

Environmental, Health and Safety Issues in Nanomaterials Workshop

The American Ceramic Society

June 9-10, 2008

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

Agriculture	Pesticides and fertilizers
Automotive	composites, epoxies, films
Biomedical	diagnostics, drug delivery
Chemical	catalysts, polymer films, coatings
Electronics	catalysts, polymer films, coatings, fiber optics
Energy	catalysts, lithium batteries, fuel additives
Environmental	sensors, catalysts
Food	additives, packaging materials, antimicrobial
Household	antimicrobials, cleaners, coatings, appliances
Personal Care	cosmetics, sunscreens, hair/skin products
Sports	composites for bats and golf clubs, shoes
Textiles	water/stain resistance, wrinkle-free, fire resistance

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?

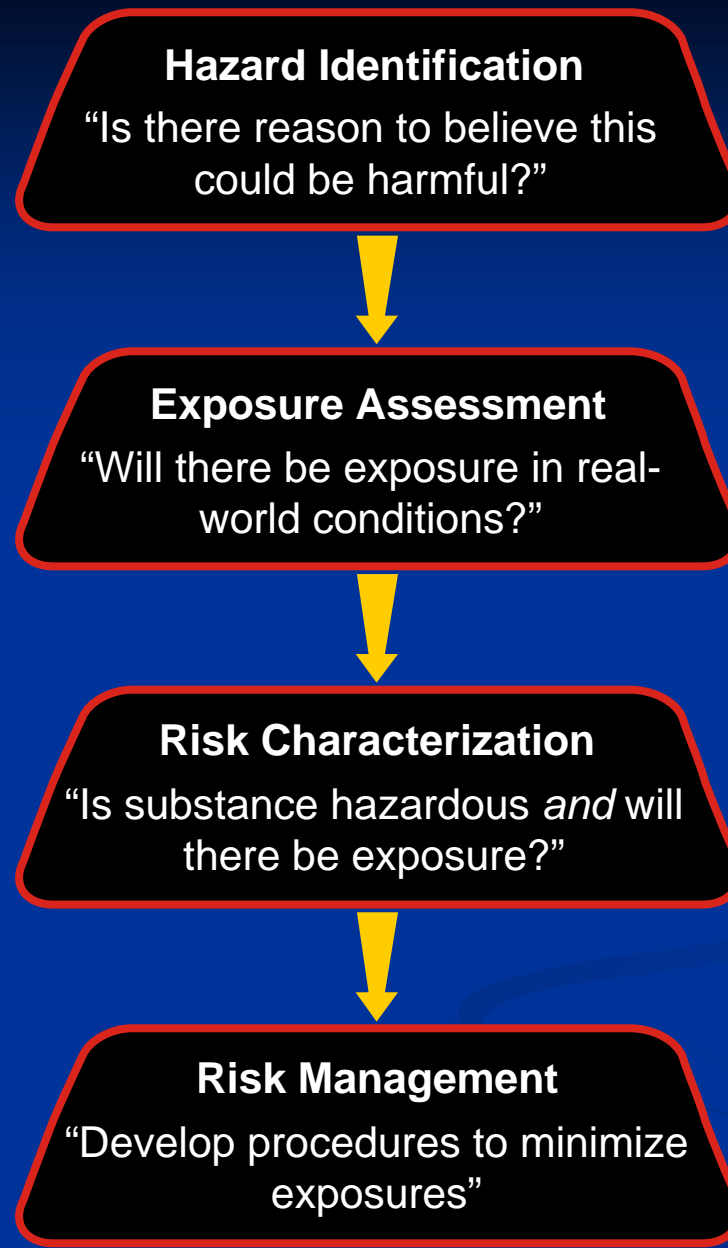
RISK = HAZARD X EXPOSURE

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

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

Unknowns and uncertainties = Risk Management approach

Key Elements of Risk Management



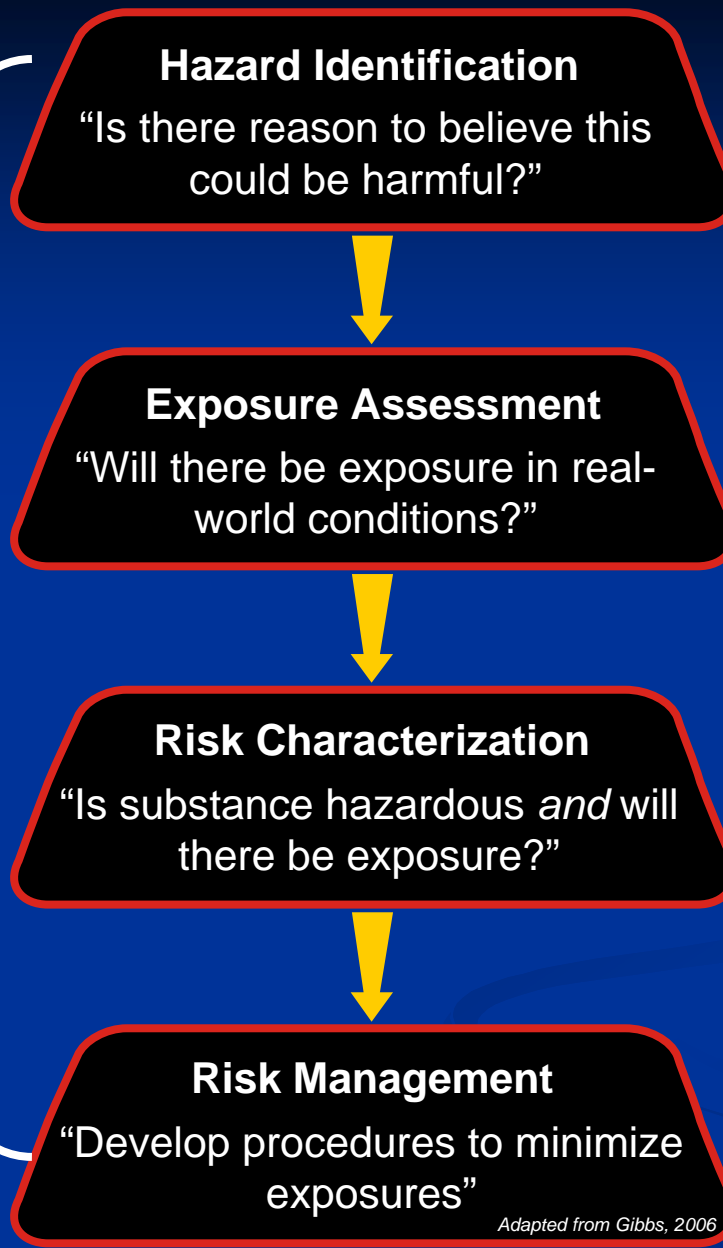
Risk Management of Engineered Nanoparticles:

The Simple Questions

Are they hazardous?

Can they be measured?

Can they be controlled?



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

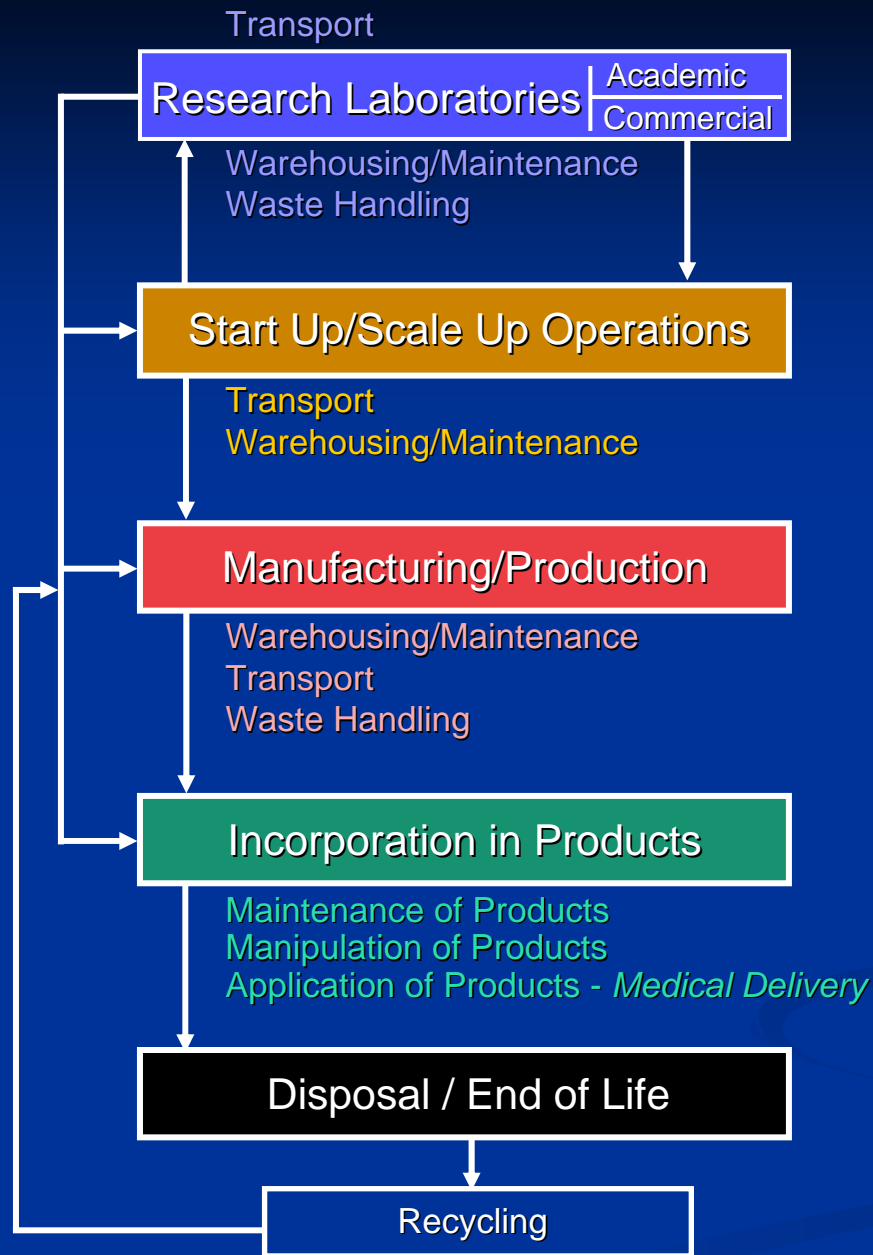
Key areas of NIOSH research supporting the Risk Management process



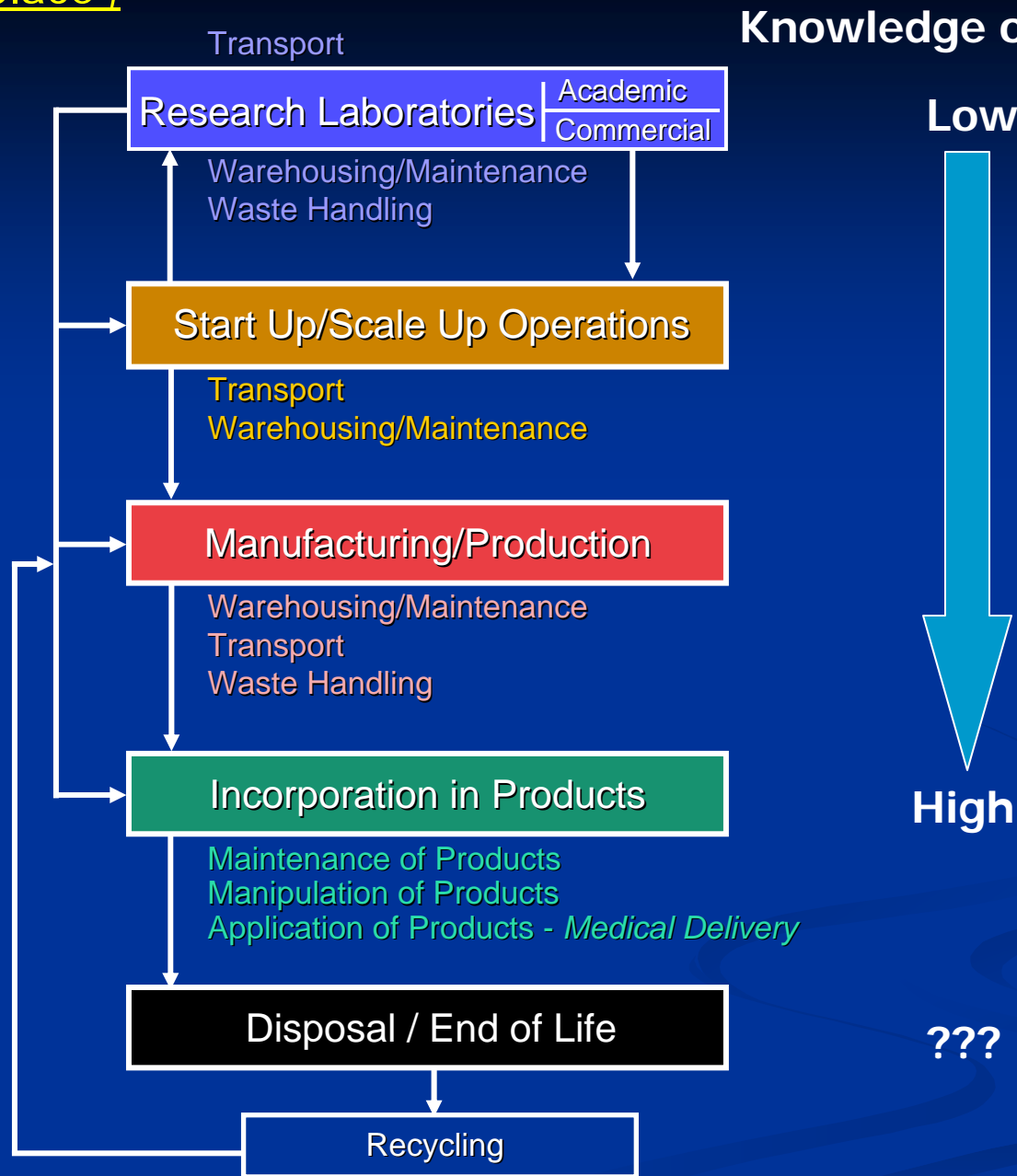
Challenge: The diversity of “Nanomaterial Production and Use”

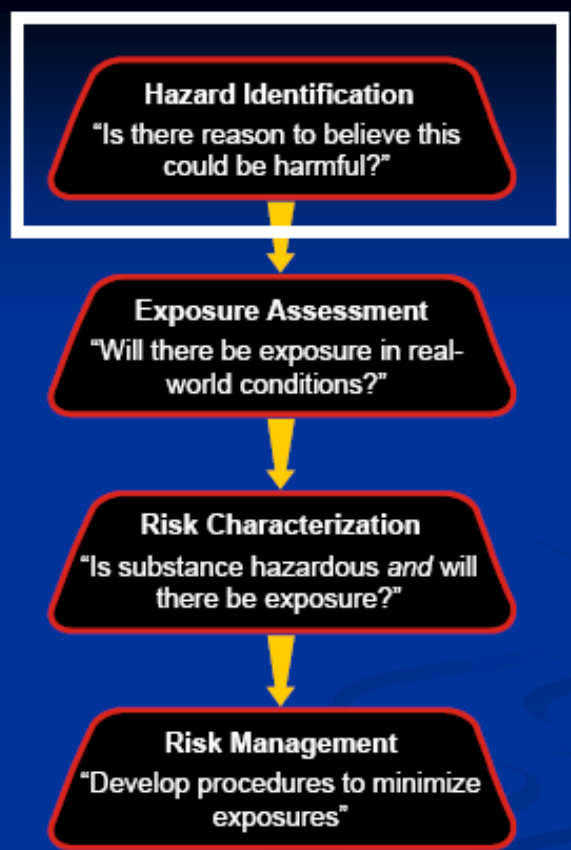


To evaluate the 'workplace',
A Life Cycle Approach
is needed.



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a Life Cycle Approach
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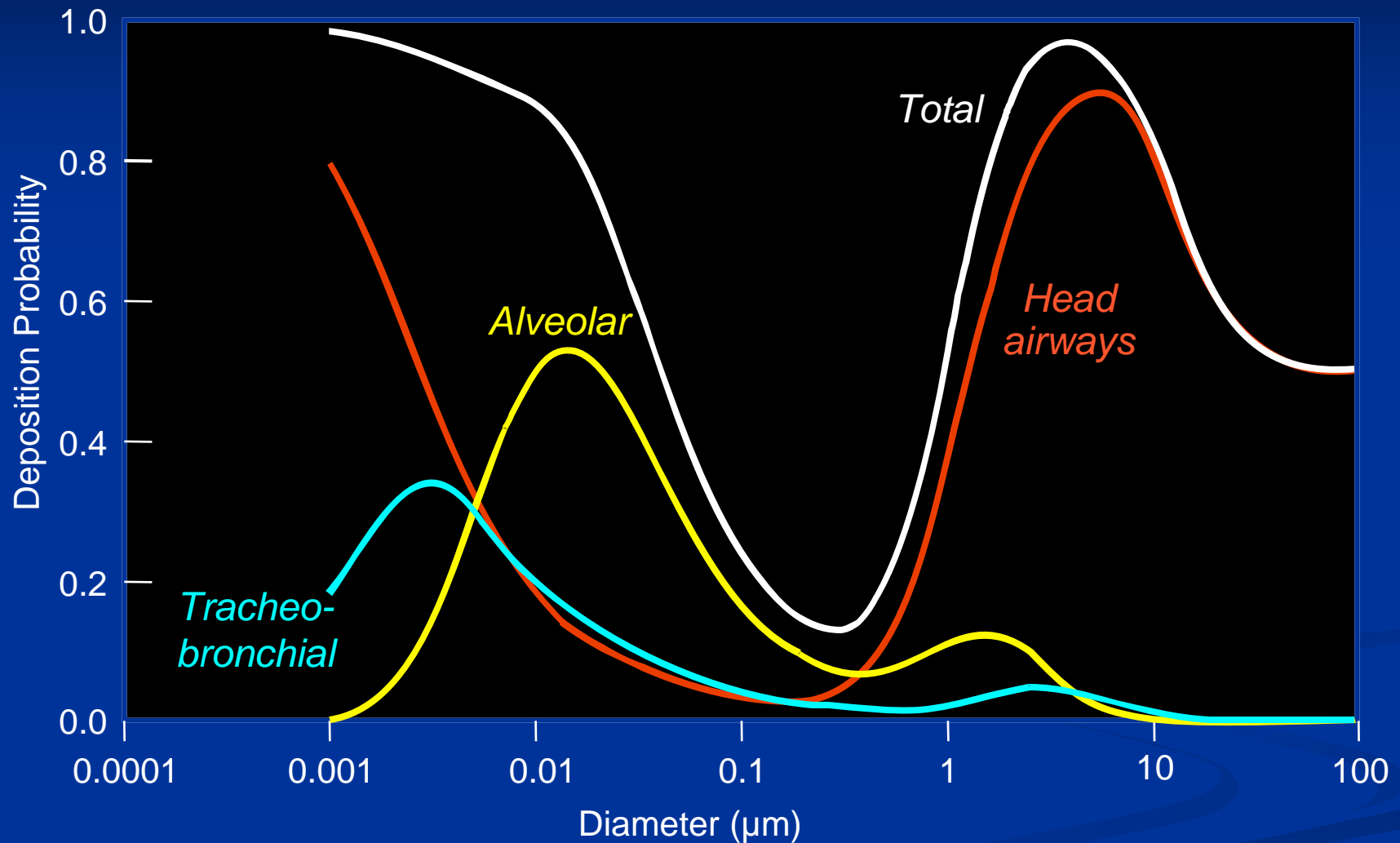




Nanotoxicology

“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

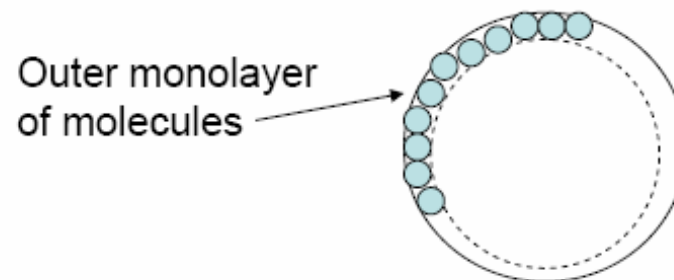
Many may be the metrics for both hazard and exposure determination

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.

Particle Size (nm)	Fraction (%) of Molecules in Outer Layer
2500 (2.5 μm)	$< 2 \times 10^{-4}$
1000 (1 μm)	$< 6 \times 10^{-4}$
100	0.006
10	0.06
1	48.8



Surface Area as a Dose Metric

- Toxicity of ultrafine TiO₂ appears much higher than fine TiO₂ *per unit mass*

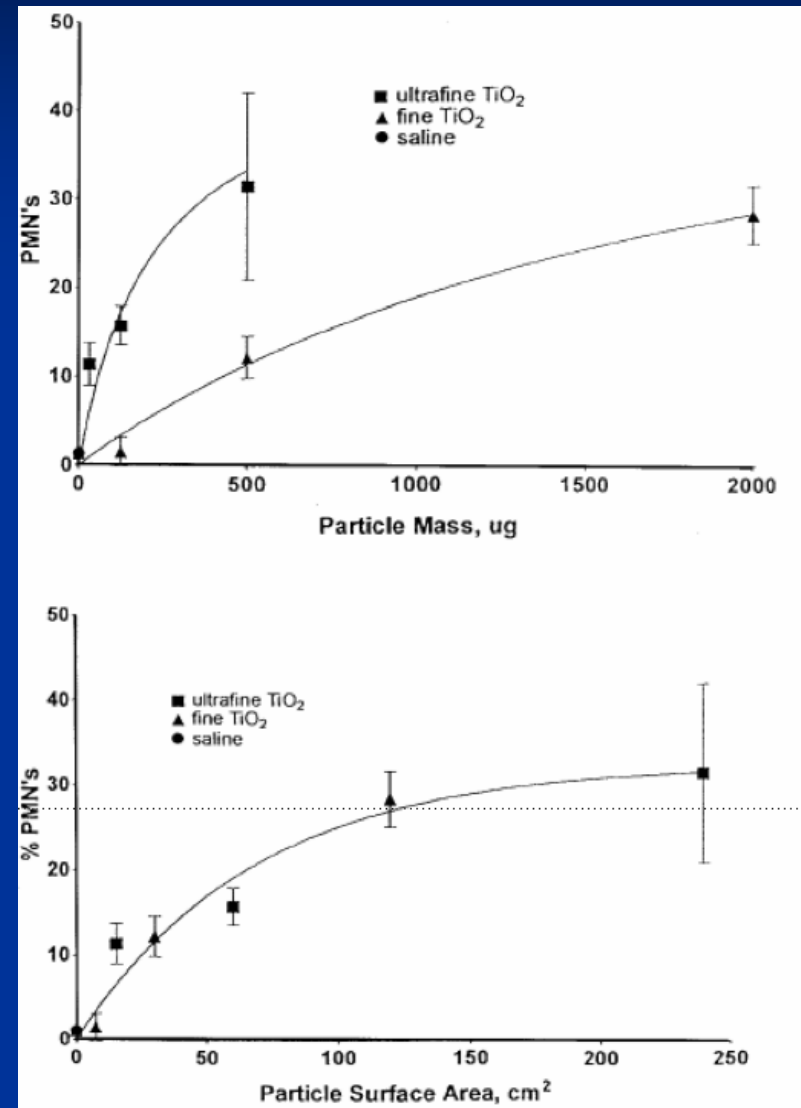


- Toxicity is equivalent when *surface area* is the exposure metric



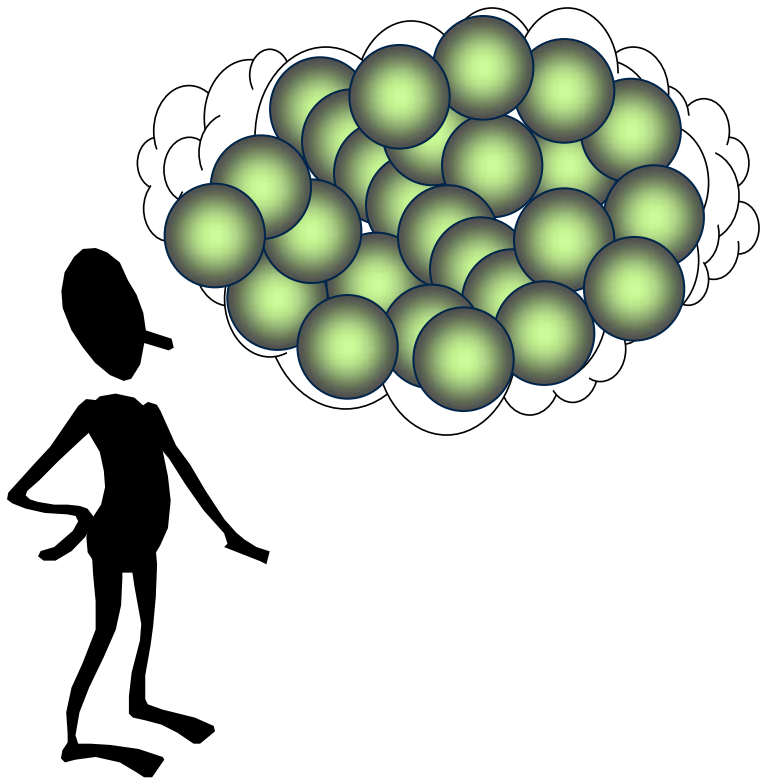
Measured polymorphonuclear neutrophils in lung lavage fluid, an index of inflammation

Oberdorster, Int Arch Occup Environ Health. 2001 Jan; 74(1):

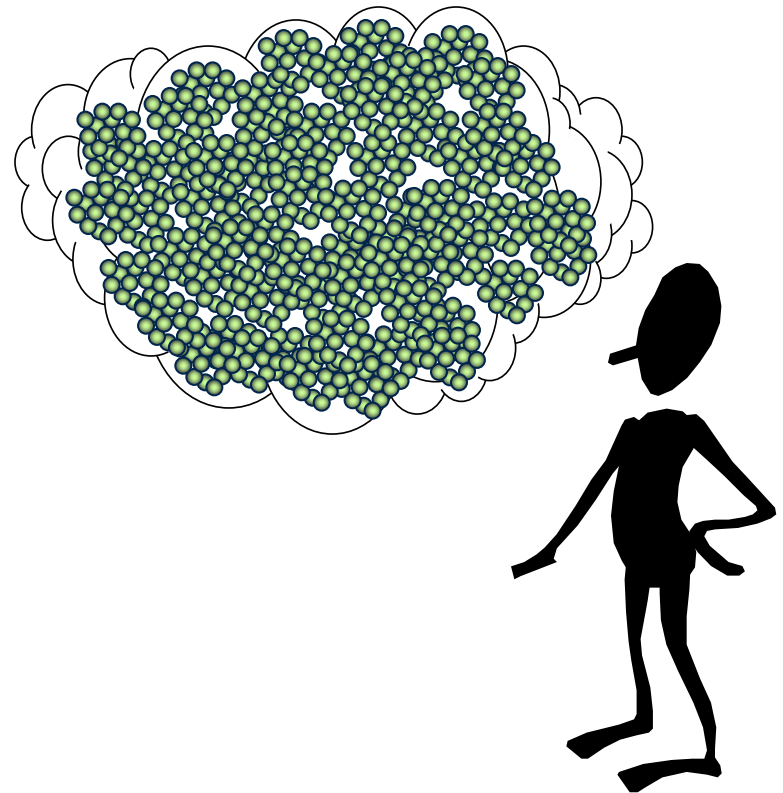


Is one of these workers at greater risk for disease?

Bulk Material



Nano Sized Particles



Research Issues

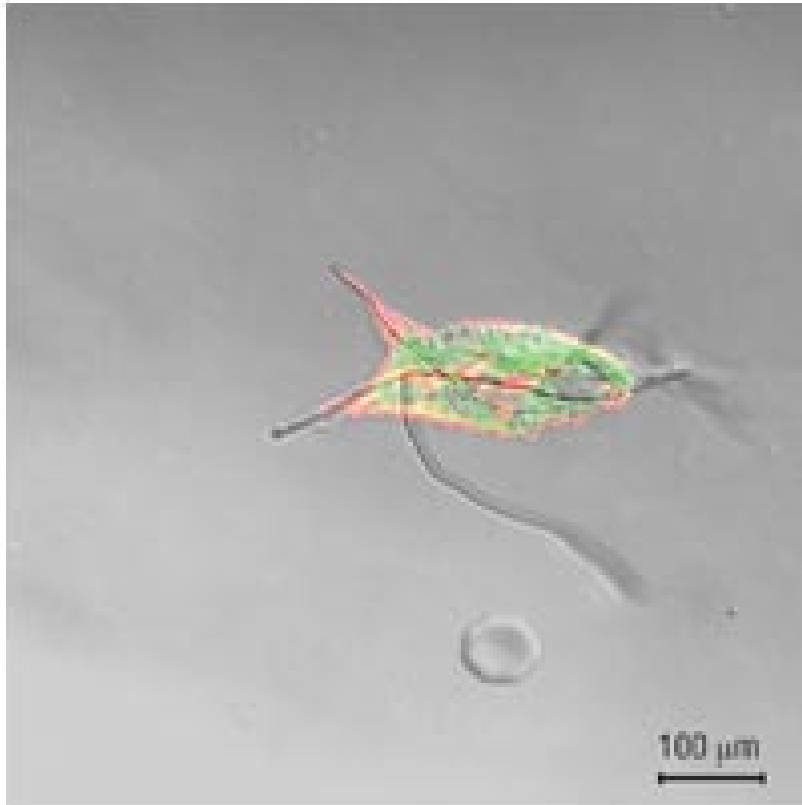
- Pulmonary Deposition, Interstitialization and Translocation
- Pulmonary Toxicology
- Systemic Effects
- Dermal Effects
- Neural Uptake and Toxicology
- Dose Metric

Nanotoxicology Summary

- Nanoparticles under investigation
 - TiO₂, 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

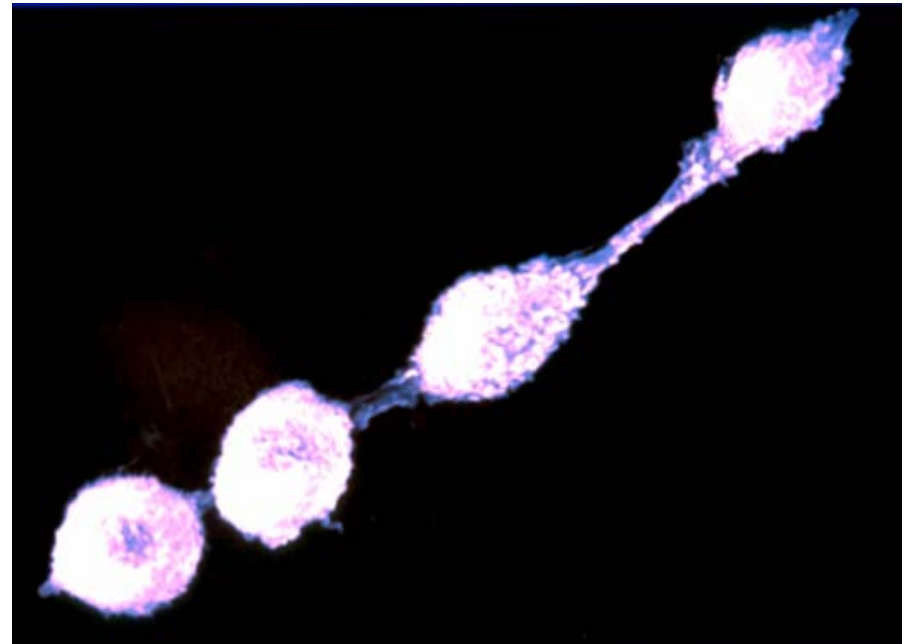
Current Research Results

Single-Walled Carbon Nanotube Toxicity to Respiratory Tract



Rat lung cells cannot digest and clear long carbon nanotubes.

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



V. Castranova, NIOSH

Poland, et al: Nature Nanotechnology

May, 2008

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

CRAIG A. POLAND¹, RODGER DUFFIN¹, IAN KINLOCH², ANDREW MAYNARD³, WILLIAM A. H. WALLACE¹, ANTHONY SEATON⁴, VICKI STONE⁵, SIMON BROWN¹, WILLIAM MacNEE¹ AND KEN DONALDSON^{1*}

¹MRC/University of Edinburgh, Centre for Inflammation Research, Queen's Medical Research Institute, 47 Little France Crescent, Edinburgh EH16 4TJ, UK
²School of Materials, University of Manchester, Grosvenor Street, Manchester M1 2PL, UK
³Woodrow Wilson International Center for Scholars, 1300 Pennsylvania Avenue, NW, Washington DC 20004-3027, USA
⁴Institute of Occupational Medicine, Research Avenue North, Riccarton, Edinburgh EH14 4AP, UK
⁵School of Life Sciences, Napier University, Colinton Road, Edinburgh EH10 5DT, UK
^{*}e-mail: ken.donaldson@ed.ac.uk

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

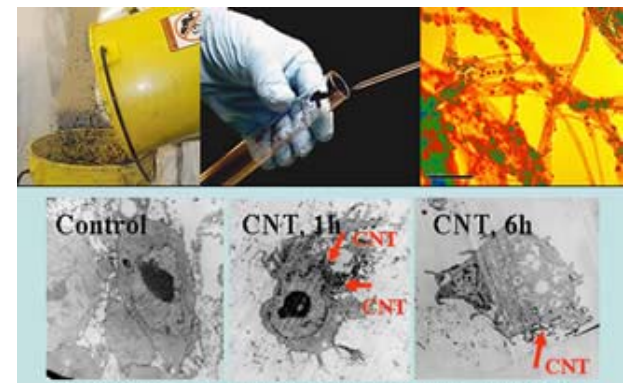
Aspiration of SWCNT resulted in:

- 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.



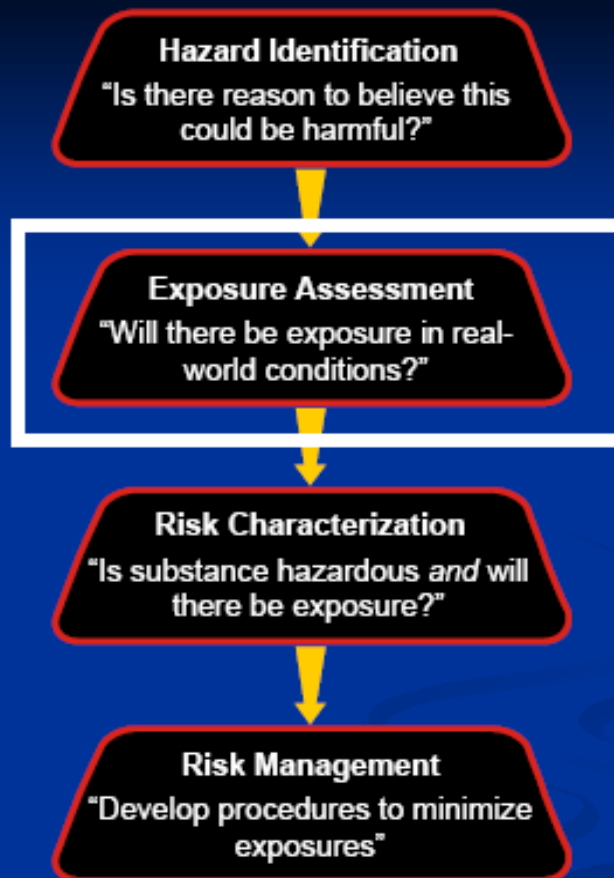
Graphics courtesy of Andrew Maynard and Anna Shvedova

Risk Assessment: Ultrafine (Nano) TiO₂

NIOSH draft recommended exposure limits (RELs):

- 1.5 mg/m³ fine TiO₂;
- 0.1 mg/m³ ultrafine TiO₂
- Reflects greater inflammation & tumor risk of ultrafine on mass basis
- 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

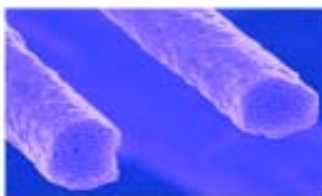


Metrics and Measurements for Exposure Assessment

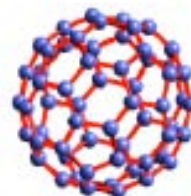
Can nanoparticles be measured?

Nanoparticles: Many shapes, many chemistries

Single and multi walled nanotubes



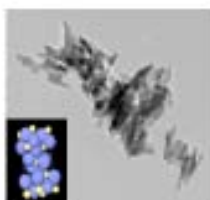
Fullerenes



Nanoshells



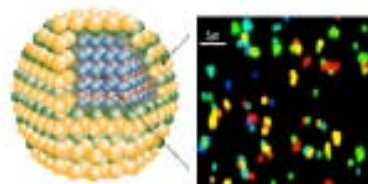
Metal oxides



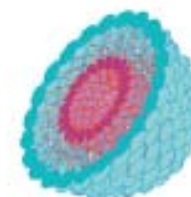
Dendrimers



Quantum dots



Nanosomes



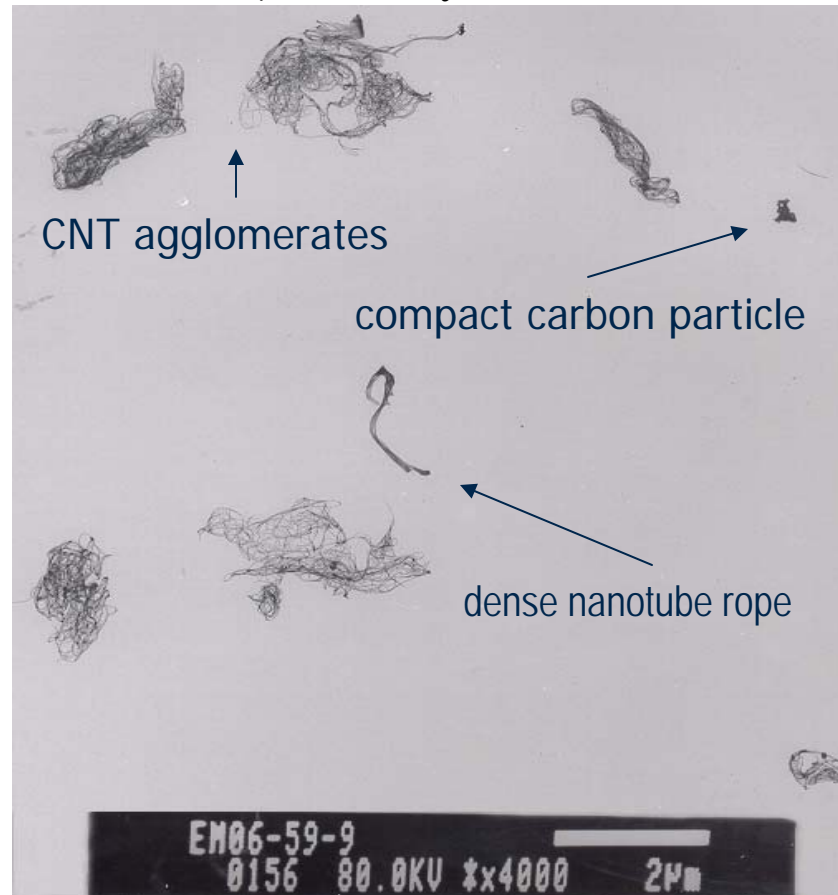
N. Walker. National Toxicology Program

Not all nanoparticles are the same

Carbon Nanotube Air Sample

Which metric to use?

0.18 – 0.32 μm aerodynamic diameter



Characterization of nanoparticles in workplaces



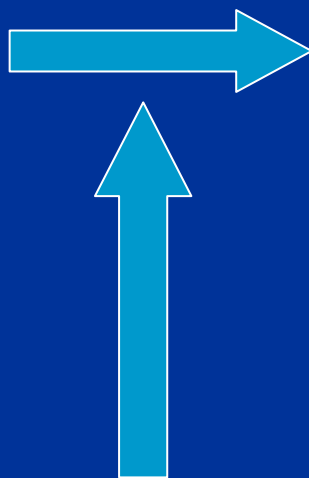
*A suite of techniques
is used ...*

Guidance on Exposure Monitoring

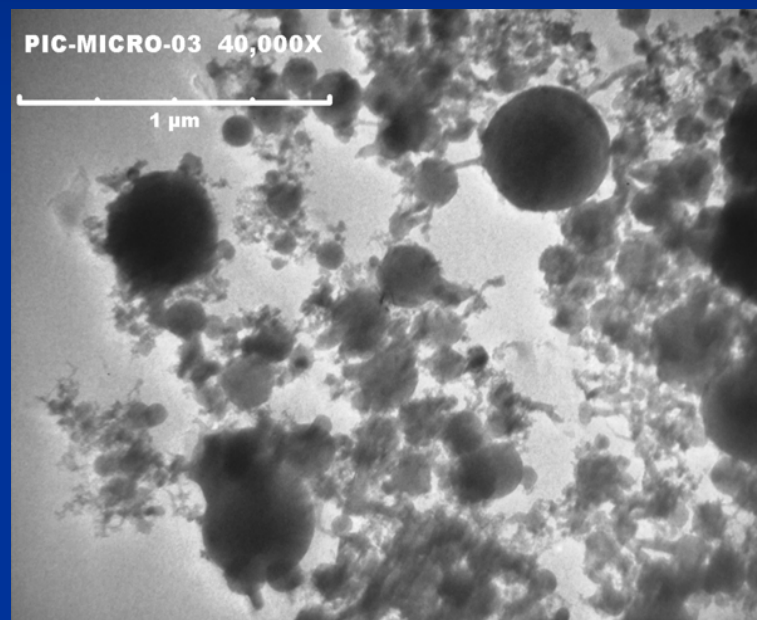
Simple Start to Complex Finish



Starting Point



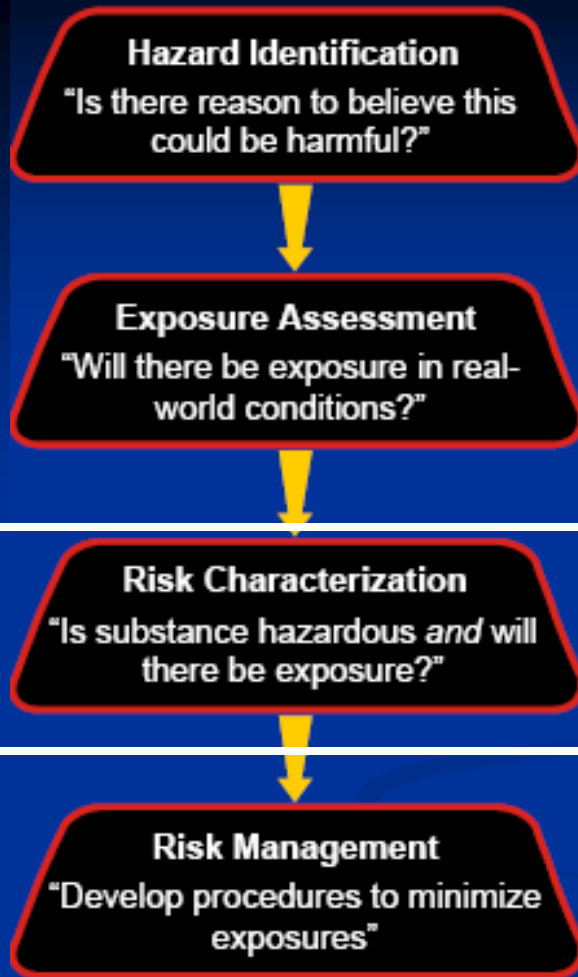
Mass, Size Distribution,
Surface Area, Etc.



TEM analysis of aerosol

The Hard Way





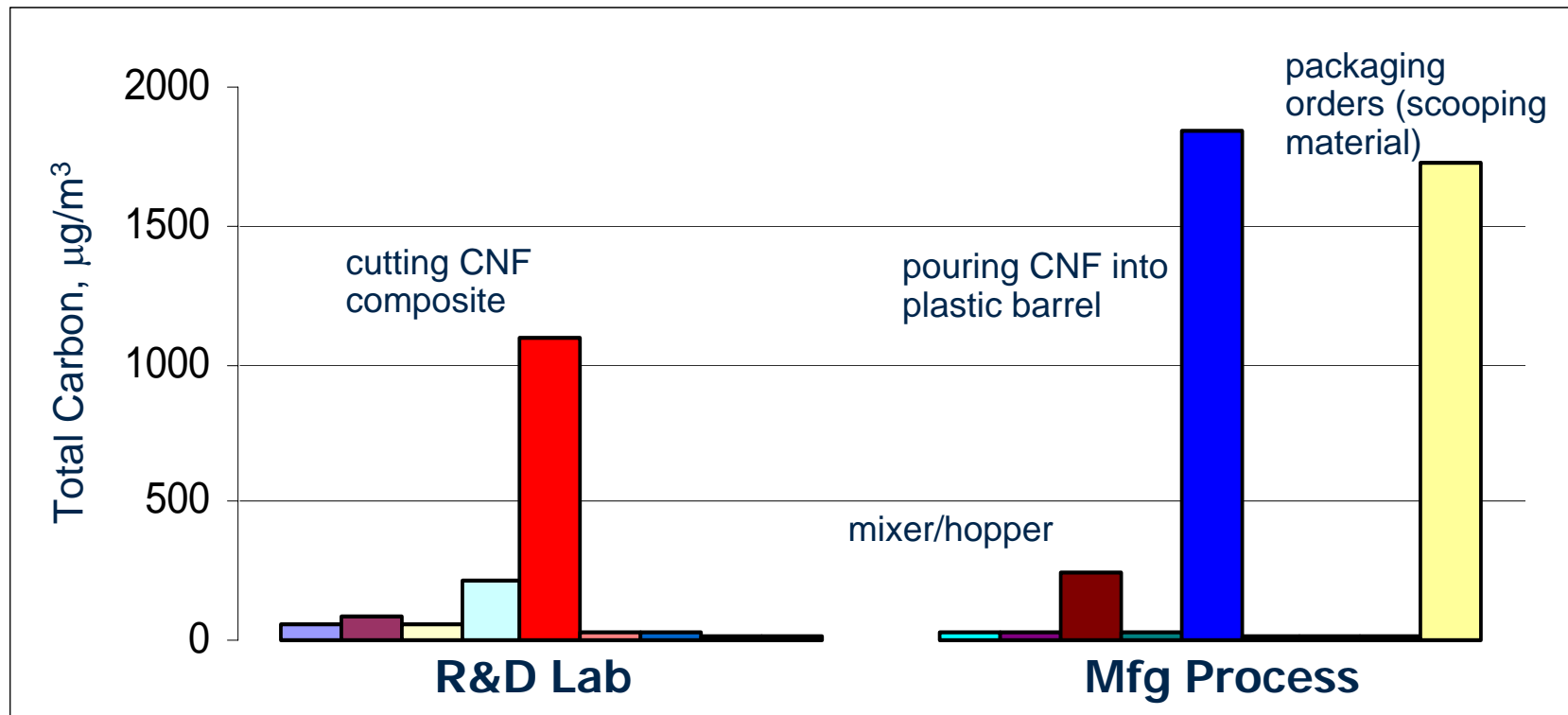
Are Workplace Exposures Occurring?

DRAFT - Summary of Nanoparticle Measurements - DRAFT

Type of Facility	Location	Type of Particle, Morphology	Singular, Agglomerated, or Both	Size of Particle	Range of "Potential" Exposure Concentrations (Duration of Task)	Nominal CPC particle counts 10-1,000 nm P/cc	Nominal Indoor background particle counts 10-1,000 nm P/cc	Nominal Outdoor background particle counts 10-1,000 nm P/cc
University Research lab	OH	Carbon Nanofibers	Agglomerated	Approx. 100 nm diameter, 1-10 microns long	80-90 $\mu\text{g}/\text{m}^3$	15,000	12,000	34,000
Metal Oxide Manufacturer		TiO ₂ , Lithium Titanate, powder	Both	100-200 nm	<100 nm: 1.4 $\mu\text{g}/\text{m}^3$ (TiO ₂) Total dust: 4 - 149 $\mu\text{g}/\text{m}^3$ (TiO ₂) <100 nm: ND (Li) Total dust: ND - 3 $\mu\text{g}/\text{m}^3$ (Li)			
Manufacturer	OH	Carbon Nanofibers	Both	Approx. 100 nm diameter, 1-10 microns long	15 - 1800 $\mu\text{g}/\text{m}^3$	100,000 P/L 300-500 nm HHPC	12,000 P/L 300-500 nm HHPC	NA
Research and Development lab		Quantum Dots, spheres	ND	2 - 8 nm	ND			
Metal Oxide Manufacturer	CA trip 1 CA trip 2	Manganese, Silver, Nickel, Cobalt, Iron oxides, spheres	Both	8 - 50 nm	67- 3819 $\mu\text{g}/\text{m}^3$	7,000 -75,000 18,000 – 30,000	10,000 12,000	15,000 NA
Research and Development lab (Pilot-Scale)	NJ	Aluminum, spheres	Both	50-100 nm	40- 276 $\mu\text{g}/\text{m}^3$	13,000	2,500	3,800
Research and Development lab		Elemental Metals - Silver, Copper, TiO ₂	ND	15 - 40 nm	ND			
Filter Media Manufacturer	KY	Nylon 6 Nanofiber	ND	70 - 300 nm diameter, continuous length	ND	15,000- 33,000	6,000	NA
Pilot Scale	WI day 1 WI day 2	Silica iron coating for cellulose	Both	4 -70 nm	1- 4 $\mu\text{g}/\text{m}^3$	25,000 8,000 – 12,000	20,000 2,000 -13,000	6,500 NA

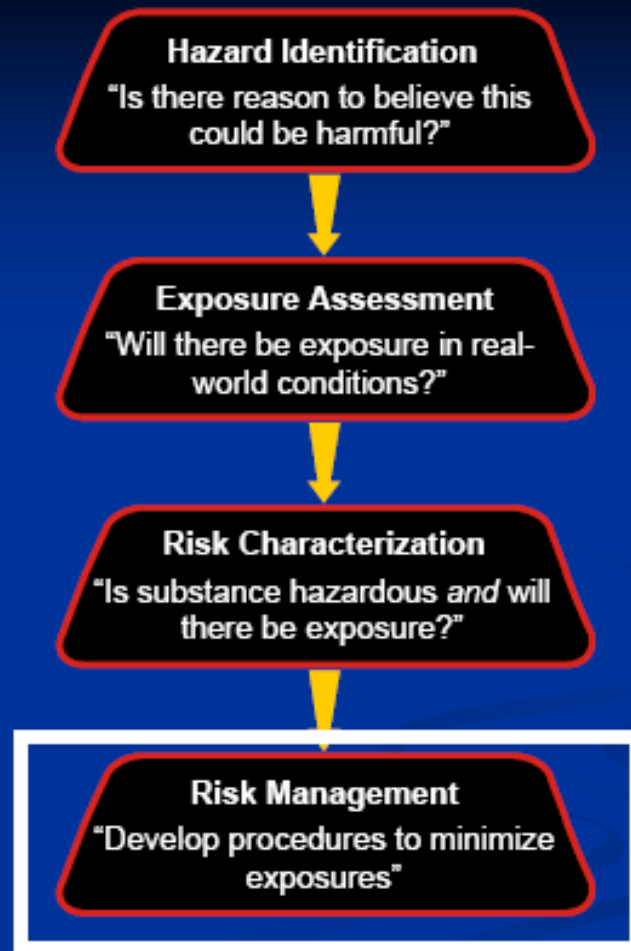
Draft: Not for distribution – Do Not Quote or Cite

CNF Air Sampling Results as Total Carbon ($\mu\text{g}/\text{m}^3$)



Did you detect the Engineered Nanoparticle of Interest?

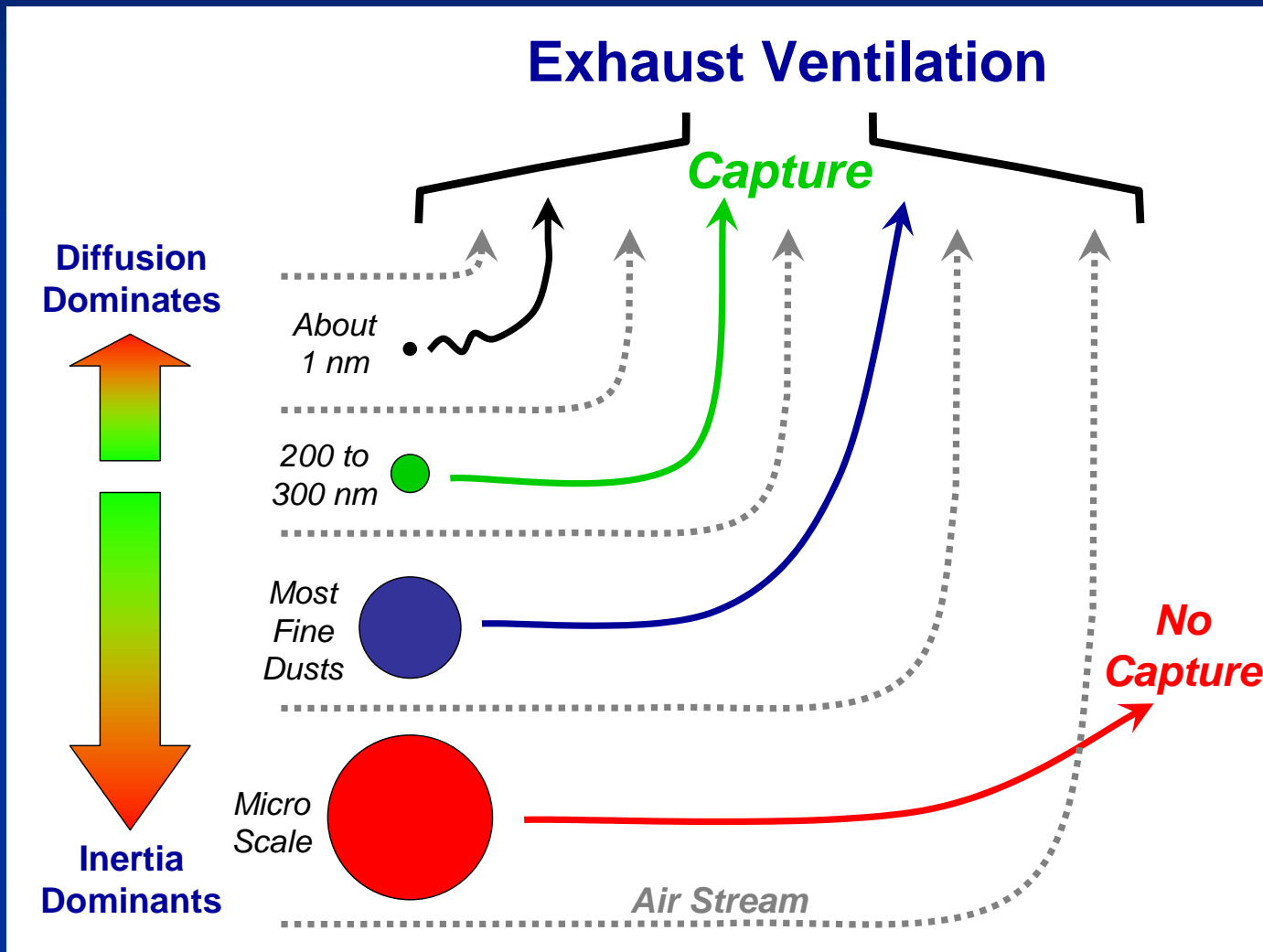




What are the limits of engineering controls and PPE?

Can nanoparticles be controlled?

Conventional Controls Should Work



Effectiveness of Local Exhaust Ventilation (LEV) in Controlling Engineered Nanomaterial Emissions During Reactor Cleanout Operations

M. Methner; L Old (ed)

[Journal of Occupational and Environmental Hygiene,](#)
Volume 5, Issue 6 June 2008 , pages D63 - D69



Conclusions of LEV Effectiveness Study

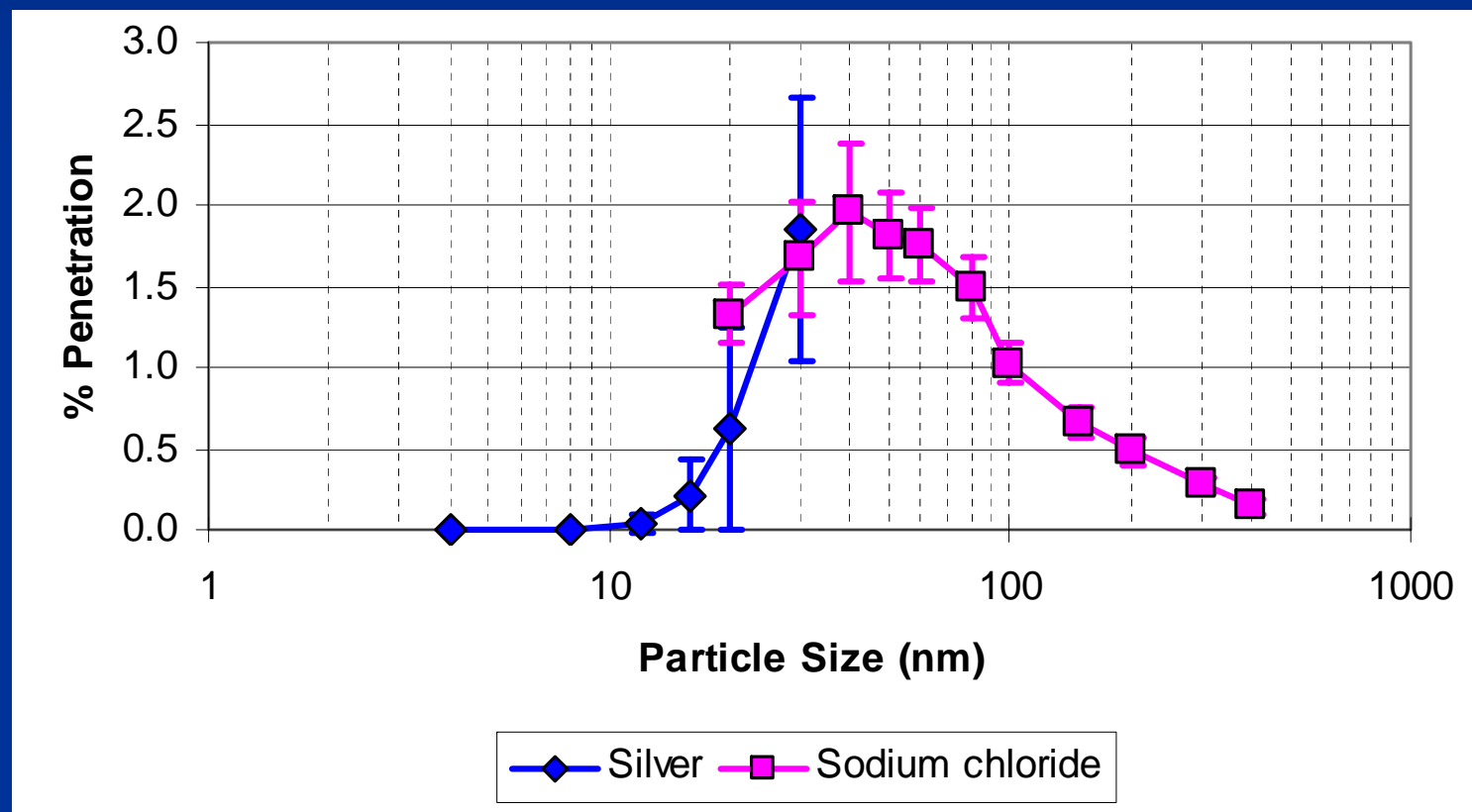
Average percent reduction from the use of a local exhaust ventilation unit

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.

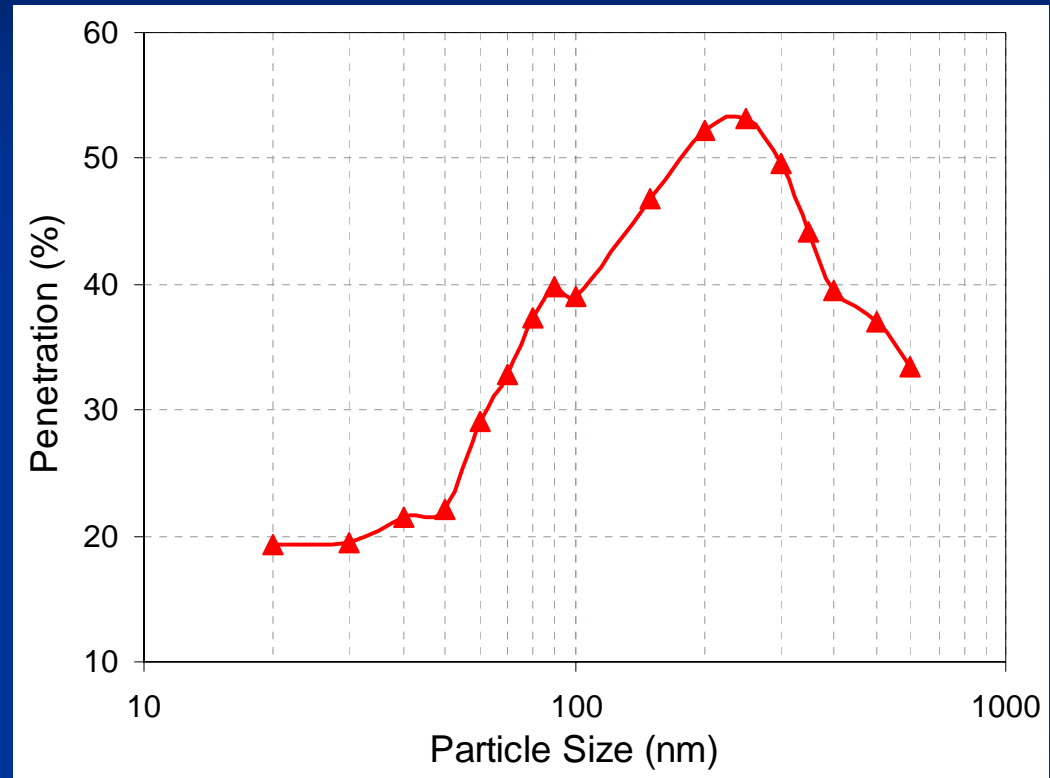


Brownian Motion Comes to the Rescue!

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

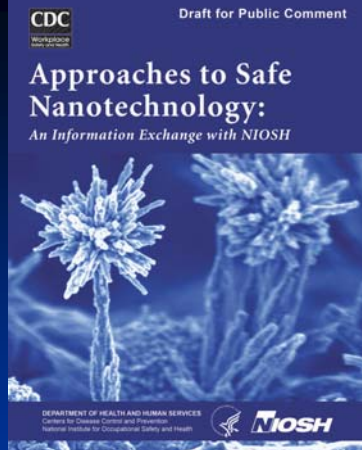


*10 cm diameter circular swatch
Single layer of needle-punched Aramid material
Face velocity = 0.63 cm/sec; Flow rate 1L/min
Data courtesy of Dr. Zhong-Min Wang (NPPTL)*

Field Studies: Findings

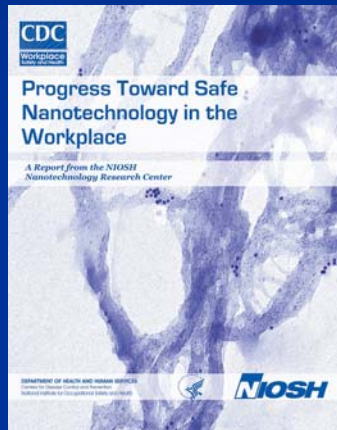
- Workplace exposures do occur: R&D to manufacturing
- Exposure assessment methods require experience and careful interpretation
- Control methods are effective for many processes
- Alternate controls may be needed for certain processes and R&D operations
- Guidance based on good risk management principles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

Information resources

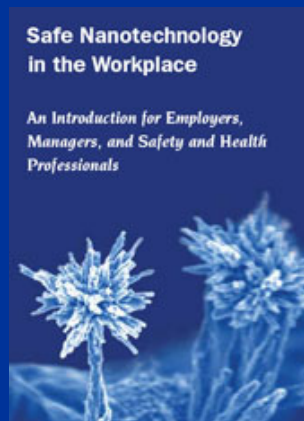


Recommendations from NIOSH

- 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

CURRENT INTELLIGENCE BULLETIN

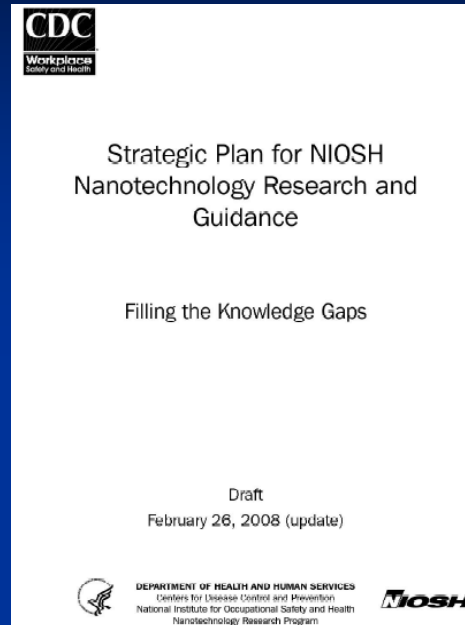
**INTERIM GUIDANCE FOR THE MEDICAL SCREENING OF WORKERS
POTENTIALLY EXPOSED TO ENGINEERED NANOPARTICLES**

November 2007

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

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Draft CIB on Medical Screening



Updated Strategic Plan:
under review

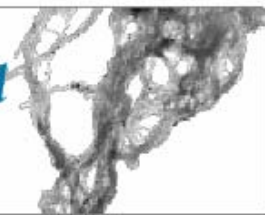
In the latest revision of "Approaches to Safe Nanotechnology"
to be released for review Summer 2008

Appendix A

**Nanoparticle Emission Assessment Technique
(NEAT) used by NIOSH for Identifying Sources and
Releases of Engineered Nanoparticles**



The Nanotechnology Field Research Team Update



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, electrospun 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) 533-8339, CGeraci@cdc.gov or Mark Methner, Ph.D., CIH at (513) 841-4325, MMethner@cdc.gov.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
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NIOSH

How Will We Get the Job Done?

Collaboration

- Share knowledge
- Use expertise
- Build experience
- Partner



Thank you!

Charles.Geraci@cdc.hhs.gov

