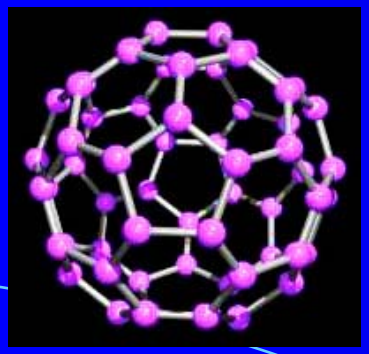

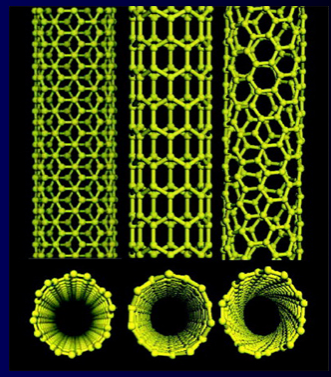

Nanotechnology:
Understanding and Managing the Potential Health Risks

Brenda E. Barry, Ph.D., R.B.P.
Senior Toxicologist
The Cadmus Group, Inc.
NEAIHA - November 16, 2006

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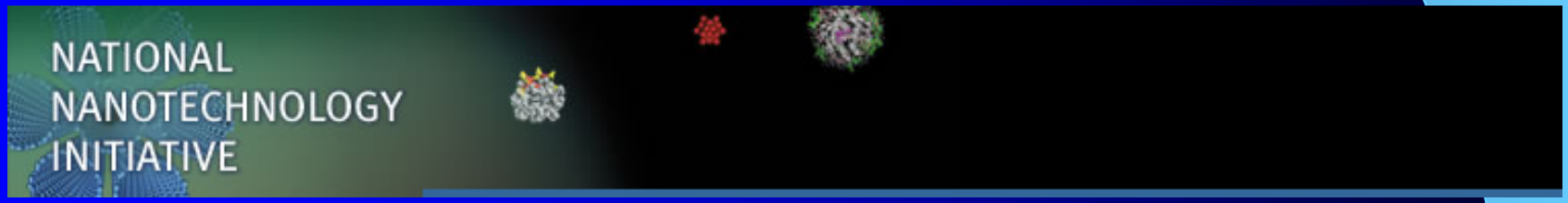
What Is Nanotechnology?

- National Nanotechnology Initiative
  - Nanotechnology is the understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications



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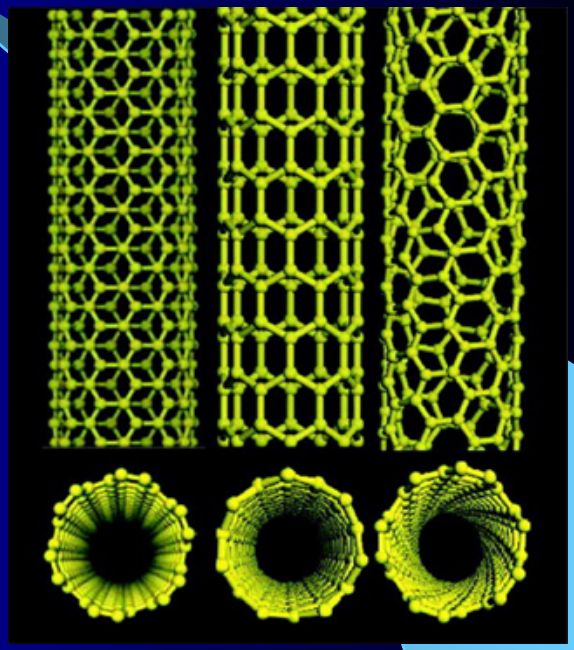
Categories of Nanomaterials

Natural

Man-Made



Engineered

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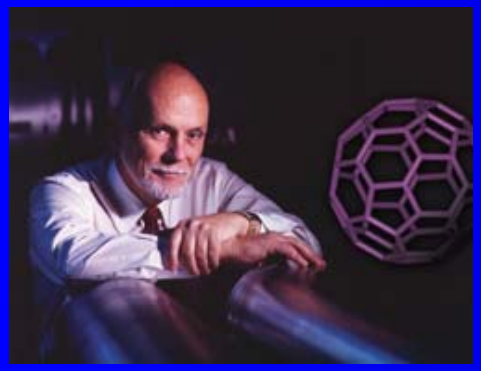
A Brief History of Nanotechnology

Feynman

- **Richard P. Feynman - 1959**
  There's Plenty of Room at the Bottom

Drexler

- **K. Eric Drexler - 1986**
  Engines of Creation



Smalley

- **Richard E. Smalley - *1996***
  Nobel Prize in Chemistry

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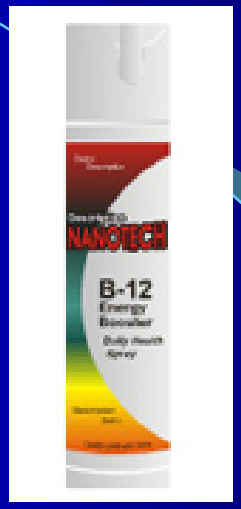
Nanotechnology Products Are Here Now

Dermatone SPF 20 Natural Formula

Curad Silver Bandages

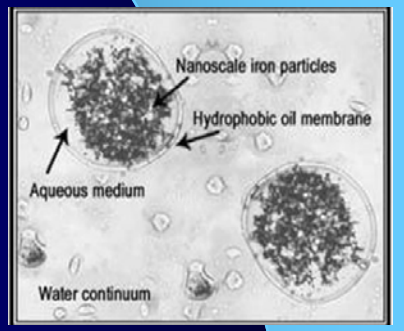


NANO B-12 Vitamin Spray

SAMSUNG Samsung Nano SilverSeal Refrigerator

Eddie Bauer Ruston Fit Nano-Tex Khakis

Wilson Double-Core Tennis Balls



NASA's Emulsified Zero-Valent Iron

Mercedes-Benz
Mercedes CLS Class

GM
Hummer H2

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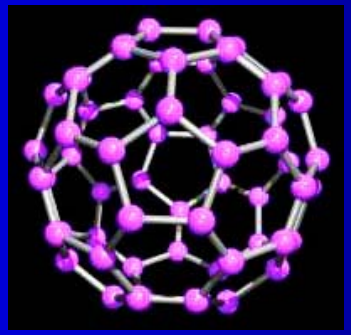
Nanotechnology Challenges

- Do nanomaterials (NM) present new and unique risks for health and safety and for the environment?
- Can the potential benefits of nanotechnology be achieved while minimizing the potential risks?



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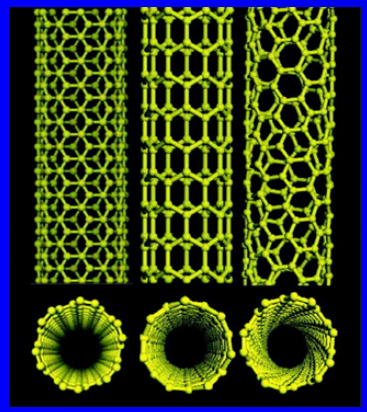
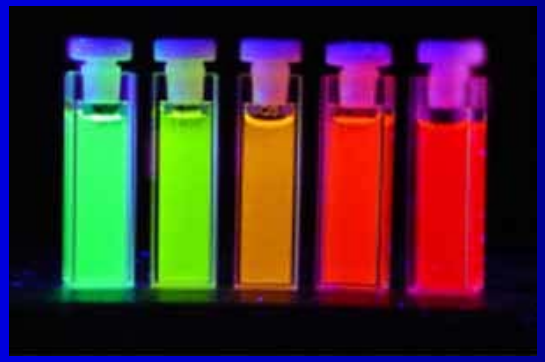
Categories of Nanomaterials

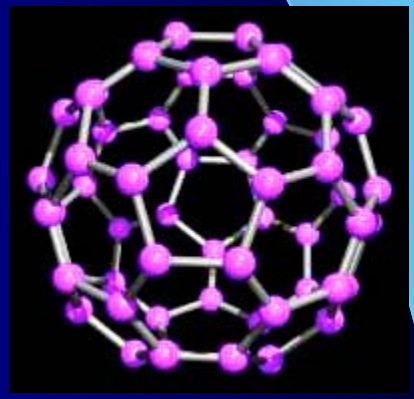
- National Academy of Sciences
  - Nanotubes
  - Nanoclays
  - Quantum dots
  - Metal oxides
- EPA
  - Carbon-based
  - Metal-based
  - Dendrimers
  - Composites



Carbon Nanotubes



Quantum Dots



Fullerenes

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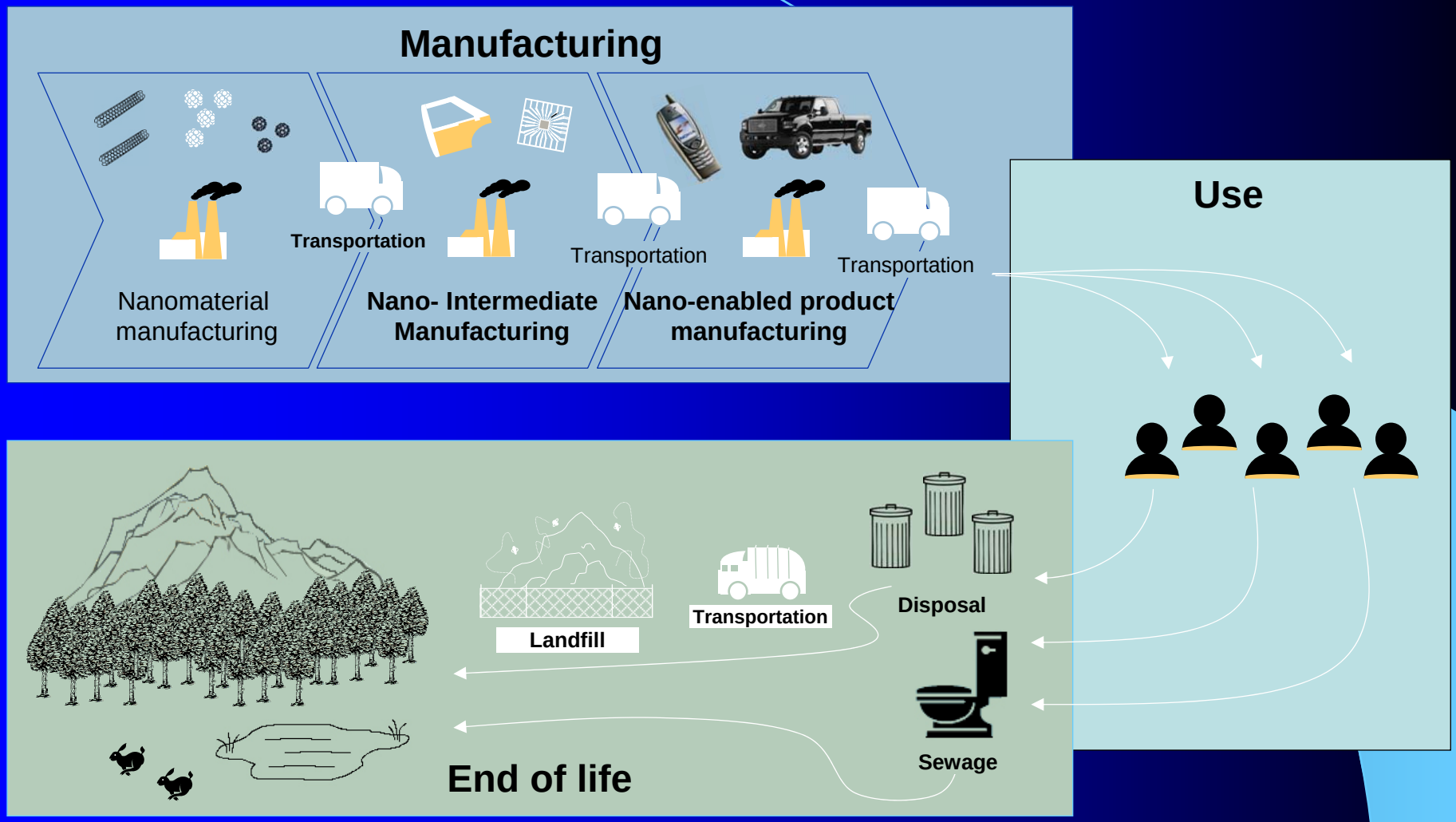
Life Cycle of Nanomaterials



From: L. Gibbs 2006

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Health, Safety, and Environmental Concerns for Nanomaterials

- Human implications
  - NM toxicity not yet well understood; nano-size materials do not behave like their bulk counterparts
  - Reactivity of NM due to large surface area
  - Potential for bioaccumulation
- Environmental implications
  - Contamination of water and soil from improper disposal of NM
  - Bio-uptake of NM and accumulation in food chain

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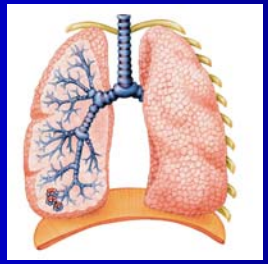
Health and Safety Concerns for Nanomaterials

- **Potential fire and explosive hazards**
  - **Decrease in particle size reduces the minimum ignition energy and increases the combustion potential**
- **Catalytic reaction hazards**
  - **Small size of nano-size particles has often been used to advantage as catalysts**
  - **Engineered nanomaterials may have unpredicted catalytic potential**

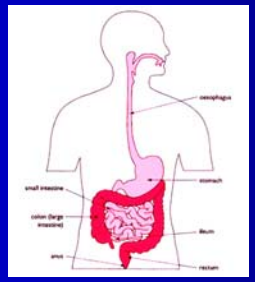
Nanotoxicology

- *Nanotoxicology* – Science of engineered nanodevices and nanostructures that deals with their effects in living organisms (Oberdorster et al. 2005)
- Potential NM exposure routes include:
  - Inhalation



  - Dermal contact

  - Ingestion



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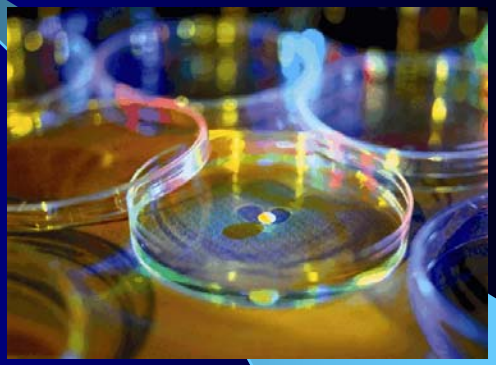
Research Approaches to Understand NM Toxicity

- ***In vitro*** **and** ***in vivo*** **approaches allow study of the mechanisms and biological effects of NM on cells and tissues under controlled conditions**



- ***In vivo*** **models include:**
  - **Inhalation chambers**
  - **Intratracheal instillation**
  - **Pharyngeal aspiration**

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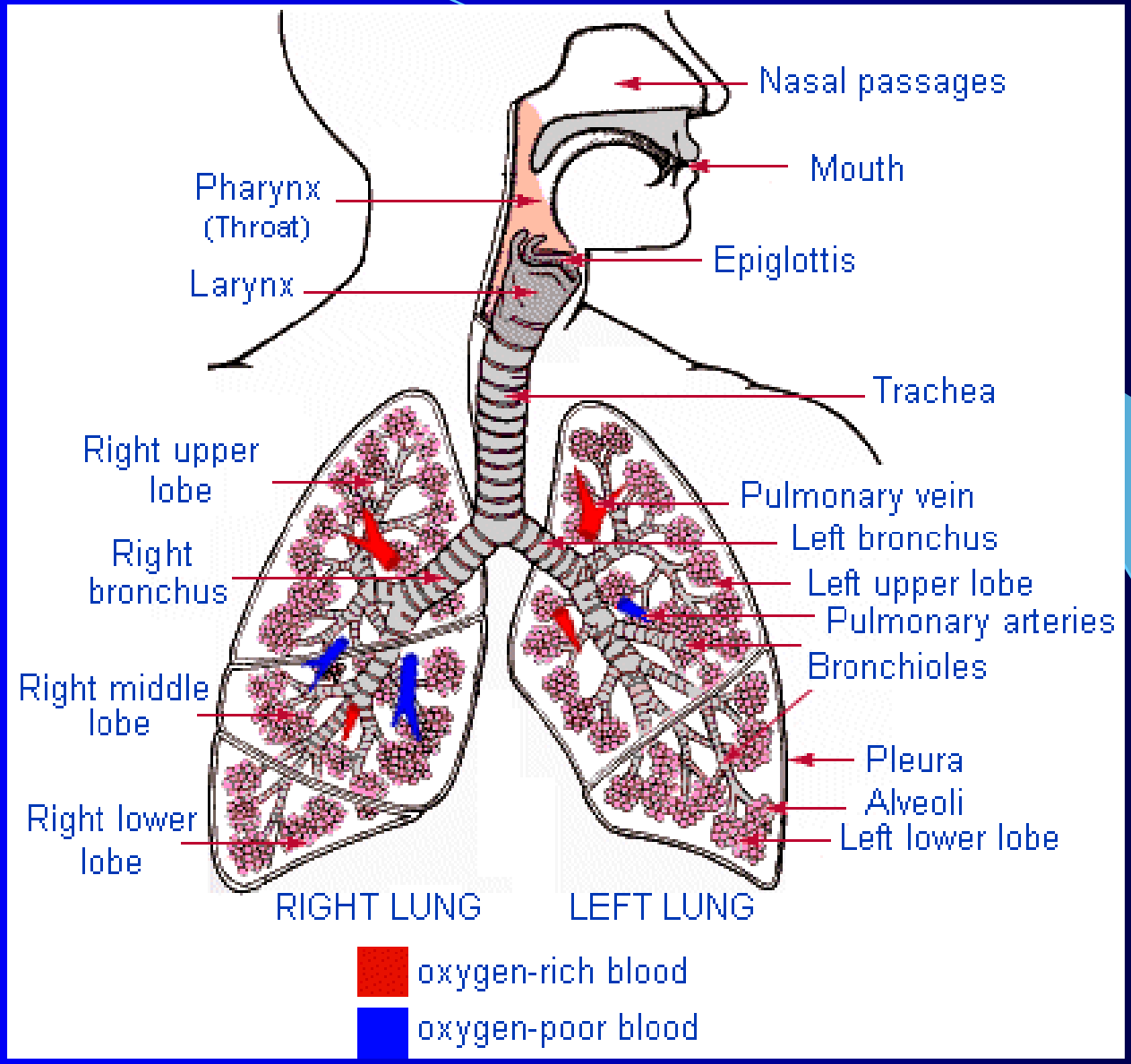
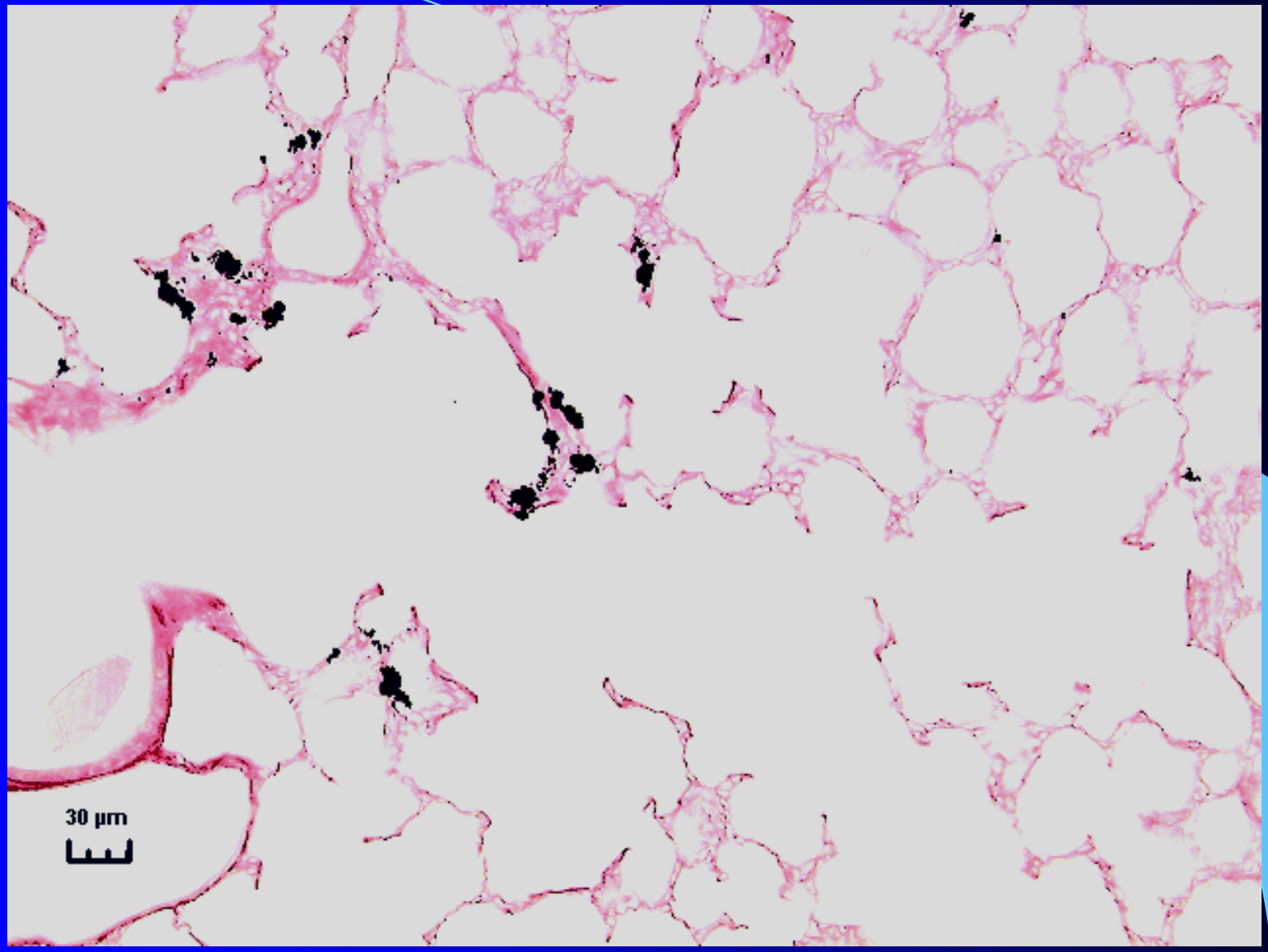
Human Respiratory Tract



Proximal Alveolar Region SWCNT Day 3



Silver-enhanced gold-labeled aggregate SWCNT, 40 ug aspiration, perfusion fixed. Mercer - NIOSH

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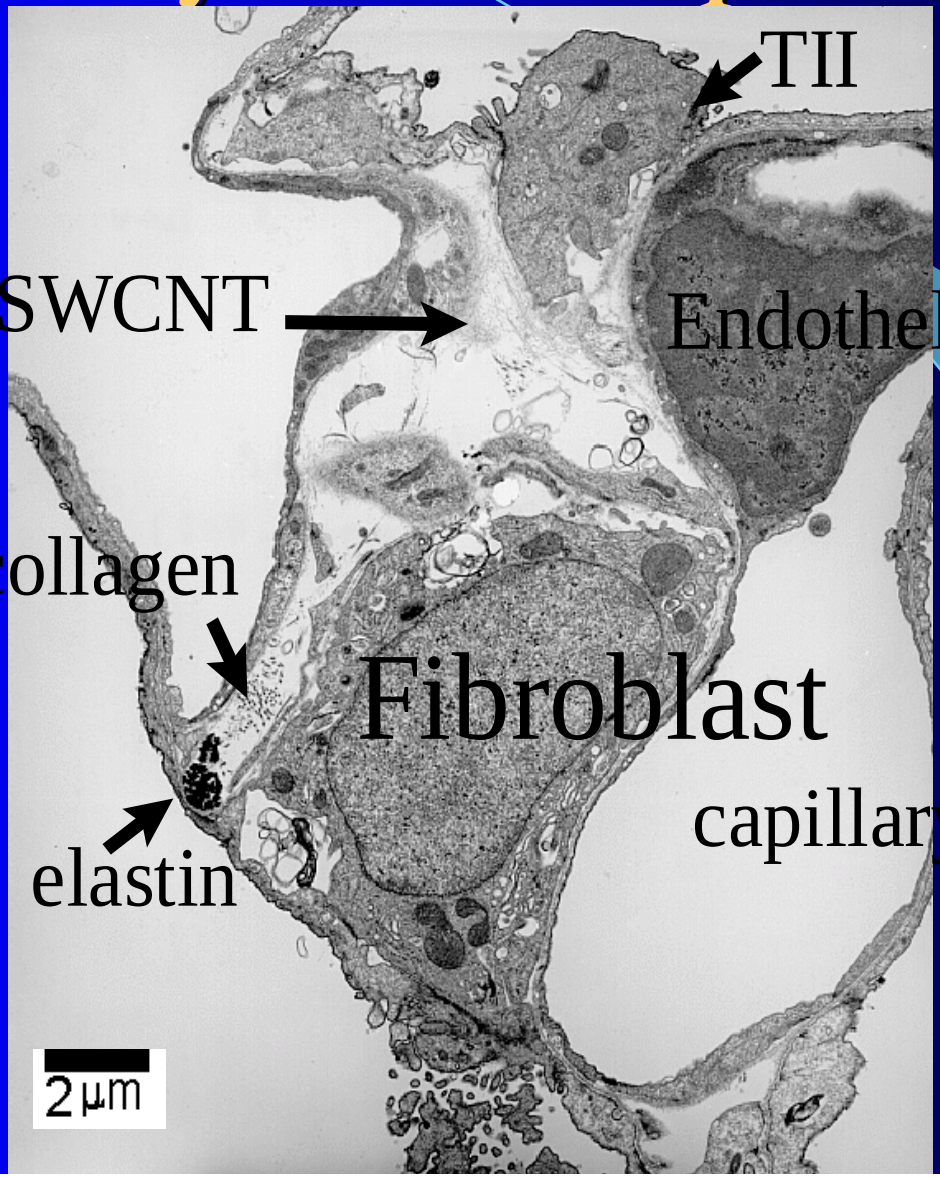
TEM of SWCNT in Interstitium 3 Days Post Exposure



Mercer -NIOSH

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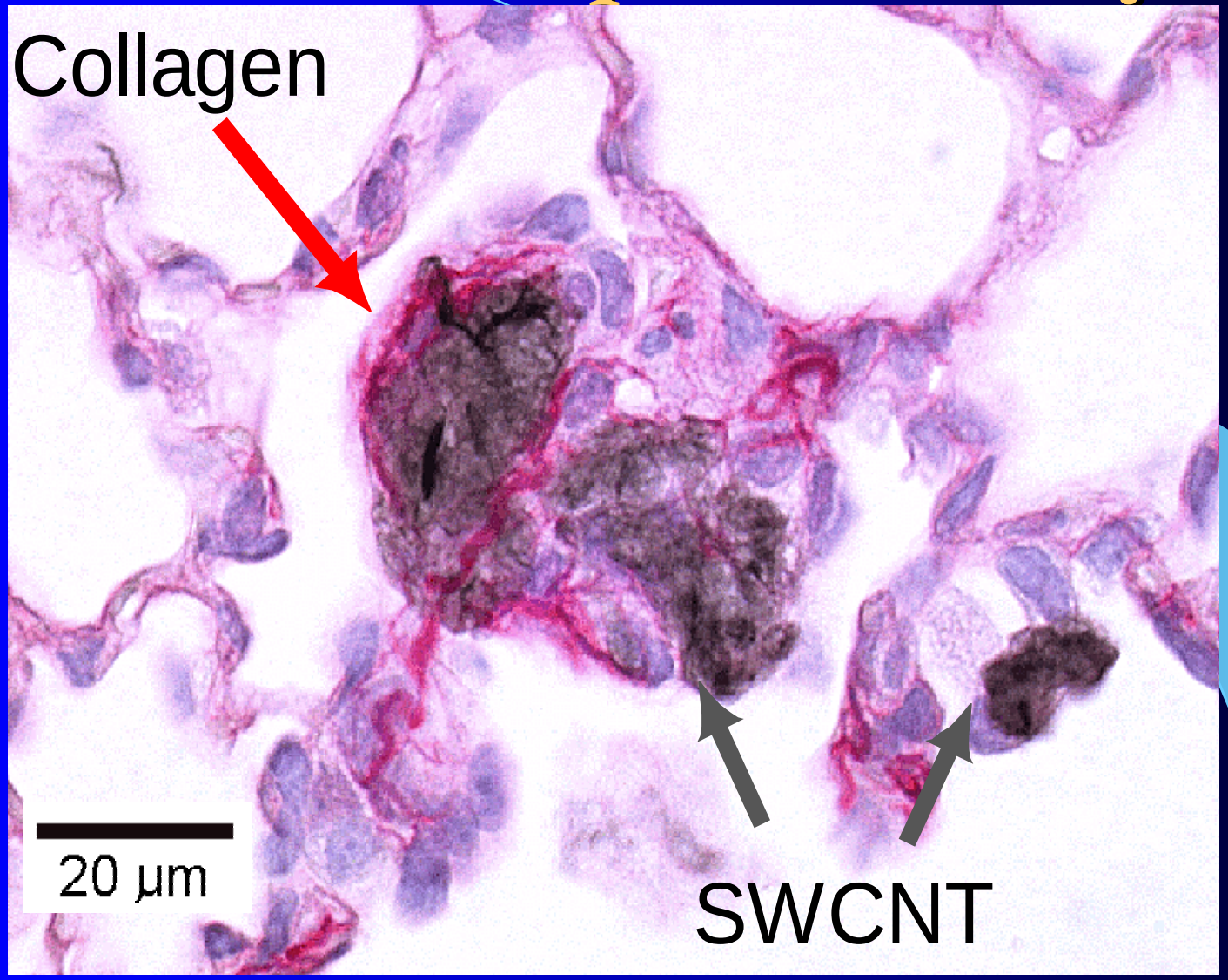
SWCNT Response 7 Days



Pharyngeal aspiration of 40ug SWCNT in C57BL/6 mice

Mercer - NIOSH

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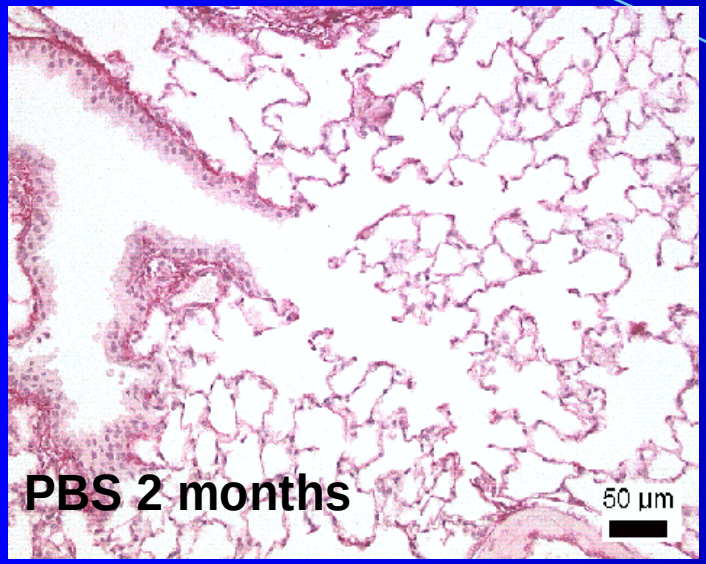
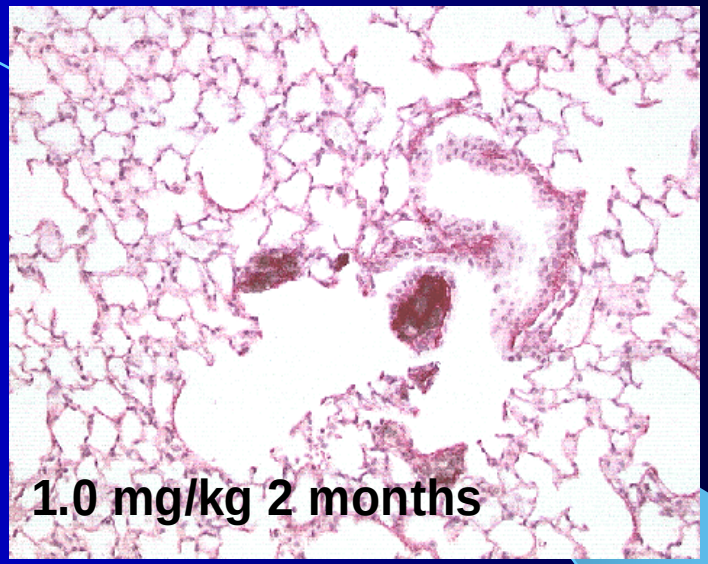
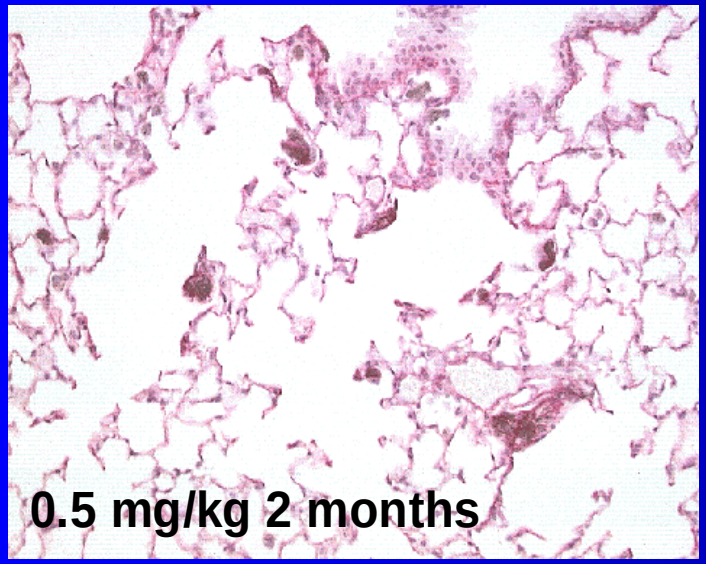
Dose Response to Aggregate SWCNT







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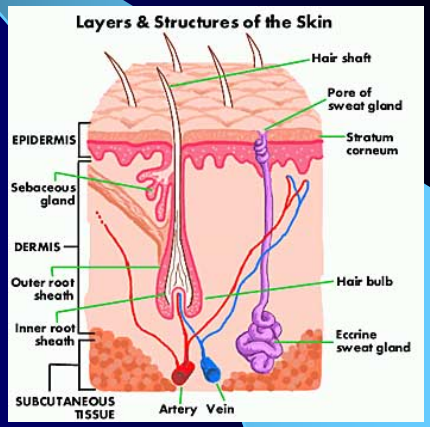
Translocation/Bioaccumulation of Nanomaterials

- Nanoparticles can cross alveolar wall into bloodstream
- Absence of alveolar macrophage response
- Distribution of NM to other organs and tissues
- Inhaled nanoparticles may reach brain through olfactory nerve

In Vitro NM Studies

- Monteiro-Riviere et al. 2006 - Isolated porcine skin flap model and HEK
  - MWCNT, substituted fullerenes, and QD can penetrate intact skin
  - Cytotoxic and inflammatory responses
- Tinkle et al. 2003 - Human skin flexion studies and beryllium exposures
  - Penetration of dermis with 0.5µm an 1µm fluorescent beads



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Functionalization of NM

- Different chemical groups added to the surface of CNT changed CNT properties and decreased their toxicity (Sayes et al. 2006)
- Addition of water-soluble functional groups can decrease the toxicity of pristine C_{60} (Sayes et al. 2004)

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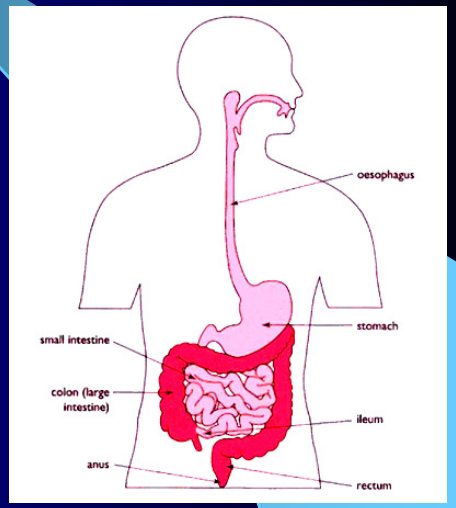
Ingestion Pathway

- Ingestion exposures can occur through direct intake of food or materials containing NM and secondary to inhalation or dermal exposures
- Some evidence suggests that ingested NM may pass through to lymphatics
- Little research to date about Ingestion exposures and the potential for distribution of NM to other tissues



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Workplace Studies

Handling Raw SWCNT

From Maynard 2005

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Workplace Studies

- Maynard and coworkers (2004) determined that aerosol concentrations of NM during handling of unrefined NM material were low
- More energetic processes likely needed to increase airborne concentrations of NM
- Gloves were contaminated with NM
- Results indicated importance of dermal contact as potential exposure route

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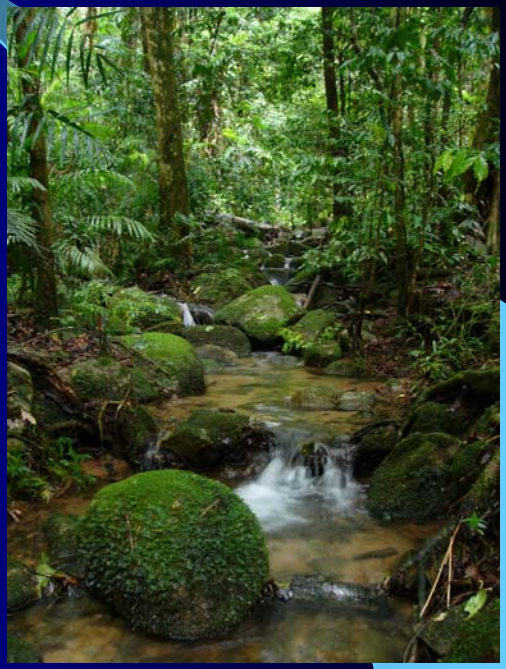
Environmental Risk Concerns Regarding NM

- What happens to NM after product use and disposal?
- What is the fate of NM in the environment?
- Do NM degrade?
- Will NM accumulate in the food chain?
- How to evaluate real world exposures to NM?



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NM and Ecotoxicology

- Exposures of largemouth bass to fullerenes for 48 hr produced lipid damage in brain tissues (E Oberdorster 2004)
- Exposures of *Daphnia* to uncoated, water soluble fullerenes for 48 hr indicated an LC_{50} of 800 ppb (E Oberdorster 2004)

Largemouth bass

Daphnia –water flea

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National Institute for Occupational Safety and Health

- NIOSH is the federal agency responsible for conducting research and making recommendations for the prevention of work-related injury and illness
- NIOSH acknowledges that the occupational health risks associated with the manufacture and use of NM are not yet clearly understood

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NIOSH Critical Topic Areas

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NIOSH Initiatives for Nanotechnology

- Approaches to Safe Nanotechnology: An Information Exchange with NIOSH - July 2006
- Strategic Plan for NIOSH Nanotechnology Research: Filling the Knowledge Gaps
- Nanoparticle Information Library
- Field team investigations to assess NM exposures
- Control Banding
  - NIOSH-RAND Workshop - October 2005

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Environmental Protection Agency

- Toxic Substances Control Act (TSCA)
  - Framework to oversee the manufacture and risk assessment of new materials
- Resource Conservation and Recovery Act (RCRA)
- Nanotechnology White Paper
  - Draft released December 2005
- Nanoscale Materials Voluntary Program

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Occupational Safety and Health Administration

- No guidance documentation yet for nanotechnology
- Participates in a federal interagency group to evaluate EHS and risk issues
- OSHA plans to develop guidance for employers and employees engaged in operations involving nanomaterials
- No standards yet proposed

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European Union and International Standards Development for NM

- EU Registration, Evaluation and Authorisation of Chemicals (REACH)
- Voluntary Standards Development
  - International Standards Organization (ISO/TC229)
  - Organisation for Economic Co-operation and Development (OECD)
  - American National Standards Institute (ANSI)
  - American Society for Testing and Materials (ASTM) International Technical Committee E56
  - Semiconductor Equipment and Materials Institute (SEMI)
  - Institute of Electrical and Electronics Engineers (IEEE)

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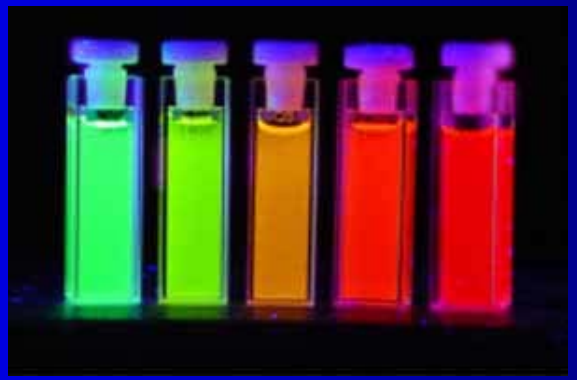
Exposure Assessment for NM

- NM pose unique challenges to traditional exposure assessment techniques
- Mass and bulk chemistry may be *less* important than particle size, surface area, and surface chemistry for NM



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EHS Approaches to Managing Potential Exposures to NM

- Engineering controls
  - Source enclosure
  - Local exhaust ventilation
  - Filters – Are HEPA adequate?
- Work practices
  - Clean work areas
  - Handwashing
  - Shower/Change of clothes

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EHS Approaches to Managing Potential Exposures to NM

- **Personal protective equipment**
  - Clothing and gloves
  - NIOSH evaluating penetration of NM through clothing and gloves
- **Respirators**
  - NIOSH-certified respirators should provide protection if properly selected and fit tested
- **Spill cleanup and proper NM disposal**
  - Select procedures that minimize inhalation and dermal exposures
- **Worker training**

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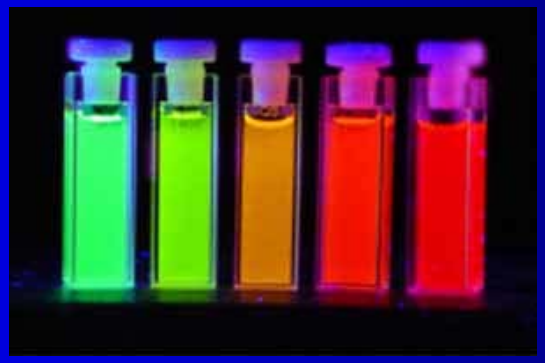
Assessing Risks of Nanomaterials

- Identify and characterize potential NM hazards
- Assess potential exposure scenarios
- Evaluate toxicity
- Characterize risk and uncertainty
- Communicate about risks



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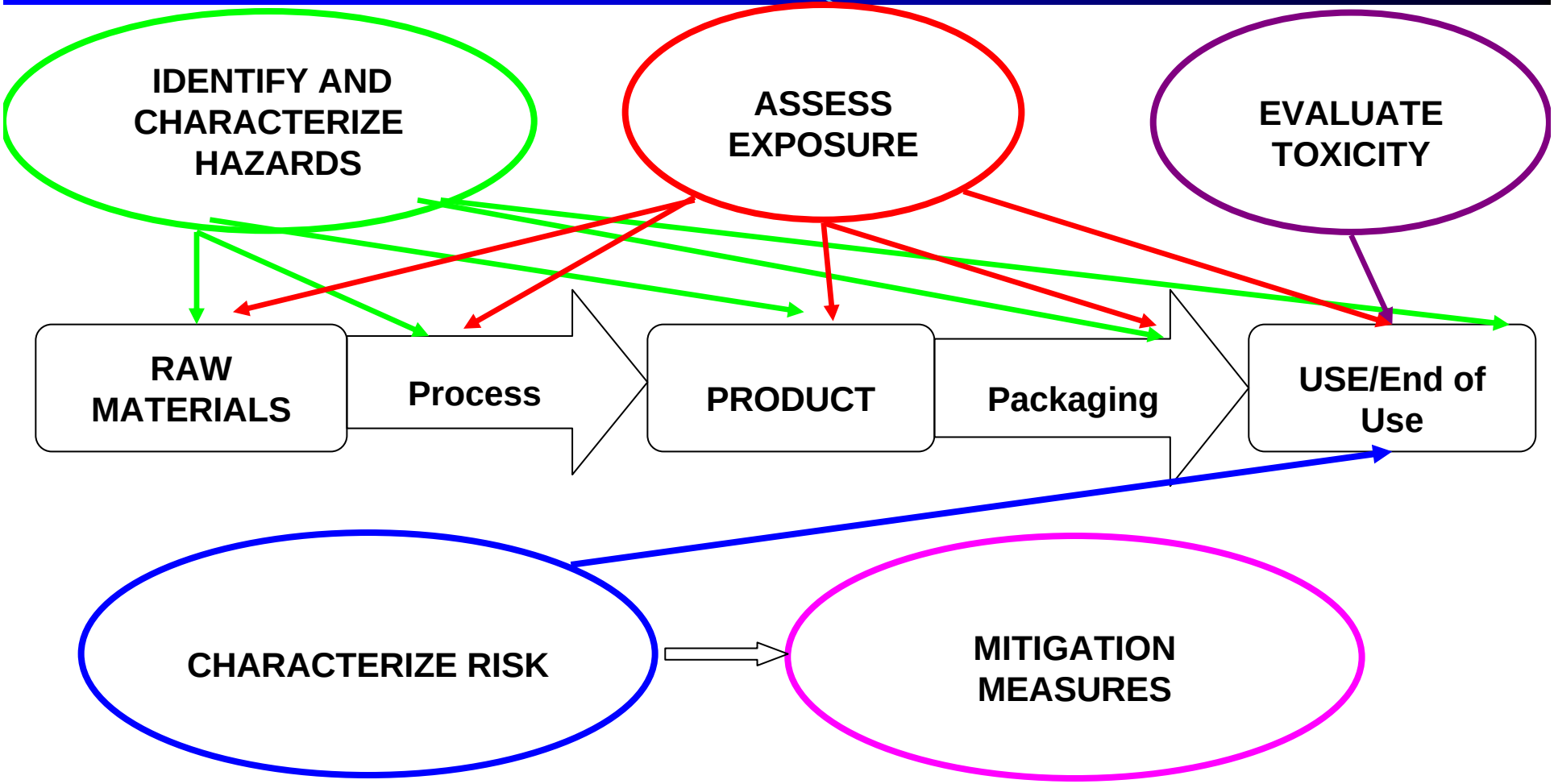
Cadmus Adaptive Risk Assessment Framework for NM



Cadmus Adaptive Risk Assessment Framework for NM

- Screening tool to identify and prioritize key health and process issues
- Dynamic approach that can be applied to a diverse array of hazards
- Identifies key uncertainties
- Adaptive aspect allows reevaluation of previous decisions when new information is available
- Direct application to health and safety concerns

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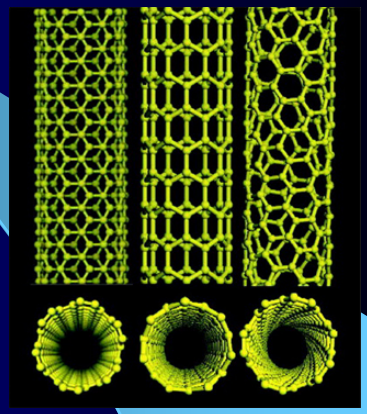
Nanotechnology
Where Are We Today?

- Limited number of NM have been evaluated to date
- Mechanisms for potential NM toxicity are an active area of research
- Specific NM properties, particularly their surface characteristics, clearly affect their toxicity



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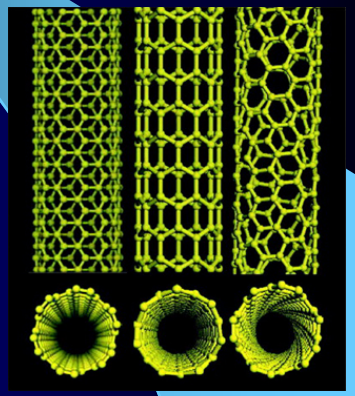
Nanotechnology and EHS Where Are We Today?

- Limited data on workplace exposures to NM
- Little known about worker health risks from exposures to NM
- Numerous current initiatives to develop/recommend best practices
- No regulatory standards or guidelines – yet!



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Nanotechnology
Where Are We Going?

Source: Boston Globe October 7, 2006

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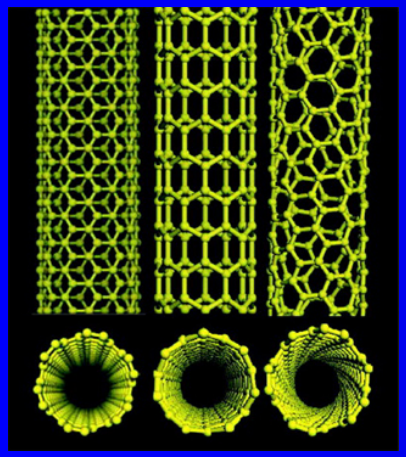
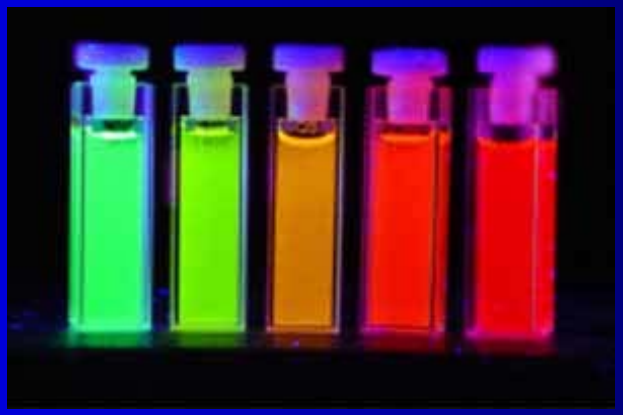
Questions???





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