio Emilia, Chemical and Earth Science Department University of Idaho, Geological Sciences Zefon International, Inc. Hibbs & Associates Pty Ltd, Certified Occupational Hygienist Calportland, Senior Environmental Manager Cardno ChemRisk, Principal Health Scientist Independent Consultant United States Environmental Protection Agency, Senior Science Advisor Brown University, Professor R.T. Vanderbilt Co., Retired, Industrial Hygienist National Institute for Occupational Safety and Health, Associate Director for Mining The Graduate School and University Center, The City University of New York, Doctoral Program in Earth and Environmental Sciences
Michele Bruce	Carbone Case	Eichrom Laboratories, Engineer Geologist New York University, Professor Icahn school of Medicine at Mount Sinai, Department of Population Health Science and Policy, Institute for Translational Epidemiology, and Department of Environmental Medicine and Public Health University of Minnesota, Associate Professor in the School of Public Health's Division of Environmental Sciences Cardno ChemRisk, Consulting Senior Science Advisor for Epidemiology Independent Chemicals Professional University of Vermont College of Medicine, Department of Pathology Ramboll, Health Sciences Practice Network Leader The City University of New York University of Rochester Medical Center, Professor University of Pittsburgh, Department of Pathology, Professor Luck Stone Corporation, Vice President of Customer and Technical Services EpidStat Institute, Senior Epidemiologist Cardno ChemRisk, President Imerys, Analytical Lab Manager Cardiff University, Professor HIL Limited, Vice President Occupational Health Alan Rogers MSc, CIH, COH, FAIOH, Alan Rogers OH&S Pty Ltd Rogers Imaging Corporation Duke Medical Center, Professor of Pathology RJ Lee Group, Principal Investigator Maxxam Analytics Microscopy Laboratory, Division Manager Citoxlab University of Rochester Medical Center, Professor of Medicine and Environmental Medicine RJ Lee Group, Registered Professional Engineer Weill Consulting Group, Principal University of Maryland, Department of Geology, Professor Emerita
Eric Louis Anthony Dan Dale Jacques Bradley Murray Shannon David Graham Robert Uschi Alessandro Mickey Martin Philip Matthew Dana John Annie Agnes John Jessica Art	Chatfield Cox Crane Drysdale Dunnigan Erskine Finkelstein Gaffney Garabrant Gibbs Glenn Graham Gualtieri Gunter Harper Hibbs Hinck Hollins Hoskins Jarabek Kane Kelse Kogel Langer	
Erell Morton Bian	Leocat Lippmann Liu	
Jeff Gary Roger Brooke Kenneth A. Robert P. Gunter Tim Doug Susan Dennis Julie Fred S. P. Vivek Chandra Alan Rick Victor Matthew S. Alan Balazs Mark Drew David Ann	Mandel Marsh McClellan Mossman Mundt Nolan Oberdorster Oury Palmore Pastula Paustenbach Pier Pooley Rao Rogers Rogers Roggli Sanchez Segrave Toth Utell Van Orden Weill Wylie	

## Individual publications with abstracts



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## THE MONTICELLO CONFERENCE ON ELONGATED MINERAL PARTICLES

Edited by David Weill, Eric Chatfield, Graham Gibbs, Ann Wylie

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Conference list

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Editorial Board

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## Proceedings of The Monticello Conference on Elongate Mineral Particles (EMP)

David Weill

Pages 1-2

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*Session I Defining EMPs Moderator: Ann Wylie ; Rapporteurs: Christy Barlow, Bob Nolan, Alan Rogers*

Research article ☐ Abstract only

## Characterization of asbestiform glaucophane-winchite in the Franciscan Complex blueschist, northern Diablo Range, California

Bradley G. Erskine, Mark Bailey

Pages 3-13

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Abstract

## Abstract


This paper presents a geologic and mineralogical investigation of asbestiform amphibole from blueschist in the Diablo Range, northern California. The analysis of fibers in air samples shows that the dominant blueschist amphibole composition ranges from glaucophane to subordinate winchite. In outcrop, blueschist amphibole exhibits a velvety luster, and its occurrence ranges from crosscutting veins to highly deformed foliated and lineated tectonites. TEM and SEM photographs reveal a highly fibrous habit typically associated with asbestiform amphiboles. Dimensional analysis reveals a mean fiber width of 0.27  $\mu\text{m}$ , and lengths and aspect ratios are shorter than reported for commercially exploitable asbestos, with a mean length of 2.8  $\mu\text{m}$  and mean aspect ratio of 11.5. The data are consistent with other research showing that the width

Research article ☐ Abstract only

## Measuring EMPs in the lung what can be measured in the lung: Asbestiform minerals and cleavage fragments

Victor L. Roggli

Pages 14-17

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### Abstract

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#### Abstract

Asbestos mineral fibers have been associated with the development of a variety of diseases in humans and experimental animals, including asbestosis, lung cancer, and mesothelioma. Asbestos includes several mineral types divided into two mineral groups, serpentine and amphibole forms. Chrysotile is the serpentine mineral classified as asbestos, whereas the amphiboles include amosite, crocidolite, tremolite, actinolite and anthophyllite.

There are a number of mineral fibers that occur with asbestiform morphology and that have been associated with various asbestos-induced diseases. These include the Libby amphiboles (associated with a vermiculite mine northwest of Libby, MT), erionite (in Turkey and North

Research article ○ Abstract only

## Characterization of lung burden EMPs

F.D. Pooley

Pages 18-20

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### Abstract

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#### Abstract

The physical characterisation of retained EMPS is extremely important in providing information regarding the aetiology of the disease they may produce. It is now accepted that the biological effects fibres may produce in lung tissue once deposited are closely related to their concentration but more critically to their variation in length and diameter. To assess the disease risk of exposure to EMPs it is necessary to accurately describe their lengths and diameter distribution.


Microscopic examination of lung burden and respirable airborne dust samples of EMPs are therefore among the most important investigations necessary to assess the risks of exposure to

Research article ○ Abstract only

## Identification and analysis of ambient EMPs

Drew R. Van Orden

Pages 21-26

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### Abstract

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#### Abstract

Mineral particles have long been observed in the ambient air and for >40 years, samples of these airborne particulate have been collected in attempt to identify and quantify the amount of asbestos particles in the air. For most of this time, regulated asbestos particles (in the shape of fibers) were the target for these analyses. However, since the turn of the century, more emphasis has been placed on finding and identifying elongate mineral particles (EMPs). For EMPs (particularly serpentine and amphibole minerals), these airborne particles have generally been associated with industrial activities and were reported as “asbestos”. Recent monitoring around construction activities involving earth moving have reported concentrations of different mineral particles at sites of varying distance from the activity. The location of detected

Research article ○ Abstract only

## Dosimetry of inhaled elongate mineral particles in the respiratory tract: The impact of shape factor

Bahman Asgharian, T. Price Owen, Eileen D. Kuempel, Annie M. Jarabek

Pages 27-35

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### Abstract

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#### Abstract

Inhalation exposure to some types of fibers (e.g., asbestos) is well known to be associated with respiratory diseases and conditions such as pleural plaques, fibrosis, asbestosis, lung cancer, and mesothelioma. In recent years, attention has expanded to other types of elongate mineral particles (EMPs) that may share similar geometry with asbestos fibers but which may differ in mineralogy. Inhalability, dimensions and orientation, and density are major determinants of the aerodynamic behavior for fibers and other EMPs; and the resultant internal dose is

recognized as being the critical link between exposure and pathogenesis. Insufficient data are available to fully understand the role of specific physicochemical properties on the potential

Research article ○ Abstract only

## Measurement of elongate mineral particles: What we should measure and how do we do it?

Eric J. Chatfield

Pages 36-46

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### Abstract

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#### Abstract

The length distributions of single fibrils of Coalinga, UICC-B and wet dispersed chrysotile were measured by transmission electron microscopy (TEM). It was found that the distributions significantly diverged above approximately 10  $\mu\text{m}$  ( $\mu\text{m}$ ) in length, corresponding to differences in published results of animal experiments. This result is in contrast to published data in which counting of an insufficient number of fibers resulted in an erroneous conclusion that the length distribution of Coalinga chrysotile fibrils was indistinguishable from those of other sources of chrysotile.

The size distributions of the respirable particle size fractions from acknowledged tremolite

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## Session I: Defining Elongated Mineral Particles (EMPs)

Pages 47-49

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*Session II Effects and Mechanisms Moderator: Roger McClellan Rapporteurs: Eric Chatfield, Murray Finkelstein, Victor Roggli*

Research article ○ Abstract only

## Predicting EMP hazard: Lessons from studies with inhaled fibrous and non-fibrous nano- and micro-particles

Günter Oberdörster, Uschi Graham

Pages 50-61

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## Abstract

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### Abstract

Inhalation exposure to elongated cleavage fragments occurring at mineral and rock mining and crushing operations raises important questions regarding potential health effects given their resemblance to fibers with known adverse health effects like amphibole asbestos. Thus, a major goal for establishing a toxicity profile for elongate mineral particles (EMPs) is to identify and characterize a suspected hazard and characterize a risk by examining together results of hazard and exposure assessment. This will require not only knowledge about biokinetics of inhaled EMPs but also about underlying mechanisms of effects induced by retained EMPs. In vitro toxicity assays with predictive power for in vivo effects have been established as useful screening tools for toxicological characterization of particulate materials including EMPs

Research article ☐ Abstract only

### Mechanistic *in vitro* studies: What they have told us about carcinogenic properties of elongated mineral particles (EMPs)

Brooke T. Mossman

Pages 62-67

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## Abstract

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### Abstract

*In vitro* studies using target and effector cells of mineral-induced cancers have been critical in determining the mechanisms of pathogenesis as well as the properties of elongated mineral particles (EMPs) important in eliciting these responses. Historically, *in vitro* models of 'mutagenesis' and immortalized cell lines were first used to test the theory that EMPs were mutagenic to cells, and 'genotoxicity', as defined as damage to DNA often culminating in cell death, was observed in a dose-dependent fashion as responses of many cell types to a number of EMPs. As two-stage and multi-step models of cancer development emerged in the 1970s and 1980s, differentiated 3D organ cultures and monolayers of lung epithelial and mesothelial cells were used to probe the mechanisms of cancer development. These studies demonstrated a

Research article ☐ Abstract only

## The asbestos-carbon nanotube analogy: An update

Agnes B. Kane, Robert H. Hurt, Huajian Gao

Pages 68-80

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### Abstract

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#### Abstract

Nanotechnology is an emerging industry based on commercialization of materials with one or more dimensions of 100 nm or less. Engineered nanomaterials are currently incorporated into thin films, porous materials, liquid suspensions, or filler/matrix nanocomposites with future applications predicted in energy and catalysis, microelectronics, environmental sensing and remediation, and nanomedicine. Carbon nanotubes are one-dimensional fibrous nanomaterials that physically resemble asbestos fibers. Toxicologic studies in rodents demonstrated that some types of carbon nanotubes can induce mesothelioma, and the World Health Organization evaluated long, rigid multiwall carbon nanotubes as possibly carcinogenic for humans in 2014. This review summarizes key physicochemical similarities and differences

Research article   ☐ Abstract only

## A case study of the translocation, bioprocessing and tissue interactions of EMP following inhalation exposure

Uschi M. Graham, Günter Oberdörster, Bruce Case, Alan Dozier

Pages 81-88

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### Abstract

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#### Abstract

Human autopsied lung sections from a resident in the Quebec asbestos region were examined. The study utilized high resolution transmission electron microscopy, scanning transmission electron microscopy (HRTEM/STEM) with the analytical capabilities of electron energy loss spectroscopy (EELS) and energy dispersive spectroscopy (EDS) detectors. We report the first analytical ultrastructural characteristics of EMPs, detailing chemical concentration gradients inside the iron-protein coatings and lateral elemental gradients in the local tissue regions. It is shown that the EMPs are subjected to bioprocessing which involves physicochemical transformations and also an elemental transport mechanism that alters the inhaled EMP as

Research article ○ Abstract only

## Towards a quantitative model to predict the toxicity/pathogenicity potential of mineral fibers

Alessandro F. Gualtieri

Pages 89-98

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### Abstract

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### Abstract

Some mineral fibers represent a health hazard because they are classified as cancer-causing chemical/physical toxicants upon (chronic) dust inhalation. Although in the last decades they have been the subject of intensive multidisciplinary investigations, the mechanisms by which mineral fibers induce toxic and pathogenic adverse effects on human health and environment are not yet fully understood. The major intricacy of the biological approach that prevents the design of a conclusive shared model of behavior of mineral fibers in a biological system stems from their very nature with intrinsic variability in chemical, molecular, structural and morphometric parameters, biodurability and surface reactivity.

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### Session II: Effects and Mechanisms

Page 99

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*Session III Human Exposure, Effects and Risks Moderator: Graham Gibbs Rapporteurs: Wayne Berman, Philip Hibbs, Morton Lippmann*

Research article ○ Abstract only

## The epidemiologic evidence for elongate mineral particle (EMP)-related human cancer risk

Paolo Boffetta, Kenneth A. Mundt, William J. Thompson

Pages 100-106

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### Abstract

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## Abstract

Epidemiologic research on the role of fibers and other elongate mineral particles (EMP) and human diseases including cancers has generated a large body of literature over the last decades; nevertheless, there remain some questions for which the scientific community appears unable to reach consensus. Reasons for genuine differences in opinion include (i) ways in which exposures have been classified; (ii) methodological limitations of the available studies, (iii) criteria for the interpretation of study results, including potential underlying biological mechanisms, and (iv) methodology for integrating the evidence. Various approaches have been proposed in recent years to address these issues, which will be illustrated using examples from asbestos, talc, taconite, synthetic mineral fibers and silicon carbide, with emphasis on potential

Research article ○ Abstract only

### Mesothelioma and other lung disease in taconite miners; the uncertain role of non-asbestiform EMP

Jeffrey H. Mandel, Nnaemeka U. Odo

Pages 107-112

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## Abstract

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## Abstract

The purpose of this paper was to assess the role of non-asbestiform amphibole EMPs in the etiology of mesotheliomas and other lung disease in taconite (iron ore) miners. Increased mesothelioma rates have been described in Minnesota taconite workers since the late 1990s. Currently, over 100 cases have been reported by the Minnesota Department of Health within the complete cohort of miners in Minnesota. Geologic sampling has indicated that only the eastern part of the iron range contains non-asbestiform amphibole elongate mineral particles (EMPs), in close proximity to the ore. This type of EMP has been less studied and also exists in talc and gold mining. A series of investigations into the state's taconite industry have been recently completed. Results from a cohort mortality study indicated an SMR of 2.77 (95%

Research article ○ Abstract only

### Refractory ceramic fibers: Fiber characteristics, potential health effects and clinical observations

Mark J. Utell, L.Daniel Maxim

Pages 113-117



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## Abstract

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### Abstract

Refractory ceramic fibers (RCFs) are amorphous fibers that belong to a class of materials termed synthetic vitreous fibers (SVFs), also called man-made mineral fibers (MMMFs), which includes alkaline earth silicate wool, glass wool, rock (stone) wool, slag wool, and special-purpose glass fibers. RCFs are more durable and biopersistent than several other SVFs, although very much less biopersistent than either amosite or crocidolite asbestos. Chronic inhalation studies indicated that rats and hamsters exposed to RCF fibers developed fibrosis and tumors. Epidemiological studies at the University of Cincinnati funded by the Industry indicated that exposed workers; (1) exhibited symptoms (e.g., dyspnea) similar to those reported in other dust-exposed populations (2) developed statistically but not clinically significant

Research article ☐ Abstract only

### Chrysotile and chrysophosphate chemical modification of the chrysotile surface and its effect on biological behavior

A.M. Langer, R.P. Nolan

Pages 118-126

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## Abstract

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### Abstract


Chrysotile asbestos was reacted with phosphorus oxychloride (POC) gas to produce a chemically modified fiber referred to as chrysophosphate. The presence of phosphorus and chlorine on the fiber surface and in small fiber bundles was verified by means of energy dispersive x-ray spectrometry and laser mass spectrometry. The altered fiber exhibits different physical-chemical properties when compared with the unaltered precursor material. In addition to marked surface changes, fibrils of the reacted material appear to be cross-linked increasing the size of particulates, fiber bundles and increasing their mechanical stability. The reacted specimens exhibit fewer fibrils reducing their surface area.

Research article ☐ Abstract only

## A comparison of asbestos fiber potency and elongate mineral particle (EMP) potency for mesothelioma in humans

David H. Garabrant, Susan T. Pastula

Pages 127-136

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### Abstract

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### Abstract

We analyzed the mesothelioma mortality in cohorts of workers exposed to crocidolite, amosite, and chrysotile to estimate asbestos fiber potency for mesothelioma, using the method of Hodgson and Darnton (2000). We relied on the original 17 cohort studies in their analysis, along with 3 updates of those studies and 3 new asbestos cohort studies published since 2000. We extended the analyses to examine the mesothelioma potency of tremolite in vermiculite from Libby, Montana, and for non-asbestiform elongate mineral particles (EMPs) in taconite iron ore, talc, and South Dakota gold mining. Mesothelioma potency ( $R_{\text{Meso}}$ ) was calculated as the percent of all expected deaths that were due to mesothelioma per fiber/cc-year of exposure. The  $R_{\text{Meso}}$  was 0.0012 for chrysotile, 0.009 for amosite, and 0.451 for crocidolite; thus

Research article   ☐ Abstract only

## Biological mechanisms of non-linear dose-response for respirable mineral fibers

Louis Anthony (Tony) Cox

Pages 137-144

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### Abstract

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### Abstract

Sufficiently high and prolonged inhalation exposures to some respirable elongated mineral particles (REMPs), notably including amphibole asbestos fibers, can increase risk of inflammation-mediated diseases including malignant mesothelioma, pleural diseases, fibrosis, and lung cancer. Chronic inflammation involves ongoing activation of the NLRP3 inflammasome, which enables immune cells to produce potent proinflammatory cytokines IL-1 $\beta$  and IL-18. Reactive oxygen species (ROS) (in particular, mitochondrial ROS) contribute to NLRP3 activation via a well-elucidated mechanism involving oxidation of reduced thioredoxin and association of thioredoxin-interacting protein with NLRP3. Lysosomal destabilization,

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### Session III: Human exposure, effects & risk

Pages 145-148

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*Session IV Future Research Moderator: David Weill Rapporteurs: Robert Glenn, Brooke Mossman, Günter Oberdörster*

Research article ○ Abstract only

### Analysis and identification of elongated mineral particles in road coated aggregates

Erell Leocat, Christophe Rielland, Patrice Letessier

Pages 149-154

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#### Abstract

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#### Abstract

The issue of Elongated Mineral Particles (EMP) in building materials has been revealed during roadworks in 2013 in France. In fact, road coating aggregates are made of specific rock gravels that can contain Naturally Occurring Asbestos (NOA), which is mainly actinolite. The legislation refers to six regulatory asbestos, that consist in asbestiform habitus of the six minerals. The current technical standard is not adapted for analyzing natural material, as it cannot distinguish the asbestiform fibers and the cleavage fragments fibers. Therefore, the Eichrom Laboratories developed an internal method for analyzing rock gravel and identifying the different kind of EMP. This analytical method is based on an accurate sample preparation and three techniques at different resolutions: a petrological analysis with a stereomicroscope, a

### *Session V Additional Manuscripts and Abstracts*

Research article ○ No access

Does qualitative examination of Elongated Mineral Particles (EMP) recovered from human and animal lungs provide reliable information on their carcinogenic and other effects?

Bruce W. Case

Pages 155-156

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## Elongate mineral particles in the natural environment

Mickey E. Gunter

Pages 157-164

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### Abstract

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#### Abstract

When considering elongate mineral particles (EMPs) in the natural environment it is important to first: 1) define what an elongate mineral is and 2) present what we as mineralogists and geologists know about their distribution. However, it is often very difficult to define the natural world, instead we physical scientists resort to describing it. For instance, we used 1,419 words spread over two pages of our mineralogy textbook (Dyar and Gunter, 2008) to describe a mineral. On the other hand, elongate has a rather simple non-quantitative definition as a particle longer than it is wide; however, to quantify it, we must select an aspect ratio. Clearly the term EMP was coined with the hopes to simplify some of the confusion resulting in the differing “meanings” of such words as asbestos, asbestiform, acicular, and most importantly

Research article ○ Abstract only

## OSHA and elongate mineral particles

Daniel T. Crane

Pages 165-167

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### Abstract

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#### Abstract

The United States Occupational Safety and Health Administration (OSHA) was established to provide guidance to protect workers from hazards in the workplace. After broadly adopting extant health and safety standards, OSHA promulgated an expanded standard for regulation of asbestos. This standard provided for regulation of six named minerals and practices to be followed. Since the initial establishment of asbestos regulation by OSHA, other elongate particles have been considered for evaluation. This discussion describes the evolution of the OSHA regulations for asbestos, what they cover and how other materials might be regulated if they are found to pose a health risk.

Research article ○ Abstract only

## Exposures estimates of the Wittenoom mining workforce and town residents – Implications associated with risk estimation for persons exposed to asbestiform riebeckite

Alan John Rogers

Pages 168-170

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### Abstract

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#### Abstract

The mining of crocidolite at Wittenoom from 1943 to 1966 is infamous due to the adverse health outcomes in the mining and milling workforce and the non-mining residents and families. Proportional latency risk analysis provided estimates that 6% of the mine workforce along with 1.9% of women and 1.1% of children residents who were environmentally exposed, have or will die from mesothelioma. The absence of environmental exposure data relevant to the period restricts the extrapolation of these historical risk outcomes being applied to the low level exposures from natural contaminant crocidolite and other amphibole fibres experienced in contemporary mining practices in the Pilbara region.

Research article ○ Abstract only

## Chrysotile asbestos cement and the Grenfell Tower fire

John A. Hoskins

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### Abstract

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#### Abstract

On 14 June 2017, a fire broke out at Grenfell Tower: a residential block in North Kensington, London, UK. Soon the whole tower was ablaze and it took firefighters over 24 h to get the fire under control. Some 71 people were confirmed or presumed dead and around 70 injured. Among the many reasons given for the blaze none discuss why a Tower Block, constructed in 1974, from materials whose fire safety had been checked was recently refurbished with materials considered by many to be flammable.

The frame of the tower had curtain walls, originally finished with 6 infill panels constructed from 4 glass windows and two 3 ply composite panels constructed with chrysotile cement.

Conference abstract ○ No access

The occurrence of pneumoconiosis in a talc mining population exposed to non-asbestos elongate mineral particle

John Kelse

Page 172

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Research article ○ No access

The mineralogy and epidemiology of cosmetic talc

Christy A. Barlow, Gary M. Marsh, Stacey Benson, Brent L. Finley

Page 173

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## APPENDIX

Research article ○ Abstract only

Standardized methods for preparation and bi-variate length & diameter counting/sizing of aerosol and tissue digestion fiber samples

David M. Bernstein, Peter Kunzendorf

Pages 174-184

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## Abstract

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### Abstract

Most fiber length distributions fit a log-normal distribution with their being many more shorter fibers present as compared to the longer fibers. As the longer fibers have been suggested to be more important for possible pathogenesis giving equal weight to all fiber lengths when sizing fibers will under sample the longer fibers. The methods described here, are based upon the optimization of fiber counting/sizing rules over a number years of experience and have been developed to provide a stable estimate of the mean number of particles and fibers present in the size ranges: particles, fibers <5  $\mu\text{m}$ ; 5–20  $\mu\text{m}$ ; and >20  $\mu\text{m}$ . These methods were first applied using TEM, however, with the development of high resolution SEM it was found that higher reproducibility could be obtained with SEM

- Full text access

## Universe of Particles

Kelly Bailey, Eric Chatfield, Graham Gibbs, Ann Wylie

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