NIOSH Guidance on Nanotechnology: Protecting Our Workers

Charles L. Geraci, Ph.D., CIH

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

The findings and conclusions in this presentation have not been formally disseminated by the National Institute for Occupational Safety and Health and should not be construed to represent any agency determination or policy.
The National Institute for Occupational Safety and Health

The U.S. Federal agency responsible for conducting research and making recommendations for the prevention of work-related injury and illness.

Mission: Generate new knowledge; convert research to practice; and collaborate globally to prevent work-related illnesses and injuries.
You have heard what nanotechnology is, now what will it do?

Anything you can imagine can be made faster, stronger, smarter, smaller, better, etc., using nanomaterial science. So, nanotechnology is coming to you, as a producer, as a user or as a consumer.

Will nanotechnology “change life” as we know it?

It has the potential, but where will we encounter it first? The Workplace!
Nanotechnology and Occupational Health

- **Nanotechnology - The Motivation**
  - Purposely *engineered* for their unique and size-dependent properties and behavior.

- **Nanotechnology - The Challenge**
  - Do these new ‘nano’ materials present new *safety and health risks*?
  - How can the benefits of nanotechnology be realized while proactively *minimizing the potential risk*?
# How Diverse is the Nanotechnology Workplace?

**Current Uses and Applications of Nanotechnology**

<table>
<thead>
<tr>
<th>Category</th>
<th>Uses and Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agriculture</td>
<td>Pesticides and fertilizers</td>
</tr>
<tr>
<td>Automotive</td>
<td>Composites, epoxies, films</td>
</tr>
<tr>
<td>Biomedical</td>
<td>Diagnostics, drug delivery</td>
</tr>
<tr>
<td>Chemical</td>
<td>Catalysts, polymer films, coatings</td>
</tr>
<tr>
<td>Electronics</td>
<td>Catalysts, polymer films, coatings, fiber optics</td>
</tr>
<tr>
<td>Energy</td>
<td>Catalysts, lithium batteries, fuel additives</td>
</tr>
<tr>
<td>Environmental</td>
<td>Sensors, catalysts</td>
</tr>
<tr>
<td>Food</td>
<td>Additives, packaging materials, antimicrobial</td>
</tr>
<tr>
<td>Household</td>
<td>Antimicrobials, cleaners, coatings, appliances</td>
</tr>
<tr>
<td>Personal Care</td>
<td>Cosmetics, sunscreens, hair/skin products</td>
</tr>
<tr>
<td>Sports</td>
<td>Composites for bats and golf clubs, shoes</td>
</tr>
<tr>
<td>Textiles</td>
<td>Water/stain resistance, wrinkle-free, fire resistance</td>
</tr>
</tbody>
</table>
The Focus: Free Engineered Nanoscale Particulate Matter—“Nanoparticles”

- Not firmly attached to a surface
- Not part of a bigger item (e.g., microchip, cell wall)
- Can result in exposure via inhalation, skin absorption or ingestion (or other nanospecific routes of exposure!)
The Charge to NIOSH
Nanotechnology: Are There Risks?

RISK = HAZARD X EXPOSURE

**Hazard:** Biological activity – toxicity. What is known and is there anything new?

**Exposure:** Where, to what, to what extent, and can it be measured?

Unknows and uncertainties = Risk Management approach


Key Elements of Risk Management

**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”
Risk Management of Engineered Nanoparticles:

The Simple Questions

**Are they hazardous?**

**Can they be measured?**

**Can they be controlled?**

---

**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”

---

Adapted from Gibbs, 2006
What is Needed:

- Good Science
- The Right Science
- Proper Interpretation
- Share and Apply
NIOSH Goals Involving Nanotechnology

- **Hazard Assessment**: Determine whether nanoparticles and nanomaterials pose risk of injuries and illnesses to workers

- **Risk Assessment**: Conduct research to develop a dose-response value and any correlation to human experience

- **Risk Management**: Promote healthy workplaces through interventions, recommendations, and capacity building

- **Collaboration**: Enhance global workplace safety and health through national and international collaboration on nanotechnology

Create a prudent and reasonable approach
Key areas of NIOSH research supporting the Risk Management process

Hazard Identification
“Is there reason to believe this could be harmful?”
- Toxicology
- Health Effects Assessment
- Safety Research

Hazard Characterization
“Under what conditions could it be harmful?”
- Toxicology
- Field Assessment
- Chemical and Physical Characteristics

Exposure Assessment
“Will there be exposure in real-world conditions?”
- Field Exposure Assessment
- Process Descriptions
- Control Technology Research
- Personal Protective Equipment (PPE) Research

Risk Characterization
“Is substance hazardous and will there be exposure?”
- Risk Assessment- Dose and Duration
- Dose Modeling
- Exposure Characterization

Risk Management
“Develop procedures to minimize exposures”
- Risk Communication
- Guidance Documents
- Information Dissemination
Challenge: The diversity of “Nanomaterial Production and Use”
To evaluate the ‘workplace’, A Life Cycle Approach is needed.
To evaluate the ‘workplace’, a Life Cycle Approach is needed.
Nanotoxicology

“Are nanoparticles hazardous?”
Predicted Deposition of Inhaled Particles in the Human Respiratory Tract

ICRP (1994) model: adult, nose breathing, at rest
Parameters That Could Affect Nanoparticle Toxicity

- Size
- Shape
- Composition
- Solubility
- Crystalline structure
- Charge
- Surface characteristic
- Attached functional groups
- Agglomeration
- Impurities

Many may be the metrics for both hazard and exposure determination.
Size and Surface Area: Why so important?

Chemical, physical, and biological interactions take place on the surface of a particle.

Nanoparticles offer more of all of these. They also present new challenges in detecting and measuring these interactions.

<table>
<thead>
<tr>
<th>Particle Size (nm)</th>
<th>Fraction (%) of Molecules in Outer Layer</th>
</tr>
</thead>
<tbody>
<tr>
<td>2500 (2.5 µm)</td>
<td>&lt; 2 x 10^{-4}</td>
</tr>
<tr>
<td>1000 (1 µm)</td>
<td>&lt; 6 x 10^{-4}</td>
</tr>
<tr>
<td>100</td>
<td>0.006</td>
</tr>
<tr>
<td>10</td>
<td>0.06</td>
</tr>
<tr>
<td>1</td>
<td>48.8</td>
</tr>
</tbody>
</table>

Outer monolayer of molecules
Surface Area as a Dose Metric

- Toxicity of ultrafine TiO2 appears much higher than fine TiO2 per unit mass
- Toxicity is equivalent when surface area is the exposure metric

Measured polymorphonuclear neutrophils in lung lavage fluid, an index of inflammation

Oberdorster, Int Arch Occup Environ Health. 2001 Jan; 74(1):
Is one of these workers at greater risk for disease?

Bulk Material

Nano Sized Particles
Research Issues

- Pulmonary Deposition, Interstitialization and Translocation
- Pulmonary Toxicology
- Systemic Effects
- Dermal Effects
- Neural Uptake and Toxicology
- Dose Metric
Nanotoxicology Summary

- Nanoparticles under investigation
  - TiO$_2$, CB, SWCNT, MWCNT, metal oxides, nanowires, and nanospheres

- Target organs
  - lung, skin, brain, cardiovascular system

- End points
  - inflammation, oxidant stress, fibrosis, translocation

- Dose Metrics
  - Surface area
  - Correlate mass, size distribution and number
Rat lung cells cannot digest and clear long carbon nanotubes.

*D. Brown, Napier Univ. and I. Kinloch, Univ. Manchester*

*V. Castranova, NIOSH*
Intraperitoneal injection of MWCNTs to investigate possible mesothelial injury

- Pathogenic behavior related to length
- Inflammation and formation of granulomas
- Long CNT fibers more active than short fibers or bundles
- Mimics the same processes as asbestos?

- Starting point: short-term study
- Does not address migration from lung to mesothelium
- Will short CNTs have same effect?

Until more research can be conducted, a prudent approach is warranted

Using Graphite OEL as an exposure guideline would be inappropriate
Hazard and Risk Picture - Carbon Nanotubes

Aspiration of SWCNT resulted in:

- Rapid but transient inflammation and damage
- Granulomas and fibrosis at deposition sites of large agglomerates of SWCNT
- Rapid and progressive interstitial fibrosis at deposition sites of dispersed SWCNT
- Results were verified with inhalation study

Message:

- SWCNTs more fibrogenic than an equal mass of ultrafine carbon black or fine quartz.
- Doses approximated exposure at the PEL for graphite (5 mg/m3) for 20 days

Message: The PEL for the ‘large’ form of a material may not be a good guide for the nano form.
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
- [www.cdc.gov/niosh/review/peer/tio2/](http://www.cdc.gov/niosh/review/peer/tio2/)

Same message: The OEL for a material in its ‘large’ form may not be appropriate for the Nano form
Metrics and Measurements for Exposure Assessment

Can nanoparticles be measured?
Nanoparticles: Many shapes, many chemistries

Not all nanoparticles are the same
Carbon Nanotube Air Sample
Which metric to use?

0.18 – 0.32 μm aerodynamic diameter

- CNT agglomerates
- Compact carbon particle
- Dense nanotube rope
Characterization of nanoparticles in workplaces

A suite of techniques is used ...
Guidance on Exposure Monitoring
Simple Start to Complex Finish

Starting Point

Mass, Size Distribution, Surface Area, Etc.

TEM analysis of aerosol
The Hard Way
Are Workplace Exposures Occurring?
## DRAFT - Summary of Nanoparticle Measurements - DRAFT

<table>
<thead>
<tr>
<th>Type of Facility</th>
<th>Location</th>
<th>Type of Particle, Morphology</th>
<th>Singular, Agglomerated, or Both</th>
<th>Size of Particle</th>
<th>Range of “Potential” Exposure Concentrations (Duration of Task)</th>
<th>Nominal CPC particle counts 10-1,000 nm P/cc</th>
<th>Nominal Indoor background particle counts 10-1,000 nm P/cc</th>
<th>Nominal Outdoor background particle counts 10-1,000 nm P/cc</th>
</tr>
</thead>
<tbody>
<tr>
<td>University Research lab</td>
<td>OH</td>
<td>Carbon Nanofibers</td>
<td>Agglomerated</td>
<td>Approx. 100 nm diameter, 1-10 microns long</td>
<td>60-90 μg/m³</td>
<td>15,000</td>
<td>12,000</td>
<td>34,000</td>
</tr>
<tr>
<td>Metal Oxide Manufacturer</td>
<td></td>
<td>TiO₂, Lithium Titanate, powder</td>
<td>Both</td>
<td>100-200 nm</td>
<td>&lt;100 nm: 1.4 μg/m² (TiO₂) Total dust: 4 - 149 μg/m³ (TiO₂) &lt;100 nm: ND (Li) Total dust: ND - 3 μg/m³ (Li)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manufacturer</td>
<td>OH</td>
<td>Carbon Nanofibers</td>
<td>Both</td>
<td>Approx. 100 nm diameter, 1-10 microns long</td>
<td>15 - 1800 μg/m³</td>
<td>100,000 P/L 300-500 nm HHPC</td>
<td>12,000 P/L 300-500 nm HHPC</td>
<td>NA</td>
</tr>
<tr>
<td>Research and Development lab</td>
<td></td>
<td>Quantum Dots, spheres</td>
<td>ND</td>
<td>2 - 8 nm</td>
<td>ND</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metal Oxide Manufacturer</td>
<td>CA trip 1</td>
<td>Manganese, Silver, Nickel, Cobalt, Iron oxides, spheres</td>
<td>Both</td>
<td>8 - 50 nm</td>
<td>67 - 3619 μg/m³</td>
<td>7,000 - 75,000</td>
<td>10,000</td>
<td>15,000</td>
</tr>
<tr>
<td>Research and Development lab(Pilot-Scale)</td>
<td>CA trip 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>18,000 - 30,000</td>
<td>12,000</td>
<td>NA</td>
</tr>
<tr>
<td>Research and Development lab</td>
<td>NJ</td>
<td>Aluminum, spheres</td>
<td>Both</td>
<td>50-100 nm</td>
<td>40 - 276 μg/m³</td>
<td>13,000</td>
<td>2,500</td>
<td>3,800</td>
</tr>
<tr>
<td>Research and Development lab</td>
<td></td>
<td>Elemental Metals - Silver, Copper, TiO₂</td>
<td>ND</td>
<td>15 - 40 nm</td>
<td>ND</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filter Media Manufacturer</td>
<td>KY</td>
<td>Nylon 6 Nanofiber</td>
<td>ND</td>
<td>70 - 300 nm diameter, continuous length</td>
<td>ND</td>
<td>15,000- 33,000</td>
<td>6,000</td>
<td>NA</td>
</tr>
<tr>
<td>Pilot Scale</td>
<td>WI day 1</td>
<td>Silica iron coating for cellulose</td>
<td>Both</td>
<td>4 -70 nm</td>
<td>1 - 4 μg/m³</td>
<td>25,000</td>
<td>20,000</td>
<td>6,500</td>
</tr>
<tr>
<td></td>
<td>WI day 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8,000 - 12,000</td>
<td>2,000 -13,000</td>
<td>NA</td>
</tr>
</tbody>
</table>
CNF Air Sampling Results as Total Carbon (µg/m³)

- Cutting CNF composite
- Pouring CNF into plastic barrel
- Packaging orders (scooping material)
- Mixer/hopper

**R&D Lab**

**Mfg Process**
Did you detect the Engineered Nanoparticle of Interest?
What are the limits of engineering controls and PPE?

Can nanoparticles be controlled?
Conventional Controls Should Work

Exhaust Ventilation

Capture

Diffusion Dominates

About 1 nm

200 to 300 nm

Most Fine Dusts

Micro Scale

Inertia Dominants

Air Stream

No Capture
Conclusions of LEV Effectiveness Study

Average percent reduction from the use of a local exhaust ventilation unit

96 +/- 6% based on particle number concentration data

88 +/- 12% based on air sampling mass concentration data
Personal Protective Equipment: Respirators

Use of respiratory protection for nanomaterials - professional judgment and hazard assessment is needed.

Brownian Motion Comes to the Rescue!

n = 5; error bars represent standard deviations
Flow rate 85 L/min; NIOSH Approved N95 (NPPTL)
Particle Penetration Through Clothing

- Some fabric swatches behave like filter media
- Particle penetration driven by pressure differences
- Particle penetration is a function of the air permeability of the fabric

10 cm diameter circular swatch
Single layer of needle-punched Aramid material
Face velocity = 0.63 cm/sec; Flow rate 1L/min
Data courtesy of Dr. Zhong-Min Wang (NPPTL)
Field Studies: Findings

- Workplace exposures do occur: R&D to manufacturing
- Exposure assessment methods require experience and careful interpretation
- Control methods are effective for many processes
- Alternate controls may be needed for certain processes and R&D operations
- Guidance based on good risk management principles is effective
Information resources

Recommendations from NIOSH
- Summary of issues
- Approaches to consider
- Basic Guidance
- Updated as new information comes on-line
- Input requested

- Research progress in 10 key areas
- Continuing project plans
- Opportunities for collaboration

- Informational brochure series
- Available in large quantities
- Useful for communication of issues

www.cdc.gov/niosh/topics/nanotech
Appendix A

Nanoparticle Emission Assessment Technique (NEAT) used by NIOSH for Identifying Sources and Releases of Engineered Nanoparticles
In 2006, NIOSH established a Nanotechnology Field Research Team to expand its knowledge and understanding of the potential health and safety risks that workers may encounter during the research, production, and use of engineered nanomaterials. This effort has complimented NIOSH’s extensive laboratory-based research program, as well as helped NIOSH identify and more fully understand the variety of work processes used to generate and manufacture engineered nanomaterials. It has also provided NIOSH with the opportunity to observe and evaluate work practices and engineering controls used to ensure worker health and safety in the nanotechnology industry.

NIOSH has conducted site visits to several facilities around the country that are involved in the research, manufacture, or use of various types of nanomaterials including, metal and metal oxide nanoparticles, carbon nanofibers, eletrospun nanofibers, quantum dots, fullerenes, and nanocomposites. As a result, NIOSH obtained valuable information that is being used to assist in developing workplace guidance documents to protect nanotechnology workers from occupational injury and illness, and has learned that:

- basic particle counting and sizing instruments can be used to identify emissions from nanomaterial processes,
- careful interpretation of the particle data is needed to differentiate between incidental (background) and process-related nanoparticles, and
- engineering controls do minimize workplace exposure to engineered nanoparticles.

Companies interested in receiving a visit by the Field Research Team are encouraged to contact NIOSH. All site visits are initiated by the respective companies and are completely voluntary. This program is fully funded by NIOSH; therefore, there is no monetary cost to the participant. Three companies who have voluntarily received site evaluations from the NIOSH Field Research Team were recently interviewed by Nanowerk, LLC for its August/September 2007 issue of Nanorisk (www.nanorisk.org). Overall, they described the collaboration as beneficial, and encouraged other companies to take advantage of NIOSH’s expertise, services, instrumentation, and unbiased assessments.

For more information about occupational safety and health topics pertaining to engineered nanomaterials, including fact sheets about the Field Research effort and other nanotechnology research programs, please visit the NIOSH nanotechnology topic page at www.cdc.gov/niosh/topics/nanotech. To discuss the possibility of receiving a site evaluation by the NIOSH Field Research Team, contact Charles Geraci, Ph.D., CIH at (513) 533-8359, CGeraci@cdc.gov or Mark Methner, Ph.D., CIH at (513) 841-4525, MMethner@cdc.gov.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

How Will We Get the Job Done?
Collaboration
- Share knowledge
- Use expertise
- Build experience
- Partner
Thank you!

Charles.Geraci@cdc.hhs.gov