Protecting the health and safety of nanomaterial workers: a progress report

Paul A. Schulte, Ph.D.
Charles L. Geraci, PH.D., CIH

Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

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Basis for concern about health and safety effects of nanoparticles

- **Findings from air pollution epidemiology**
  - Particles < 2.5 µm associated with respiratory and cardiovascular effects

- **Studies of industrial fumes (e.g., welding fumes) and combustion (e.g., diesel) products**
  - Wide range of effects: pulmonary and eye irritation, fever, lung cancer

- **Initial animal inhalation studies of engineered nanomaterials**
  - Pulmonary fibrosis, granulomas, and inflammation
  - Lung cancer, mesothelioma-like effects
  - Cardiovascular effects: oxidative stress, plaque
Why the workplace?

- First point of potential exposure
- Exposure concentration greatest
- Early in the history of a material
- “Workplace” = R&D, Scale Up/Pilot, Manufacture, Use, Disposal
<table>
<thead>
<tr>
<th>Sector: Materials</th>
<th>Nanomaterial Type</th>
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<tbody>
<tr>
<td>Workplaces</td>
<td>Carbon Nanotubes</td>
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<td>Metal Oxides</td>
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<td>Dendrimers</td>
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<td>Fullerenes</td>
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<td>Metal Nanomaterials</td>
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<td>Nanowires</td>
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<td>Nanostructured Metals</td>
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<td>Nanoporous Materials</td>
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<td>Nanoscale Encapsulation</td>
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</table>

- Laboratory Research
- Start up/Pilot
- Manufacturing
- Production
- Disposal
- etc.
Major knowledge gaps related to nanotechnology health and safety

Hazard Identification
Is there reason to believe this could be harmful?

Exposure Assessment
Will there be exposure in real-world conditions?

Risk Characterization
Is substance hazardous and will there be exposure?

Risk Management
Develop procedures to minimize exposures

Approaches to Safe Nanotechnology (DHHS (NIOSH) Publication 2009-125)
Key elements in worker protection

**Hazard**

Nanotoxicology
What do we know?
Are there “trends?”

**Hazard Identification**
“Is there reason to believe this could be harmful?”

**Exposure Assessment**
“Will there be exposure in real-world conditions?”

**Risk Characterization**
“Is substance hazardous and will there be exposure?”

**Risk Management**
“Develop procedures to minimize exposures.”
Nanotoxicology: key findings

Pulmonary exposure to:

- Carbon nanotubes causes rapid and persistent fibrosis in mice

- Certain nanoparticles (SWCNT or TiO$_2$) can cause cardiovascular dysfunction

- MWCNT or TiO$_2$ nanowires can induce inflammatory mediators in certain regions of the brain

Courtesy of R. Mercer, NIOSH
Nanotoxicology: key findings

Carbon nanotubes

- Multi-walled nanotubes can reach the intrapleural space (site of mesotheliomia)
- Single-walled nanotubes can interfere with cell division

Courtesy of R. Mercer, NIOSH
What could a “nanoparticle” be?

**Particle Categories**
Classes of engineered nanoparticles

A. Spherical homogeneous
B. Fibrous homogeneous
C. Non-spherical homogeneous
D. Agglomerate homogeneous
E. Heterogeneous concentric
F. Heterogeneous distributed
G. Heterogeneous agglomerate
H. Active particle
I. Multifunctional particle
Same composition—different shape

Zinc oxide nanoparticles

Key elements in worker protection

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Exposure
Can it be measured?
Where is it occurring?
Metric?
Diverse exposure scenarios evaluated
Evidence of exposure

Weighing MWCNT’s

PBZ sample collected on a polycarbonate filter and analyzed by SEM
Evidence of exposure

Harvesting SWCNT’s, scraping product from wall of Carbon Arc Reactor

Task-based “At source” air sample
<table>
<thead>
<tr>
<th>Type of Facility</th>
<th>Type of Particle, Morphology</th>
<th>Size of Particle</th>
<th>Range of “Potential” Exposure Concentrations</th>
</tr>
</thead>
<tbody>
<tr>
<td>University Research lab</td>
<td>Carbon Nanofibers</td>
<td>Approx. 100 nm diameter, 1–10 microns long</td>
<td>60-90 µg/m³ Total Carbon</td>
</tr>
<tr>
<td>Metal Oxide Manufacturer</td>
<td>TiO₂, Lithium Titanate, powder</td>
<td>100–200 nm</td>
<td>&lt;100 nm: 1.4 µg/m³ (TiO₂) Total dust: 4-149 µg/m³ (TiO₂) &lt;100 nm: ND (Li) Total dust: ND -3 µg/m³ (Li)</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>Carbon Nanofibers</td>
<td>Approx. 100 nm diameter, 1–10 microns long</td>
<td>15 - 1800 µg/m³ Total carbon</td>
</tr>
<tr>
<td>Research and Development lab</td>
<td>Quantum Dots, spheres</td>
<td>2–8 nm</td>
<td>ND</td>
</tr>
<tr>
<td>Metal Oxide Manufacturer</td>
<td>Manganese, Silver, Nickel, Cobalt, Iron oxides, spheres</td>
<td>8–50 nm</td>
<td>67 - 3619 µg/m³ Mg, Ag, Ni, Co, Fe</td>
</tr>
<tr>
<td>Research and Development lab (Pilot-Scale)</td>
<td>Aluminum, spheres</td>
<td>50–100 nm</td>
<td>40 - 276 µg/m³ Al</td>
</tr>
<tr>
<td>Research and Development lab</td>
<td>Elemental metals: Silver, copper, TiO₂</td>
<td>15–40 nm</td>
<td>ND</td>
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<tr>
<td>Filter Media Manufacturer</td>
<td>Nylon 6 Nanofiber</td>
<td>70–300 nm diameter, continuous length</td>
<td>ND</td>
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</table>
Recent published summary of field exposure assessments

*Nanoparticle Emission Assessment Technique (NEAT) for the Identification and Measurement of Potential Inhalation Exposure to Engineered Nanomaterials — Part A*

and

*Part B: Results from 12 Field Studies*

M. Methner, L. Hodson, C. Geraci

National Institute for Occupational Safety and Health (NIOSH), Nanotechnology Research Center, Cincinnati, Ohio
Collaboration

- Share knowledge
- Use expertise
- Build experience
- Partner

The NIOSH Nanotechnology field team is available for field assessments. Contact us.
Key elements in worker protection

- **Hazard Identification**
  “Is there reason to believe this could be harmful?”

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  “Will there be exposure in real-world conditions?”

- **Risk Characterization**
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- **Risk Management**
  “Develop procedures to minimize exposures.”

Risk: Hazard x Exposure
Quantitative Risk Assessment in developing Recommended Exposure Limits for nanoparticles

**Rat**

- Dose-response model (*particle surface area dose in lungs*)
- Calculate tissue dose -- BMD

**Human**

- Recommended exposure limit
- Working lifetime exposure concentration*
- Equivalent tissue dose
- Technical feasibility
- Variability/uncertainty

*Compare rat-based risk estimates with confidence intervals from human studies

Assume equal response to equivalent dose

**Human lung dosimetry model**

*Species differences in lung mass or surface area*
Risk Assessment: ultrafine (nano) TiO$_2$

- NIOSH draft recommended exposure limits (RELs)
  - 1.5 mg/m$^3$ fine TiO$_2$
  - 0.1 mg/m$^3$ ultrafine TiO$_2$
  - Reflects greater inflammation & tumor risk of ultrafine on mass basis

- This recommendation will be released from NIOSH in the Autumn of 2010

- Key message: The OEL for a material in its “large” form may not be appropriate for the nano form.
Hazard and risk picture: carbon nanotubes

- SWCNTs more fibrogenic then an equal mass of ultrafine carbon black or fine quartz
- Doses approximated exposure at the PEL for graphite (5 mg/m$^3$) for 20 days
- MWCNT can penetrate the pleura
  - More data needed
- Similar message: The OEL for the “large” form of a material may not be a good guide for the nano form.

Key NIOSH project: Current Intelligence Bulletin on Carbon Nanotubes

Key responses: Industry OELs
Key elements in worker protection

Recognize and Manage Risk

- What works?
- What has been used?
- What can be reapplied?

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Conventional controls should work

Exhaust Ventilation
Capture
Inertia Dominants
Diffusion Dominates

About 1 nm
200 to 300 nm
Most Fine Dusts
Micro Scale

No Capture
Air Stream
Filtration performance of an example NIOSH approved N95 filtering facepiece respirator

n=5; Error bars represent standard deviations
TSI 3160; Flow rate 85 L/min
Basic Guidance from NIOSH

- Updated and re-issued in 2009
- Based on direct experience and applied research results
- Updated as new information is developed
- A starting point for building a responsible nanomaterial management program

www.cdc.gov/niosh/topics/nanotech
Interim guidance issued by NIOSH

- Value of medical screening
- Lack of specific health end point
- Hazard Surveillance
- Potential for Exposure Registry
Nanotechnology Conference: Medical Surveillance, Exposure Registries and Epidemiological Research for Workers Exposed to Nanomaterials | CDC/NIOSH

NIOSH Safety and Health Topic:

Nanotechnology

Nanomaterials and Worker Health: Medical Surveillance, Exposure Registries, and Epidemiologic Research

July 21-23, 2010
Keystone Conference Center

Invitation

The National Institute for Occupational Safety and Health (NIOSH) and the Mountain and Plains Education and Research Center invite you to attend the conference on "Nanomaterials and Worker Health: Medical Surveillance, Exposure Registries, and Epidemiologic Research." The conference will be held on July 21–23, 2010, at the Keystone Resort and Conference Center in Keystone, Colorado.

The aim of the conference is to identify gaps in information and address questions focusing on occupational health surveillance, exposure registries, and epidemiologic research involving nanotechnology workers. In each of these areas, this conference will:

- Share existing knowledge;
- Identify major issues;
- Examine successful approaches;
- Explore new approaches, techniques, and models.

This conference will enable members of the occupational safety and health community concerned with nanomaterials and the health of workers exposed to these materials to address fundamental questions and seek practical solutions for carrying out occupational health surveillance, developing exposure registries, and conducting epidemiological research. The conference will include invited and submitted papers, breakout sessions to allow for small group discussions, and poster presentation.

http://www.cdc.gov/niosh/topics/nanotech/keystone2010/default.html
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- Sector: **Materials**
- Sector: **Energy**
- Sector: **Food**
- Sector: **Electronics**
- Sector: **Medicine**

etc.
Dilemmas in identifying workers exposed to engineered nanoparticles

Schulte, 2009

Estimated number of workers actually exposed to engineered nanoparticles

Global employment est. (Roco & Bainbridge, 2005)

USA employment est.

Number of Workers Exposed

10,000,000

1,000,000

100,000

10,000

1000

1959

1990’s

2000

2010

2015

2025

Feynman’s vision

Beginning of commercialization

Schulte, 2009
Exposure registries

- Used in public health for over 50 years
- May serve as a societal response to hazardous exposures
- May serve as preparatory step for epidemiological studies
Questions about exposure registries

- Who would manage them?
- What data would be collected?
- Who would have access to the data?
- Could any investigator with a research proposal have access to the registry?
- Are there non-research implications and responsibilities for those who manage registries?
- Are there expectations for those who participate in them?
Thank you!

Pschulte@cdc.hhs.gov