Nanomaterials: Naughty or Nice?

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Product Safety Engineering Society (PSES)
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Science or Science Fiction?

“Nanoparticles are small enough to get places nobody’s ever had to worry about before.”

(Michael Chrichton, *Prey*)
LETTERS

Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study

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Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study

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graphene cylinders, typically a few nanometers in diameter, which can range in length from a few micrometres to millimetres. Single-walled nanotubes (SWNTs) consist of one such cylinder, and multi-walled nanotubes (MWNTs), as used in this study, comprise 2 to 50 such cylinders concentrically stacked with a common long axis. This structure gives nanotubes an unusual
Agenda

• Brief “nano 101”
• Environmental health & safety (EHS) issues
  – Risk assessment of nanomaterials
    • Exposure
    • Toxicity
• Conclusions and recommendations
Nanomaterials 101

- Substances <100 nm in size
  - Dust mite (~200,000 nm)
  - Human hair (~80,000 nm)
  - Red blood cells (~5,000 nm)

- Novel materials created by engineering on the atomic level

- Unique properties based on quantum physics and large surface area
The Term “Nanomaterials” is Meaningless!

[photo removed due to copyright / permissions]

What are Nano-Engineered Materials?

<table>
<thead>
<tr>
<th>ENGINEERED</th>
<th>INCIDENTAL</th>
<th>NATURAL</th>
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<tbody>
<tr>
<td>• Carbon-based (nanotubes, fullerenes)</td>
<td>• Particles from:</td>
<td>• Particles from:</td>
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<tr>
<td>• Metal oxides</td>
<td>• Combustion</td>
<td>• Plants, trees, forest fires</td>
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<td>• Quantum dots</td>
<td>• Industrial processes, grinding, welding</td>
<td>• Oceans, bodies of water</td>
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<tr>
<td>• Nanowires</td>
<td>• Vehicles (e.g., diesel)</td>
<td>• Erosion, dust</td>
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<td>• Dendrimers</td>
<td>• Construction</td>
<td>• Volcanic eruptions</td>
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<td>• Composites</td>
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[photo removed due to copyright / permissions]

Adapted from Savage and Walker (2006).
Growth of Nanotechnology in Consumer Products

Source: Woodrow Wilson International Center for Scholars; www.nanotechproject.org
Applications of Nanomaterials

- Vehicles
- Aerospace
- Structures
  - Buildings
  - Bridges
  - Elevator to space
- Personal care items
- Medical devices

- Chemicals
  - Fuel additives
  - Lubricants
  - Catalysts
- Power generation
- Electronics
- Clothing
- Remediation
Questions...

• Occupational & consumer health
  – Will this be the next asbestos?

• Environmental health
  – Will this be the next PCB, DDT, or [insert favorite chemical here]?

• Manufacturing & marketing
  – Will this be the next genetically modified foods (GMO)?
Survey of Current Work Practices and EHS Programs

- Results of survey of 64 companies who use or research nanomaterials
- Telephone questionnaire on EHS issues
- All information self-reported (no verification)
Findings of ICON Report

• Actual EHS practices did not differ from conventional safety practices
  – Engineering controls, PPE, clean-up methods, waste management
  – Practices often based on properties of bulk material or solvent carrier
  – North America appeared to lead the way regarding implementation of EHS programs

• Few organizations reported workplace monitoring or provided formal guidance

• Most organizations recommended disposing of nanomaterials as hazardous waste

• Most reported that biggest impediment was lack of information on hazards
Regulations and Quality Controls

Depending on the industry, common regulations and qualification testing specifications are expected to include:

- Environmental Protection Agency
- International Standard Organization
- American Society for Testing and Materials
- Institute of Environmental Science and Technology
- Underwriters Laboratories

These specifications allow for a model for reporting and suggested experimental techniques. The techniques and protocol development is ongoing.
EHS Research Areas of Federal Agencies

Source: Adapted from Geraci (2006). AIHce.
The Challenge:

• Are existing regulatory frameworks and guidance sufficient for nano-engineered materials?

• Do new regulations/frameworks need to be devised and implemented?

• In either case, what is the underlying data upon which to base policy?

See also review by Davies (2005).
EHS: Release and Exposure

Source: Adapted from Tsuji et al. (2006).
Much Is Already Known

• Nano-sized particles have been in production for decades
  – Carbon black for manufacture of rubber products and pigments
  – Titanium, aluminum, zirconium, and fumed silica as thixotropic agents in pigments and cosmetics
  – Products used in the semiconductor and micro-electronics industry
  – “Micronized” titania in sunscreens
Much Is Already Known continued

- Epidemiologic studies of certain workers exposed to both macro- and nano-scale substances show effects only at very high levels
  - Metal fume fever in welders of zinc
  - Foundry workers exposed to aluminum

- On the other hand, studies of atmospheric UFPs (PM$_{10}$, PM$_{2.5}$, PM$_{0.1}$) linked to short-term increases in morbidity and mortality
Key Exposure Issues for Human Health and the Environment

• **Degree of containment or encapsulation**
  - Presence of coatings?
  - Matrix properties?
  - Product integrity during wear and weathering?

• **Environmental fate and transport**
  - Increased solubility and mobility?
  - Aggregation/precipitation potential?
  - Propensity for bioaccumulation?
  - Effect of surface coatings and treatments?

• **What are the relevant exposure measures and available technology?**

• **What is the effectiveness of current approaches for occupational and consumer protection?**
Manufacturing, Synthesis, and Production Process

QUALITY CONTROL

Raw Materials → Manufacturing Process → Final Product → Production

Worker Exposure

Unused Material
- Byproducts, product disposal after use

Public or Environmental Exposure

Waste Streams
- Waste during processing
Potential Exposures During Manufacturing, Synthesis, and Production

- **Synthesis process/particle formation**
  - Gas phase (air)
  - Vapor phase (surface)
  - Colloidal (liquid suspension)
  - Attrition (liquid suspension)

- **Sources (examples)**
  - Reactor leakage
  - Product recovery
  - Spray drying
  - Spillage, drying

Potential pathways for inhalation or dermal exposure:

- Airborne contamination (inhalation)
- Handling of raw materials (dermal)
- Cleaning/maintenance (inhalation)
- Spillage (inhalation, dermal)
No Agreed Upon Method for Measuring Airborne Exposures

- Conventional methods may not be practical
- Several approaches:
  - Adopt current mass-based approaches
  - Measure size distribution
  - Monitor number concentration
  - Monitor aerosol surface area concentrations
- For nano-engineered materials, surface area and shape become relevant metrics as well
What are Current Exposure Measurement Options?

- Condensation particle counter (CPC)
- Differential mobility analyzer (DMA)
- Electrical low pressure impact (ELPI)
- Aerosol surface area measurement
AEROTRAK™ 9000: Nanoparticle Aerosol Monitoring

- Portable, battery operated
- Real-time surface area measurement and read-out
- Can display 8-hour TWAs and statistical summaries of surface area data
- Alarm set-point can be set for use in workplace monitoring
- Can be used to log exposures for record-keeping purposes

TSI Model 3550 Nanoparticle Surface Area Monitor

• Matches lung deposition of particles
• Measures surface area of fraction of particles that deposit in tracheobronchial or alveolar regions of human respiratory tract
• 10 nm to 1000 nm range capability
Possible EHS Strategies for Exposure Control in Manufacturing and Production

- Devise and implement SOPs with safety in mind
- Particle monitoring methods to identify leaks in reactors and other possible emissions
- Design processes that limit worker exposure
  - Total enclosure of the process
  - Partial enclosure with local exhaust ventilation/filtration
  - Mix nano-engineered materials in liquid slurries
  - Use proper personal protective equipment
  - Control ventilation (e.g., air exchanges per hour)
  - HEPA filtration on all tooling exhausts, re-circulated air
  - HEPA vacuums for cleaning spills
  - Cleaning methods for walls and surfaces
- Monitor during exposure periods and/or limit time per shift
- Conduct materials science evaluation to allow for evaluation and eventual incorporation of “safer” properties into product design
- Control banding
### Potential Control-Banding Approach (Conceptual Model)

**Exposure Index**

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- **Specialist advice**
- **Containment**
- **Engineering control**
- **General ventilation**

**Exposure Index** = “Dustiness” or propensity to become airborne, amount used

**Impact Index** = Bulk hazard, surface area, surface activity, shape, size

Source: Maynard (2006)
Materials Science: Factors Affecting Exposure Potential

- **Performance**
  - Durable
  - Encapsulated
  - Stable

- **Process**
  - Mixing
  - Heating
  - Application

- **Properties**
  - Toughness
  - Adhesion
  - Friability
  - Environmental resistance
  - Diffusion rates

- **Structure**
  - Polarity
  - Crystallinity
  - Reactivity
Materials Science and Exposure Potential

- **Particle behavior**
  - Dispersion/agglomeration/aggregation

- **Durability of coatings/product integrity**
  - Chemistry and microstructure determine behavior over time, e.g., weathering, friability, wear, leaching

- **Binder effect**
  - Affinity of binders and particles
  - Resistance to chemical dissolution
  - Encapsulation

Source: [http://fcs.itc.it](http://fcs.itc.it)  
Source: [http://ipt.arc.nasa.gov/cntpolymer.html](http://ipt.arc.nasa.gov/cntpolymer.html)
Engineer Safety into Products

• Use knowledge of factors that determine nanoparticle toxicity to reduce reactivity, dispersion, etc.
  – Less toxic particles with greater wealth of toxicity information
  – Surface coatings
  – Encapsulate or embed in matrix which prevents release of free nanoparticles
Toxicology of Nano-Engineered Particles: A Matter of Size?

• **Ability to cross biological barriers**
  - Cell membrane
  - GI tract
  - Skin
  - Blood-brain
  - Deeper airways
  - Lungs-blood
  - Placenta

• **Higher reactivity**
  - Large relative surface area
  - Surface charge, photocatalytic activity
  - Increased oxidative stress and injury
Effect of Size on Toxicity

**Dogma:**
- Toxicity is a function of particle surface reactivity
- Smaller particles have much larger surface area per mass
- Therefore, the smaller the particle, the greater the toxicity per mass

**100 g Iron:**
- Diameter = 2.9 cm
- Surface Area = 26.1 cm²

**100 g Iron:**
- Diameter = 50 nm
- Surface Area = 1,520 m²
Some Evidence That Smaller Size Increases Toxicity

• Lung inflammation studies
  – TiO$_2$: 21 nm v. 300 nm inhaled by rats
    • Basis of NIOSH’s lower worker exposure limits for ultrafine v. fine scale particles
  – TiO$_2$: 20 nm v. 250 nm instilled in rats and mice
  – UFP instilled in mice

• However, TiO$_2$ inhalation studies used different crystal types—a more toxic type for the 21 nm particles
Smaller Size Does Not Necessarily Confer Greater Toxicity

- Nano anatase TiO$_2$ rods and dots were not more toxic than rutile fine-scale TiO$_2$ particles when instilled in rat lungs
- Smaller TiO$_2$ particles were not more cytotoxic in vitro
- Toxicity of quartz particles was more dependent on surface characteristics than particle size

http://www.cdc.gov/niosh/review/public/tio2/
Size is Not Everything

• Shape, surface properties, crystal type
  – Toxicity of TiO$_2$ anatase $\gg$ TiO$_2$ rutile

• Chemistry
  – Lung inflammation: (UFP, CNTs, quartz) $>$ TiO$_2$ $>$ MgO
  – *In vitro* solubility and cytotoxicity:
    Fe$_2$O$_3$ = asbestos $>$ ZnO $>$ TiO$_2$ = CeO$_2$ = ZrO$_2$
    but….
  – Soluble essential metals may be easily handled in the body once absorbed
“Lessons Learned”

• **Asbestos**
  – Dimension, chemical composition, biopersistence, and durability play a role in disease
  – Respiratory uptake and deposition patterns may be similar

• **Welding fume**
  – Respiratory uptake and deposition patterns may be similar
  – Translocation via neuronal transport?

• **Ultrafine particles**
  – Wealth of information on pulmonary toxicity
  – Translocation to other organs may play a role
  – Cytokine release and other mechanisms may be involved in cardiovascular outcomes
Conclusions and Recommendations
State of the Knowledge for NMs

• What we know we know
  – Health effects of UFPs, air pollution, fibers
  – Control technologies for ultrafines
  – Some important factors affecting toxicity and chemistry
  – Short-term, high dose toxicity of some nanomaterials

• What we’re still figuring out
  – Relevant measurement and characterization techniques
  – Hazards of novel engineered particles
  – Extent of translocation in the body and fate/transport in the environment for novel materials
  – Health risks in workers and their families from chronic exposures to novel materials
  – Effectiveness of controls

Source: Adapted from Schulte and Salamanca-Buentello (2006)
The Good News...

- Substantial awareness of the issue
- Processes are “similar” to other chemical production processes
- Valuable materials – not thrown around
- Likely to be difficult to become airborne
- Current PPE likely adequate (NIOSH)
- Airborne materials may quickly agglomerate or disperse (also those in solution)
- Filtration probably effective for airborne nano-engineered particles
- Many applications have little potential for release of particles

Source: Adapted from Aitken (2006).
But We Should Act Now!

- **Manufacture/synthesis**
  - Work in well ventilated area
  - Mix product within enclosed vessels or in liquid slurry
  - Encapsulate nanoparticles to prevent release
  - Evaluate “best practices,” SOPs, labeling requirements, registrations—document and implement
  - Educate workers and incorporate into decisions

- **Use/misuse**
  - Evaluate exposure of new product, as well as older product (potentially worn or degraded)
  - Use “lessons learned” from other materials, when applicable
  - Materials science analysis for exposure potential

- **Be suitably cautious and be proactive!**
Recommendations

- Evaluate the potential for exposure throughout the particles life cycle
- Conduct materials science analysis of product matrix
- Evaluate factors that determine toxicity (e.g., chemical composition, aggregation potential, etc.)
- Performance-based testing
  - Many regulatory limits (e.g., water discharge limits) are performance-based (e.g., aquatic toxicity testing)
- Design tests to distinguish if products containing nano-engineered materials are different to those without these materials.