Exposure Assessment and Sampling Issues for Nanotoxicology and Safe Handling of Nanoparticles in the Workplaces

AIHA Roundtable 201
Toxicology and Exposure Assessment Issues for Nanotechnology: An Update for IHs
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National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
We are developing a comprehensive exposure assessment scheme that will enable us to:

- Anticipate,
- Recognize,
- Evaluate, and
- Control potential health risks for nanotechnology by applying a science-based approach to understanding and managing the critical elements over which we have control.
Ideally, this will enable a comprehensive assessment of all task-specific exposure pathways

Adapted from NIOSH: Day et al. 2007
Ideally, tasks will cover the full spectrum of activities
Ideally, the pathway assessments will include:

- **Material composition**
  - Purity
  - Surface coating
    - Including functionalization
- **Toxicity**
  - Inflammation
  - Fibrosis
  - Cancer
  - Other
- **Potential mechanisms for toxicity**
  - Oxidant stress
  - Chemical action
  - Physical action
  - Other
- **Reference material linkages**
- **Dustiness and fraction dispersed**
- **Primary particle size distribution**
- **Agglomerate or aggregate particle size distribution**
- **Particle durability and solubility**
- **Surface area**
- **Exposure dynamics**
  - Average concentration
  - Peak concentration
  - Cumulative concentration-time
- **Relative importance of the pathways**
  - Including PPE used
There would be a comprehensive job-exposure matrix (JEM) for each worker.

<table>
<thead>
<tr>
<th>Job</th>
<th>Exposure Period 1</th>
<th>Exposure Period 2</th>
<th>Exposure Period 3</th>
<th>...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Job 1</td>
<td>Time($J_1, P_1$)</td>
<td>Time($J_1, P_2$)</td>
<td>Time($J_1, P_3$)</td>
<td>...</td>
</tr>
<tr>
<td>Job 2</td>
<td>Time($J_2, P_1$)</td>
<td>Time($J_2, P_2$)</td>
<td>Time($J_2, P_3$)</td>
<td>...</td>
</tr>
<tr>
<td>Job 3</td>
<td>Time($J_3, P_1$)</td>
<td>Time($J_3, P_2$)</td>
<td>Time($J_3, P_3$)</td>
<td>...</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

Where Time($J_i, P_j$) is the worker’s time on job $i$ during exposure period $j$. 
A comprehensive equation for anticipating and controlling health effects

Health Risk = \frac{(\text{MAR} \times \text{DR} \times \text{ARF} \times \text{RF} \times \text{CF} \times \text{BR} \times \text{T} \times \text{DCF})}{V}

where:

- MAR is the Material-at-Risk (grams)
- DR is the Damage Ratio
- ARF is the Airborne Release Fraction
- RF is the Respirable Fraction
- CF is a Control Factor
- BR is the Breathing Rate
- T is the Time duration of exposure (minutes)
- DCF is the Dose Conversion Factor
- V is the effective volume in which the material is dispersed (m³)
A Nano-EHS Roadmap

Part of nano R&D budget
Lab manager involvement
Staff participation
Decision makers / mgmt

Funding / Mgmt Support
Laboratory Access / Relationship building
Process Mapping
Risk Communication

Defined roles / responsibilities
Cultural / Political support
Control Banding
Staff

Latest nano H&S information
Basic IH practices
Engineering controls
PPE
Training
Occupational Health Surveillance

Compliments of
Lynn Bowman

UDRI
A Control Banding Approach for Safe Handling of Nanoparticles in the Workplace

1. Health Hazard Banding
   - Identify Nanoparticle of Interest
   - Determine Appropriate Health Hazard Band
     - A, B, C or D
   - Evaluate Determinants of Exposure
     - Dustiness, Process, Quantity, Frequency, Duration
   - Determine Appropriate Control Band
     - "Laboratory" Scale 1 - 2
     - "Production" Scale 1 - 4
   - Verify Effectiveness of Controls
     - Are results acceptable for the assigned Health Hazard Band?
       - yes
       - no
         - Modify Controls

2. Control Banding
   - Conduct Periodic Re-Evaluations

3. Control Verification

4. Periodic Review
Health Hazard Banding Step

Identify Nanoparticle of Interest

Has the specific nanoparticle been assigned to a Health Hazard Band?

yes

no

Has another nanoparticle in the same chemical family been assigned to a Health Hazard Band? (e.g. metal oxides)

yes

no

Is the nanoparticle free of surface modifications that could affect toxicity?

yes

no

Have adequate animal and/or in vitro toxicity studies been conducted to determine hazard to human health?

yes

no

Use Hazard Band Tables to Determine Appropriate Health Hazard Band

Conduct Toxicity Studies (In Interim, Assign Nanoparticle to Health Hazard Band “C”)

Proceed to the Control Banding steps
Control Banding Step

Evaluate Determinants of Exposure
Dustiness and Process (i.e., potential for aerosolization), Quantity, Frequency and Duration

Dustiness
Classify material as solid, suspension, granular/agglomerated, powder, or highly dispersable

Process
Determine potential for particle release due to equipment, level of containment, process energy and degree of manual handling

Quantity
Research quantities (e.g., mg – g)
Scale up (e.g., g – kg)
Production (e.g., kg and above)

Frequency and Duration
(include appropriate attention to the potential for exceeding short term excursion values)

Determine Appropriate Control Band
Use the Control Band Table as Guidance
(include appropriate attention to the potential for acute toxicity)

Laboratory Band 1 or 2

Production Band 1, 2, 3 or 4
Control Verification Step

1. Identify All Operations that can result in Exposure
2. Select Employees and/or Work Areas to be Sampled
3. Does the nanoparticle have a validated sampling and analytical method* or an acceptable surrogate?
   - Yes: Measure Worker Exposures
   - No: Measure Indicators of Exposure
4. Analyze Estimated or Measured Results
   - Yes: Are results acceptable for the assigned Health Hazard Band?
     - Yes: Periodically Re-Verify Adequacy of Exposure Controls
     - No: Modify Controls
   - No: Modify Controls

* Chemical analysis, gravimetric analysis, total surface area determination, etc.
Periodic Re-evaluation Step

Re-Evaluate Health Hazard Banding when:
- New toxicology data are generated
- Medical surveillance trending suggests adverse effects
- Occupational illness is reported

Re-Evaluate Control Banding when:
- Production volume or frequency changes
- Duration of operations with exposure risk changes
- A new nanoparticle is handled
- Physical form changes (for example, powders rather than suspensions)
- New equipment is designed or installed
- New toxicology data are generated
- Medical surveillance trending suggests adverse effects
- Occupational illness is reported
- Periodically, to meet regulatory requirements for respiratory protection or other personal protective equipment

Re-Evaluate Control Verification when:
- There are changes in the workforce
- Process or process equipment modifications are made
- Production volume, speed or frequency changes
- A validated sampling and analytical method is developed
- Qualitative indicators of exposure suggest a change in control effectiveness

Modify the Banding Elements as Appropriate
A Control Banding Approach
for Safe Handling of Nanoparticles in the Workplace

1. Health Hazard Banding
   - Identify Nanoparticle of Interest
   - Determine Appropriate Health Hazard Band
     - A, B, C or D
   - Evaluate Determinants of Exposure
     - Dustiness, Process, Quantity, Frequency, Duration
   - Determine Appropriate Control Band
     - "Laboratory" Scale 1 – 2
     - "Production" Scale 1 - 4

2. Control Banding
   - Verify Effectiveness of Controls
   - Are results acceptable for the assigned Health Hazard Band?
     - yes
     - no

3. Control Verification
   - Modify Controls

4. Periodic Review
   - Conduct Periodic Re-Evaluations
1

Health Hazard Banding

Identify Nanoparticle of Interest

Determine Appropriate Health Hazard Band
A, B, C or D
### Similar to historical control bands for exposures to chemicals by inhalation

<table>
<thead>
<tr>
<th>Band No.</th>
<th>Range of Exposure Concentrations</th>
<th>Hazard Group</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;1 to 10 mg/m³ dust, &gt;50 to 500 ppm vapor</td>
<td>Skin and eye irritants</td>
<td>Use good industrial hygiene practice and general ventilation.</td>
</tr>
<tr>
<td>2</td>
<td>&gt;0.1 to 1 mg/m³ dust, &gt;5 to 50 ppm vapor</td>
<td>Harmful on single exposure</td>
<td>Use local exhaust ventilation.</td>
</tr>
<tr>
<td>3</td>
<td>&gt;0.01 to 0.1 mg/m³ dust, &gt;0.5 to 5 ppm vapor</td>
<td>Severely irritating and corrosive</td>
<td>Enclose the process.</td>
</tr>
<tr>
<td>4</td>
<td>&lt;0.01 mg/m³ dust, &lt;0.5 ppm vapor</td>
<td>Very toxic on single exposure, reproductive hazard, sensitizer</td>
<td>Seek expert advice.</td>
</tr>
</tbody>
</table>
## Possible Hazard Band Scheme for Nanoparticles in the Workplace

<table>
<thead>
<tr>
<th>Hazard Band</th>
<th>Range of Exposure Concentrations</th>
<th>Type or Degree of Hazard</th>
<th>General Character of Control Band</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong></td>
<td>100 to 500 µg/m³ dust</td>
<td>Slight and reversible ?</td>
<td>Good industrial hygiene practice with open handling or local exhaust ventilation</td>
</tr>
<tr>
<td></td>
<td>? Other criteria ?</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>B</strong></td>
<td>10 to 100 µg/m³ dust</td>
<td>Moderate and reversible ?</td>
<td>Local exhaust ventilation or enclosed processes.</td>
</tr>
<tr>
<td></td>
<td>? Other criteria ?</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>C</strong></td>
<td>1 to 10 µg/m³ dust</td>
<td>Severe and reversible or moderate and irreversible ?</td>
<td>Enclosed processes.</td>
</tr>
<tr>
<td></td>
<td>? Other criteria ?</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>D</strong></td>
<td>&lt;1 µg/m³ dust</td>
<td>Severe and irreversible ?</td>
<td>Isolated or remote handling.</td>
</tr>
<tr>
<td></td>
<td>? Other criteria ?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Health Hazard Banding Step

1. Identify Nanoparticle of Interest

   - Has the specific nanoparticle been assigned to a Health Hazard Band?
     - yes
     - no

   - Has another nanoparticle in the same chemical family been assigned to a Health Hazard Band (e.g., metal oxides)?
     - yes
     - no

   - Have adequate animal and/or in vitro toxicity studies been conducted to determine hazard to human health?
     - yes
     - no

2. Use Hazard Band Tables to Determine Appropriate Health Hazard Band

3. Conduct Toxicity Studies (In Interim, Assign Nanoparticle to Health Hazard Band “C”)

4. Proceed to the Control Banding steps
Evaluate Determinants of Exposure

*Dustiness, Process, Quantity, Frequency, Duration*

Determine Appropriate Control Band

"Laboratory" Scale 1 – 2
"Production" Scale 1 - 4

2 Control Banding
Control Banding Step

Evaluate Determinants of Exposure
Dustiness and Process (i.e., potential for aerosolization), Quantity, Frequency and Duration

Dustiness
Classify material as solid, suspension, granular/agglomerated, powder, or highly dispersable

Process
Determine potential for particle release due to equipment, level of containment, process energy and degree of manual handling

Quantity
Research quantities (e.g., mg – g)
Scale up (e.g., g – kg)
Production (e.g., kg and above)

Frequency and Duration
(include appropriate attention to the potential for exceeding short term excursion values)

Determine Appropriate Control Band
Use the Control Band Table as Guidance
(include appropriate attention to the potential for acute toxicity)

Laboratory Band 1 or 2

Production Band 1, 2, 3 or 4
Dustiness
Classify material as solid, suspension, granular/agglomerated, powder, or highly dispersable

Process
Determine potential for particle release due to equipment, level of containment, process energy and degree of manual handling

Quantity
Research quantities (e.g., mg – g)
Scale up (e.g., g – kg)
Production (e.g., kg and above)

Frequency and Duration
(include appropriate attention to the potential for exceeding short term excursion values)
“Traditional” Control banding concept for exposure management

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Amount Used</th>
<th>Dustiness</th>
<th>Hazard Group (R-Phrase)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Approach</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. General Ventilation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Engineering Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Containment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Specialist Advice</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hazard Group A</th>
<th>Low Dustiness</th>
<th>Medium Dustiness</th>
<th>High Dustiness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Medium</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Large</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hazard Group B</th>
<th>Low Dustiness</th>
<th>Medium Dustiness</th>
<th>High Dustiness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Medium</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Large</td>
<td>1</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hazard Group C</th>
<th>Low Dustiness</th>
<th>Medium Dustiness</th>
<th>High Dustiness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Medium</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Large</td>
<td>2</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hazard Group D</th>
<th>Low Dustiness</th>
<th>Medium Dustiness</th>
<th>High Dustiness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Medium</td>
<td>3</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Large</td>
<td>3</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hazard Group E</th>
<th>Low Dustiness</th>
<th>Medium Dustiness</th>
<th>High Dustiness</th>
</tr>
</thead>
<tbody>
<tr>
<td>For all hazard group E substances, choose control approach 4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NIOSH: TJ Lentz
Control Banding Step

Evaluate Determinants of Exposure
- Dustiness and Process (i.e., potential for aerosolization), Quantity, Frequency and Duration

Dustiness
- Classify material as solid, suspension, granular/agglomerated, powder, or highly dispersable

Process
- Determine potential for particle release due to equipment, level of containment, process energy and degree of manual handling

Quantity
- Research quantities (e.g., mg – g)
- Scale up (e.g., g – kg)
- Production (e.g., kg and above)

Frequency and Duration
- Include appropriate attention to the potential for exceeding short term excursion values

Determine Appropriate Control Band
- Use the Control Band Table as Guidance (include appropriate attention to the potential for acute toxicity)

Laboratory Band
- 1 or 2

Production Band
- 1, 2, 3 or 4
Verify Effectiveness of Controls

Are results acceptable for the assigned Health Hazard Band?

Modify Controls

Control Verification
Control Verification Step

1. Identify All Operations that can result in Exposure

2. Select Employees and/or Work Areas to be Sampled

3. Does nanoparticle have a validated sampling and analytical method* or an acceptable surrogate?
   - yes: Measure Worker Exposures
   - no: Measure Indicators of Exposure

4. Analyze Estimated or Measured Results

5. Are results acceptable for the assigned Health Hazard Band?
   - yes
   - no: Modify Controls

6. Periodically Re-Verify Adequacy of Exposure Controls

* Chemical analysis, gravimetric analysis, total surface area determination, etc.
Conduct Periodic Re-Evaluations

4 Periodic Review
4 Periodic Re-evaluation Step

Re-Evaluate Health Hazard Banding when:
- New toxicology data are generated
- Medical surveillance trending suggests adverse effects
- Occupational illness is reported

Re-Evaluate Control Banding when:
- Production volume or frequency changes
- Duration of operations with exposure risk changes
- A new nanoparticle is handled
- Physical form changes (for example, powders rather than suspensions)
- New equipment is designed or installed
- New toxicology data are generated
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- Periodically, to meet regulatory requirements for respiratory protection or other personal protective equipment

Re-Evaluate Control Verification when:
- There are changes in the workforce
- Process or process equipment modifications are made
- Production volume, speed or frequency changes
- A validated sampling and analytical method is developed
- Qualitative indicators of exposure suggest a change in control effectiveness

Modify the Banding Elements as Appropriate
Re-Evaluate *Health Hazard Banding* when:

- New toxicology data are generated
- Medical surveillance trending suggests adverse effects
- Occupational illness is reported
Re-Evaluate Control Banding when:

- Production volume or frequency changes
- Duration of operations with exposure risk changes
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Re-Evaluate Control Verification when:

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Periodic Re-evaluation Step

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1. Health Hazard Banding
   - Identify Nanoparticle of Interest
   - Determine Appropriate Health Hazard Band: A, B, C or D
   - Evaluate Determinants of Exposure: Dustiness, Process, Quantity, Frequency, Duration

2. Control Banding
   - Determine Appropriate Control Band: “Laboratory” Scale 1 - 2, “Production” Scale 1 - 4
   - Verify Effectiveness of Controls

3. Control Verification
   - Are results acceptable for the assigned Health Hazard Band?
     - yes
     - no: Modify Controls

4. Periodic Review
   - Conduct Periodic Re-Evaluations

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Information Resources on the NIOSH Nanotechnology Topic Page

• Approaches to Safe Nanotechnology: A Dialogue with NIOSH

• The Nanoparticle Information Library
  – Particle-specific information
    • Physical and chemical form
    • Origin
    • Available toxicity data
  – A contributor database to facilitate networking
  – Direct search links to:
    • NIOSH Pocket Guide to Chemical Hazards
    • Registry of Toxic Effects of Chemical Substances (RTECS)
    • Wilson Center research database
    • ICON EHS Bibliography
  – Options for including control information and lessons learned

www.cdc.gov/niosh/topics/nanotech
Nanotechnology

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Narayan Hosmane
Northern Illinois University

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The potential health implications of nanoparticles are currently being investigated by NIOSH and others, and this aspect of our library is in development. Click Here for an example of some nanoparticles for which health information is available.

Single-crystalline barium titanate nanowires are synthesized more...
VOLUNTEER PARTNERS NEEDED FOR THE NIOSH NANOTECHNOLOGY FIELD RESEARCH EFFORT

• The NIOSH field research team is available to visit and assess processes involving research, production, and use of nanomaterials.

• The team will characterize materials, processes, potential worker exposures, work practices, and control procedures.

• Information and recommendations will be shared with the volunteer partner.

• Information will be used by NIOSH to update the guidance that appears in *Approaches to Safe Nanotechnology* on the our NanotechnologyTopic Page.

There is no cost to participate!!!

If your organization is interested in volunteering to participate, please contact one of us!!!!

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  – Eileen Kuempel
  – Bon-Ki Ku
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  – Greg Day
  – Vince Castranova

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  – Renae Goldman, 3M
  – Carey Newton, Ely Lilly
  – Ellen Faria, Johnson and Johnson
Questions?

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.

Mention of company names or products does not constitute endorsement by NIOSH.

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