Navy and Marine Corps Public Health Center
47th Navy Occupational Health and Preventive Medicine Conference

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Navy Occupational Health and Preventive Medicine Conference, 17 March 2008

ENGINEERED NANOMATERIALS:

What you might need to know!

An Update

Christopher Carroll, MSES, CIH

USACHPPM
Readiness thru Health

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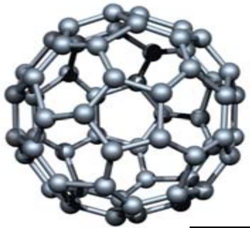
Nanotechnology:

The Next Technological Revolution?

Why Should You Care?

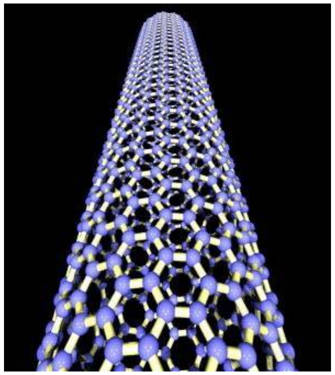
- DoD and other Federal Departments investing a lot of money in R&D
- More and more products down the road
- May see nanomaterial regulations from EPA, OSHA, FDA, DoD, etc. in years ahead

Nanometer and Nanoparticle Definitions



Nanometer (nm): 10^{-9} m or 0.001 μm

***About the diameter of a C_{60} fullerene**



***About the diameter of a single-walled carbon nanotube**

- **Nanoparticle: a particle about < 100 nm (< 0.10 μm) in one, two or three dimensions? – depends on whose definition**

***About < 1/1,000th the width of human hair**
***About the size of the smallest mitochondria in cells**

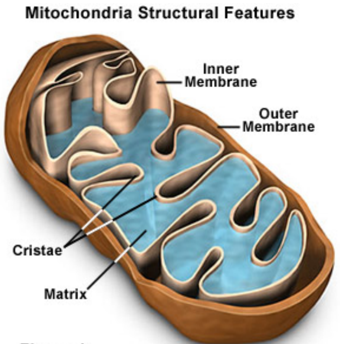
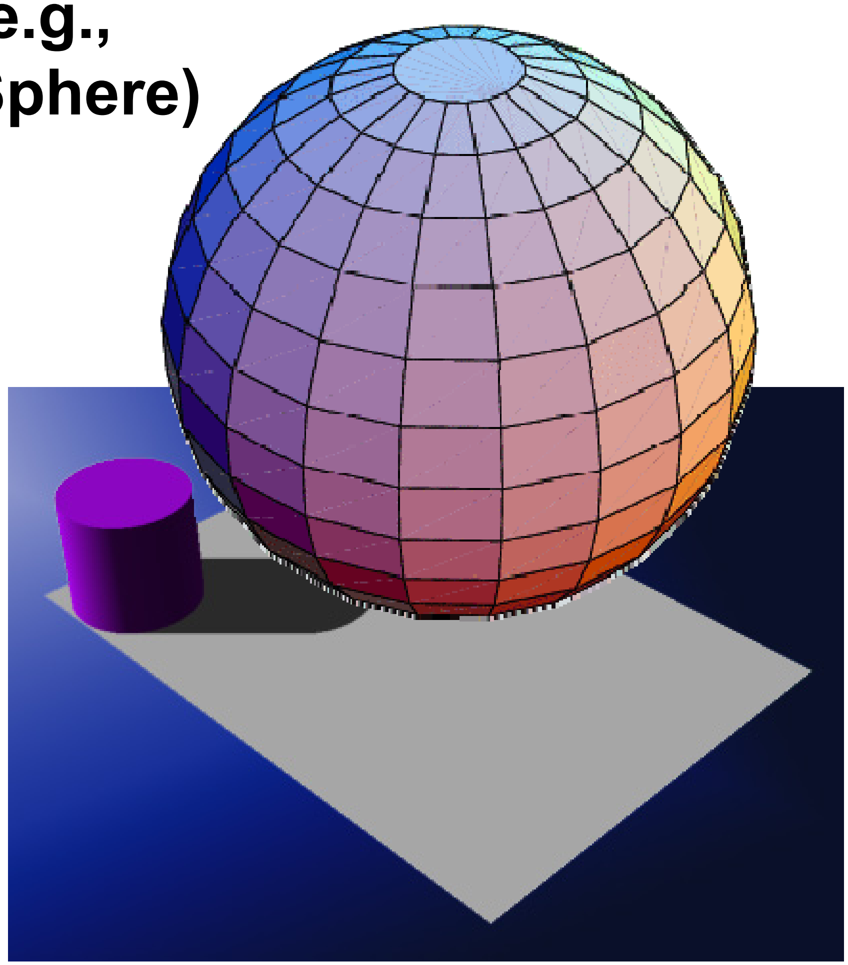


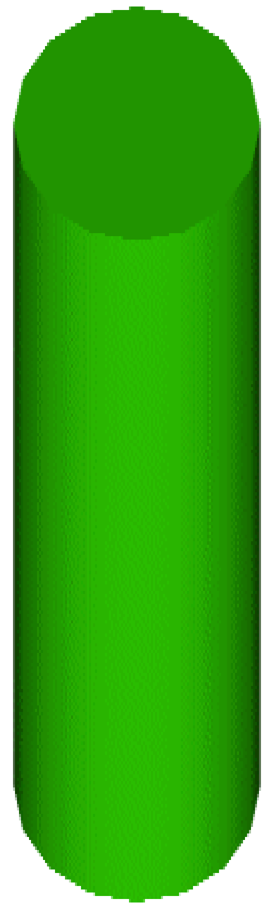
Figure 1

Definitions: Nanoparticle or Nanoscale Object or Particle?

< 100 nm in one, two, or three dimensions?

3-D Object (e.g., Sphere)





2-D Object (e.g., fiber, rod)

1-D Object (e.g., Plate)

ISO TC 229 Nanotechnologies Under Development

International Organization for Standardization

- **Technical Specifications:**
  - Terminology and definitions for nanoparticles
  - Terminology and definitions for carbon nanomaterials
- **Technical Reports:**
  - Outline of nanomaterials classification (Nano tree)

BSi, British Standards Nanotechnology Terminology, December 2007

- PAS 131 Terminology for medical, health and personal care applications of nanotechnologies
- PAS 132 Terminology for the bio-nano interface
- PAS 133 Terminology for nanoscale measurement and instrumentation
- PAS 134 Terminology for carbon nanostructures
- PAS 135 Terminology for nanofabrication
- PAS 136 Terminology for nanomaterials

ENGINEERED NANOPARTICLES/NANOMATERIALS

- Dendrimers
- Nanosomes
- Quantum dots
- Nanoshells
- Nanoscale metal oxides
- Fullerenes
- Nanotubes
- Nanofoam
- Nanohorns
- Nanofibers

ENGINEERED NANOPARTICLES/NANOMATERIALS

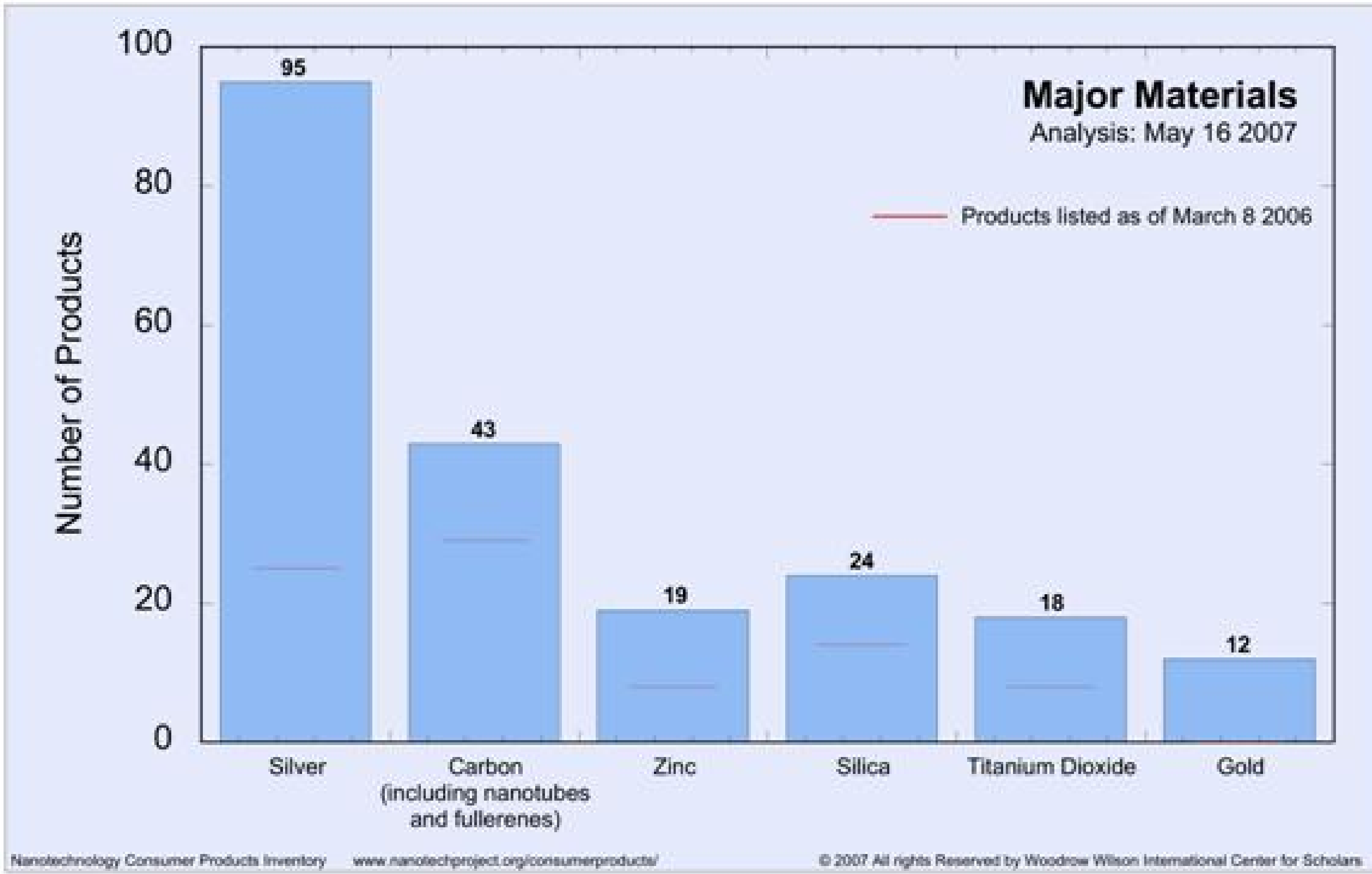
- Nanosheets
- Nanowires
- Nanoplates
- Nanotrees
- Nanoflowers
- Nanosprings
- Nanobelts
- Nanorings

Major Engineered Nanomaterials in Commercial Products

http://www.nanotechproject.org/inventories/consumer/

May 07: Over 475 products; Feb 08: Over 606 products

Source: Woodrow Wilson International Center for Scholars



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Engineered Nanomaterials

- **Bulk nanomaterial -** nanostructured throughout in all three dimensions
  - **One Phase:**
    - **Nanocrystalline copper,** strength depends on size of nanocrystals forming the copper bulk
  - **Multiphase:**
    - **Ceramic zeolites** widely used as support materials in industrial catalysts
    - **Diblock copolymers** which form nanoscale ordered structures depending on temp. and copolymer composition

Engineered Nanomaterials

- **Surface nanomaterial -** only the surface is nanostructured
  - **Surface is nanostructured and bulk consists of same material:**
    - **nanostructured surfaces used in implants to favor cell growth**
  - **Un-patterned film of nanoscale thickness on a substrate of a different material:**
    - **anti-fouling treatments of cars and windows**
    - **anti-reflection coatings of glasses**
  - **Patterned film on a substrate, where the film is either nanoscale in thickness, or the pattern has nanoscale dimensions along the surface**
    - **most of the read/write heads of harddisks**

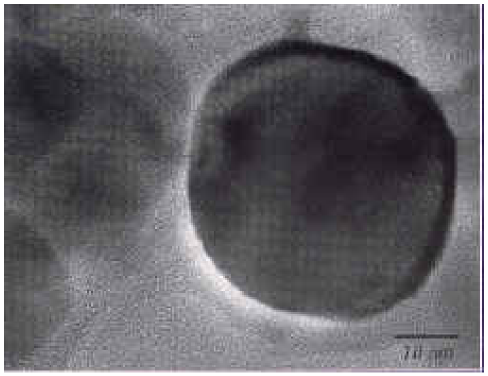
Engineered Nanomaterials

- **Nanoscale particles** that are either
  - **Unbound**
    - **Powder**
    - **Nanoscale particles suspended in air**
    - **Nanoscale particles suspended in a liquid such as water**
  - **Bound on the surface of another solid structure**
    - **Catalysts are usually manufactured as nanometer sized particles on an inert surface material**
  - **Bound within a different solid material**
    - **Advanced composite material consisting of carbon nanotubes mixed/dispersed within a cured polymer**

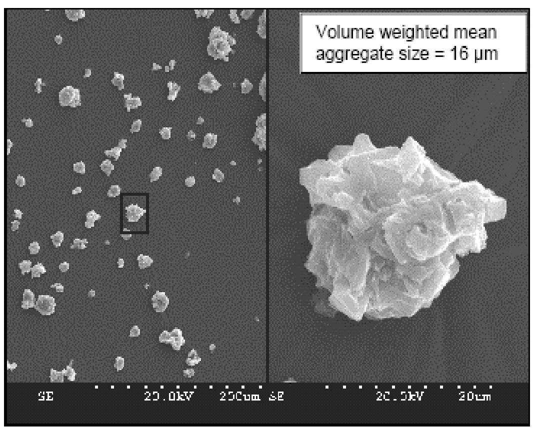
Engineered Nanomaterials

- Particles that have an internal or surface structure at the nanoscale, but the particle, itself, is larger than nanoscale
  - Particle > 100 nm that is an **agglomerate** of discrete nanoscale particles
  - Particle > 100 nm that is an **aggregate** of discrete nanoscale particles

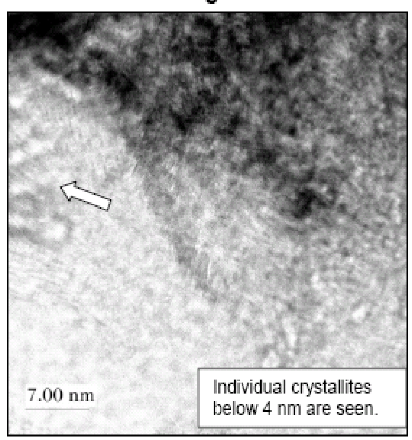
Aggregated
Titanium Dioxide Nanoparticles



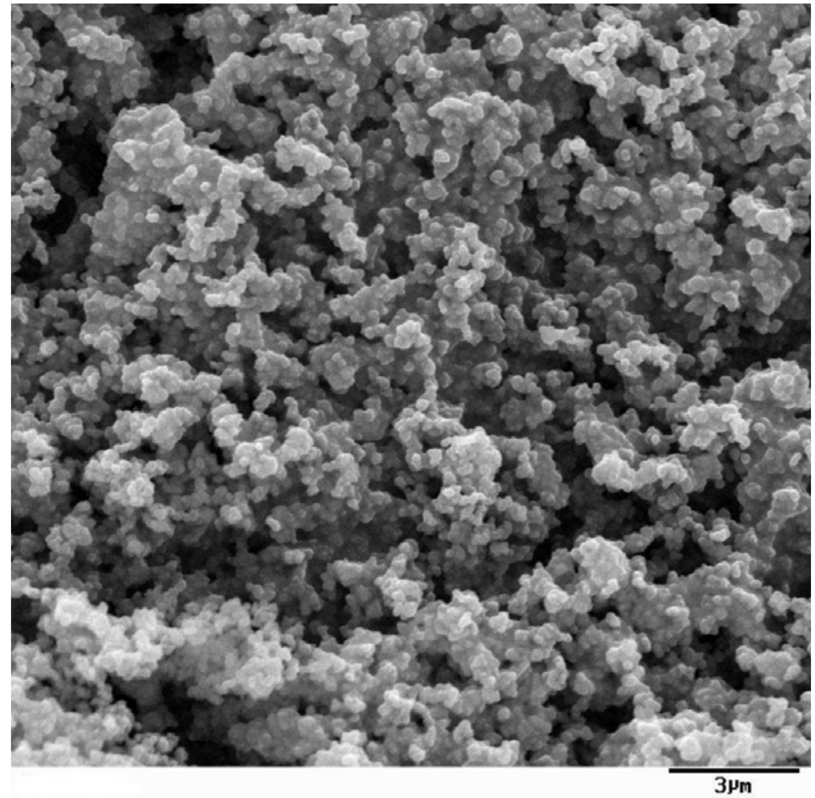
Scanning Electron Microscopy Image



Transmission Electron Microscopy Image



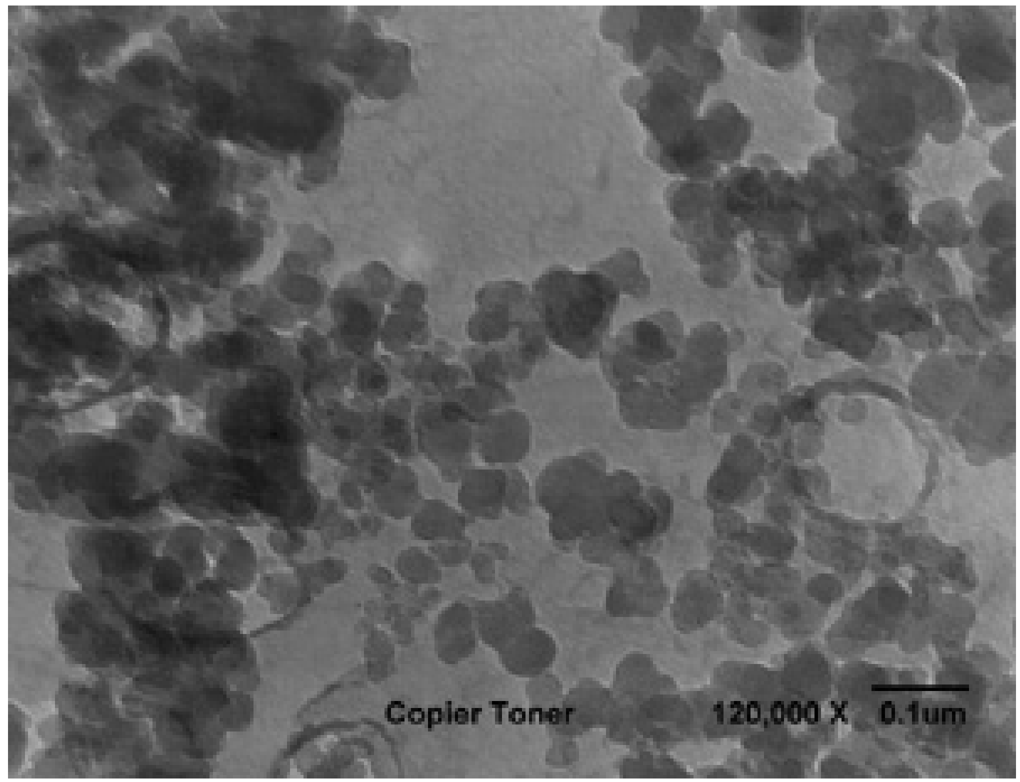
Primary particles strongly bonded together (e.g., fused, sintered, or metallically bonded together)



Aggregate: Discrete group of particles of which the individual components are not easily broken apart

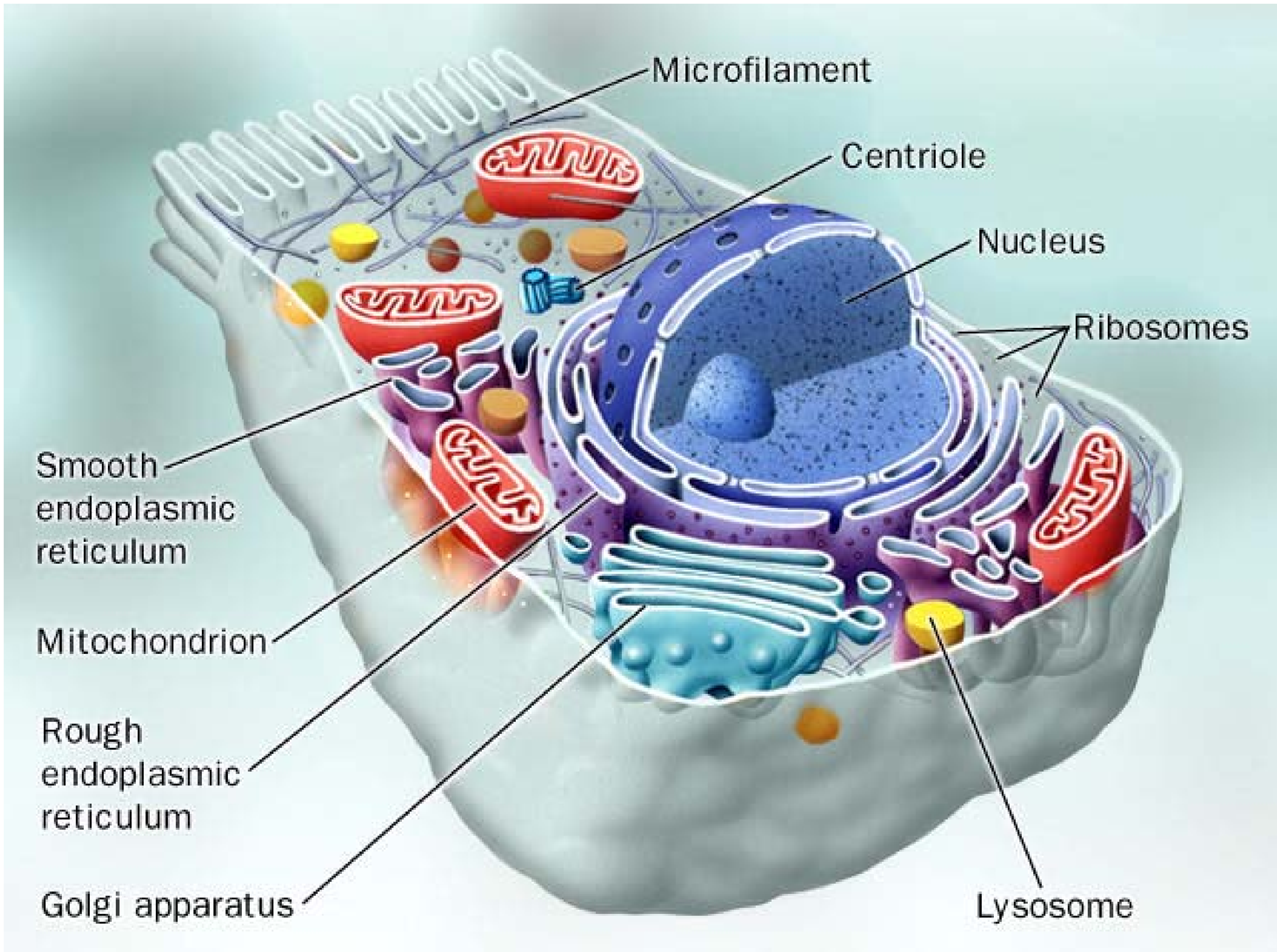
Carbon Black: Agglomerates of Aggregates

A group of particles that may break apart into smaller particles upon processing, etc.

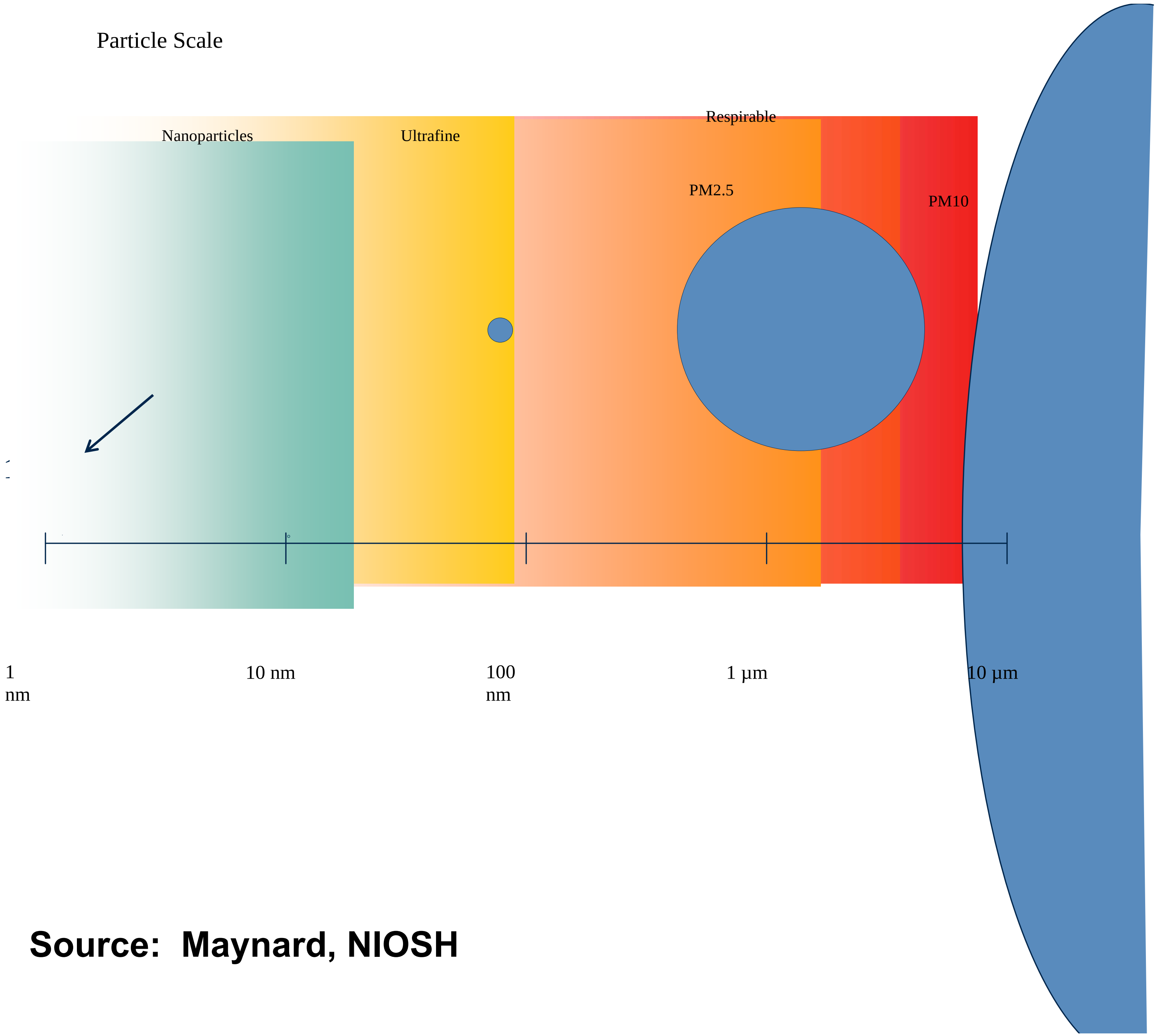


Held together by relatively weak forces (e.g., Van der Waals or Capillary)

Human Cell


Microfilament
Centriole
Nucleus
Ribosomes
Smooth
endoplasmic
reticulum
Mitochondrion
Rough
endoplasmic
reticulum
Golgi apparatus
Lysosome

Particle Scale



Source: Maynard, NIOSH

Nanotechnology Definition

- **Nanoscale science, engineering, and technology encompassing any of the following:**
- **1. Understanding and control of matter at dimensions approximately less than 100 nm (in one or more dimensions)**
- **2. Using the physical, chemical, and biological properties of materials that differ in fundamental and valuable ways from the properties of individual atoms, molecules and bulk matter to create improved materials, devices and systems that exploit these new properties**
- **3. Imaging, measuring, modeling, and manipulating matter at the nanoscale**

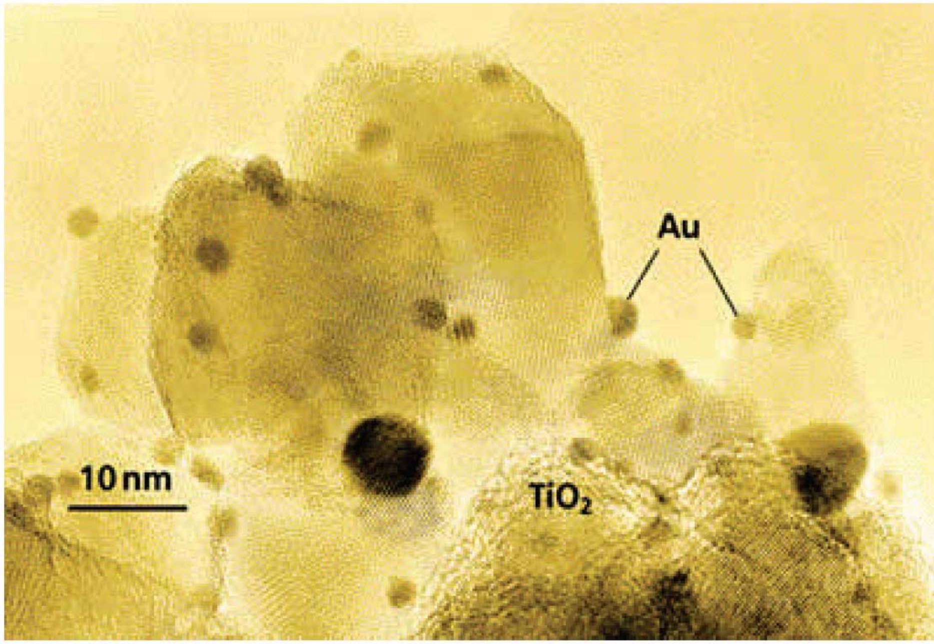
Nanoscale materials are made from either of two approaches:
“bottom-up” **(e.g., beginning with atoms or molecules)**
“top-down” **(refining or reducing bulk materials)**

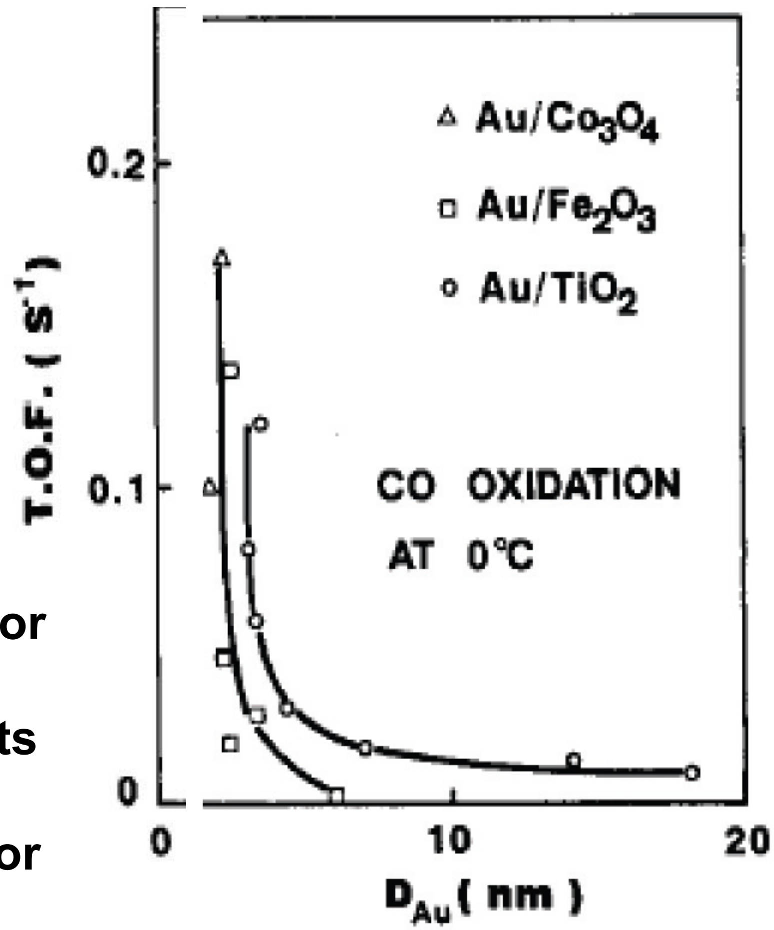
Bulk Form of Gold

Inert – not a catalyst

used in dental fillings, corrosion-resistant coatings.

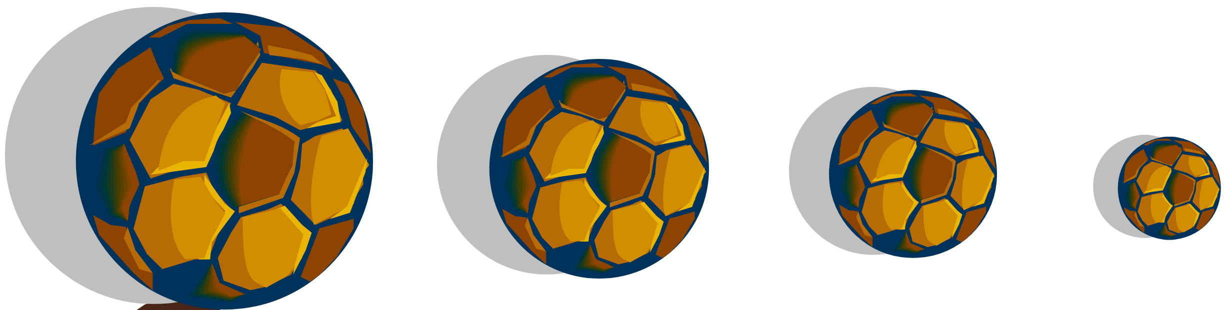
Gold Nanoparticle Catalytic Behavior

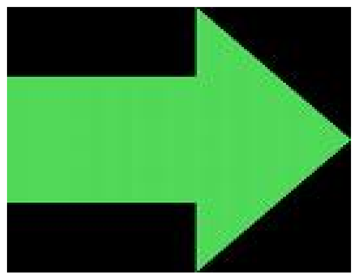




Source: NNI Report, Nanoscience Research for Energy Needs. Transmission electron micrograph of gold (Au) nanoparticle catalysts on a titania (TiO2) support. The remarkable catalytic behavior of the gold nanoparticles for CO oxidation is shown on the right as a function of their size

Person becomes a stronger Person
NON-TRANSITIVE NANOPARTICLE





e.g., nanocrystalline Al 2X stronger than larger Al particles

e.g., nanocrystalline Ni as strong as steel

Does NOT exhibit size-related intensive properties

Has properties that fall on a continuum that can be smoothly extrapolated from the behavior of the larger particles

Some of Our Health Concerns Over Engineered Nanoparticles Are Driven By Our Experiences With:

- Anthropogenic incidental/unintentional respirable or fine particulate matter which contains some fraction of nanoparticles

  ***Air pollution (e.g., vehicle exhaust, etc.)**

  ***Occupational (welding, soldering, asphalt fumes, etc.)**

  ***Human nature activities (e.g., cigarette smoking, candles, fireplaces, etc.)**

Circulation Research Journal of the American Heart Association

American Heart Association
Learn and Live

- Araujo, et. al., Ambient Particulate Pollutants in the Ultrafine Range Promote Early Atherosclerosis and Systemic Oxidative Stress, Cir. Res., 17 Jan. 2008
- **Exposed genetically susceptible mice in mobile animal facility close to a Los Angeles freeway**
- **Compared proatherogenic effects in mice:**
  - **Concentrated ultrafine particles < 0.18 µm AED**
  - **Concentrated $PM_{2.5}$ particles <2.5 µm AED**
  - **Filtered air**

Circulation Research
Journal of the
American Heart Association

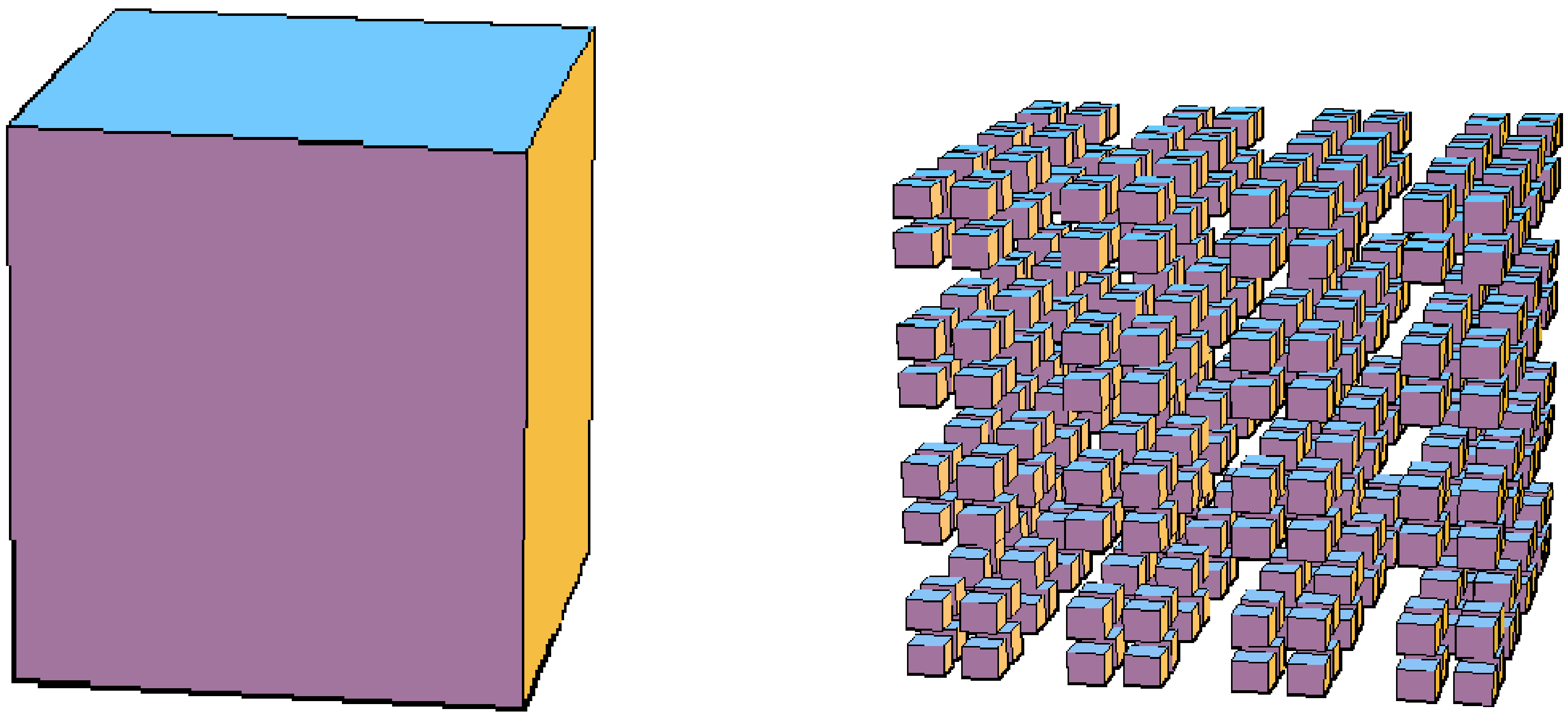
American Heart Association®
Learn and Live℠

- Ultrafine particle-exposed mice had significantly larger early atherosclerotic lesions than mice exposed to $PM_{2.5}$ or filtered air
- **UFPs data demonstrated that they:**
  - are more proatherogenic
  - exert the strongest prooxidative effects
  - are associated with the largest decrease in HDL protective activity
  - may constitute a significant CV risk and are of considerable significance from a regulatory perspective

Toxicology

- **Toxicology Studies Have Found:**
- **On a mass to mass basis:**
  - **Certain Insoluble Nanoparticles are More Toxic and Tumorigenic than Larger Particles of Similar Composition**

Surface Area and Health Implications



Source: Maynard, NIOSH

Hansen, et. al., (2007) 'Categorization framework to aid hazard identification of nanomaterials', Nanotoxicology, 1 - 8

- Vast majority of the 428 studies reviewed demonstrate:
  - (i) Adverse effects on tested animals or cell lines, and
  - (ii) serious lack of characterization of the nanoparticles tested
    - difficult to identify which key characteristics - or combinations of key characteristics - determine the hazards documented in (eco)toxicological studies of nanoparticles.

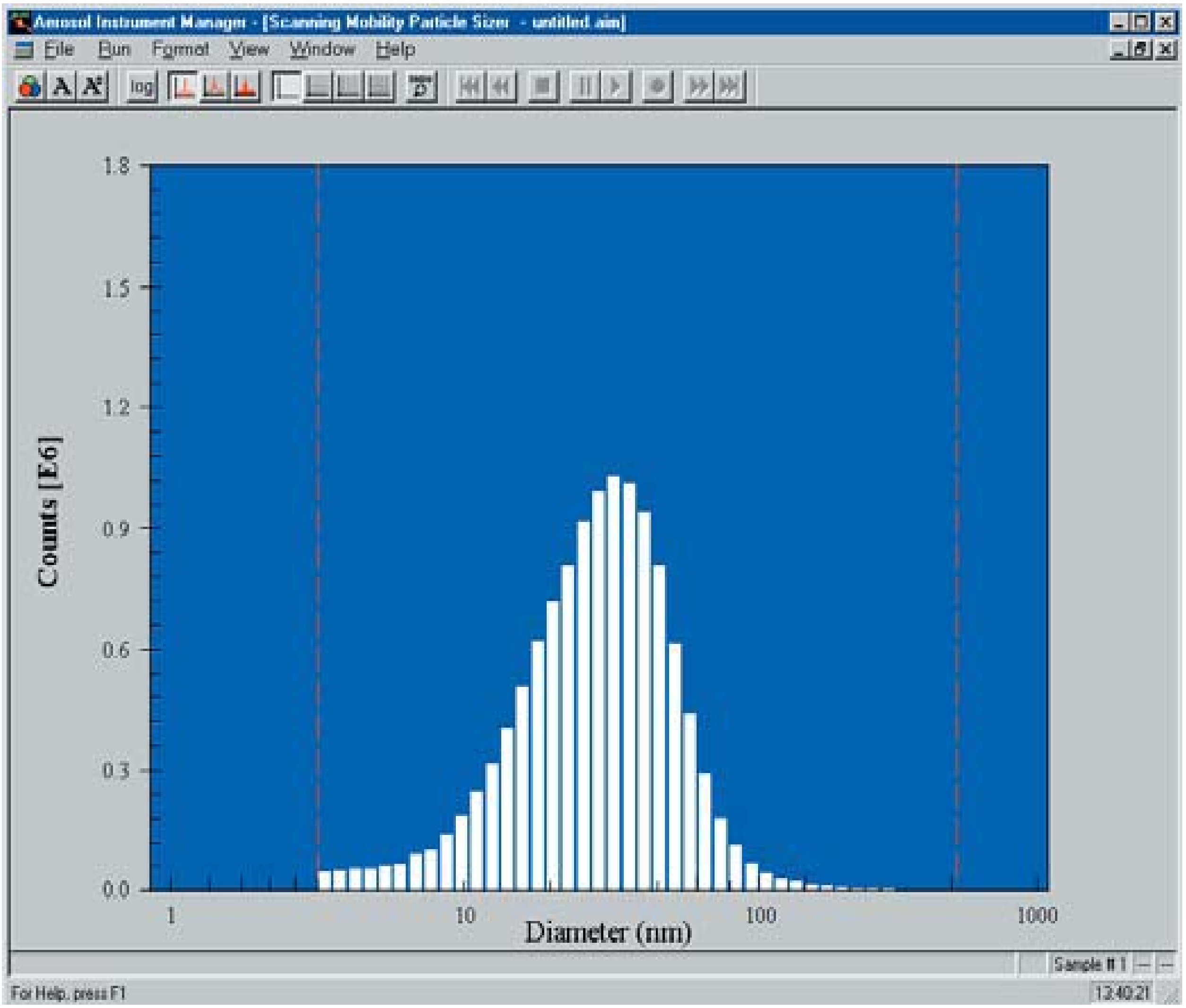
NIOSH Interim Guidance for Medical Screening of Workers Potentially Exposed to Engineered Nanoparticles, DRAFT, Dec 07

- Some types of engineered nanoparticles have been shown in experimental animal studies to cause
  - adverse **lung** effects (e.g., pulmonary inflammation and progressive fibrosis)
  - **cardiovascular** effects (e.g., inflammation, blood platelet activation, plaque formation, and thrombosis)

Nanoparticle Toxicity Determinants

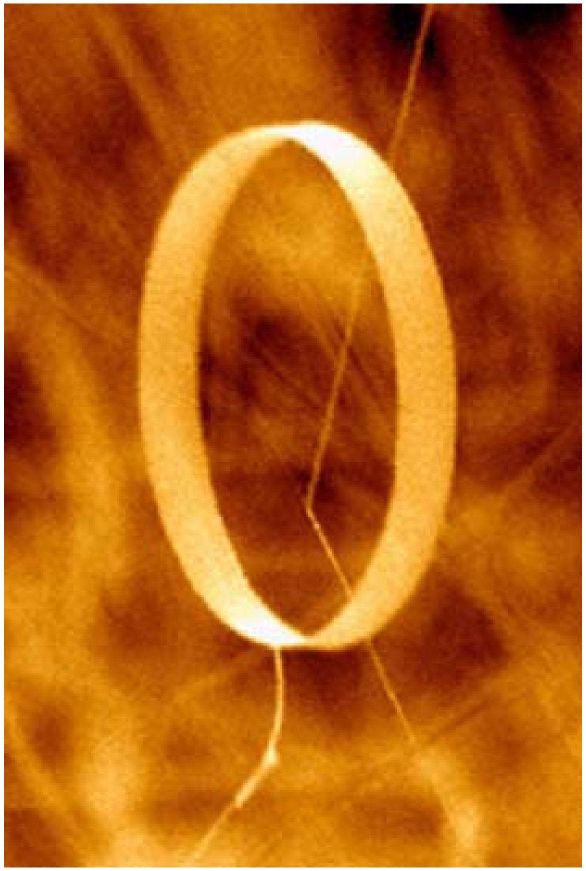
- Size and size distribution
- Shape
- Surface area: external, internal
- Surface chemistry: composition, charge, reactivity, energy/wettability, adsorbed species, contamination
- Chemical composition: spatially averaged (bulk), spatially resolved heterogeneous composition
- Crystallinity: amorphous or crystalline
- Crystalline form (e.g., rutile or anatase TiO2)
- Porosity: nonporous, microporous, mesoporous
- Trace impurities/contaminants (e.g., metal catalysts, PAHs, etc)
- Agglomeration/aggregation state
- Biopersistence/durability/solubility

Size and Size Distribution



Shape

Zinc oxide nanostructures synthesized by a vapor-solid process. (Images: Prof. Zhong Lin Wang, Georgia Tech)

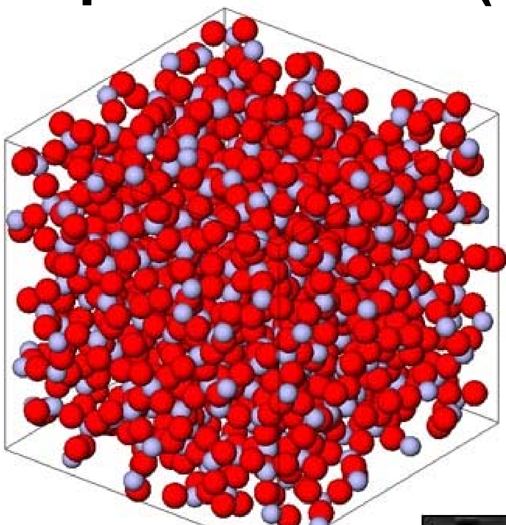


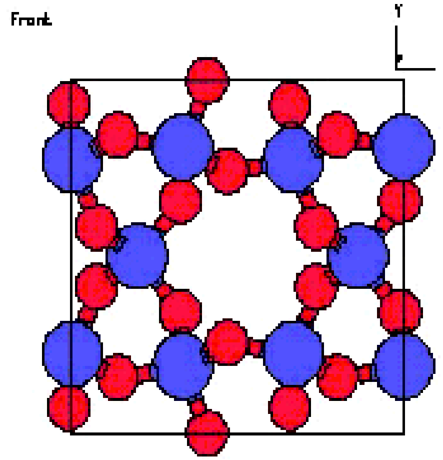
Amorphous or Crystalline

O=Si=O

Amorphous Silica (SiO_2)

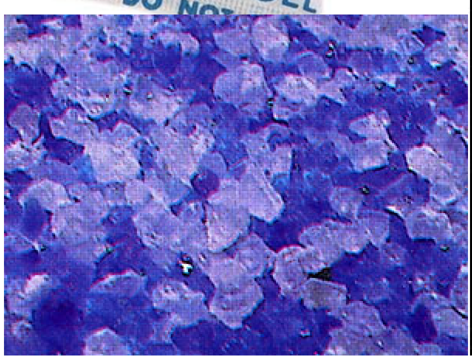
Crystalline Silica (SiO_2)

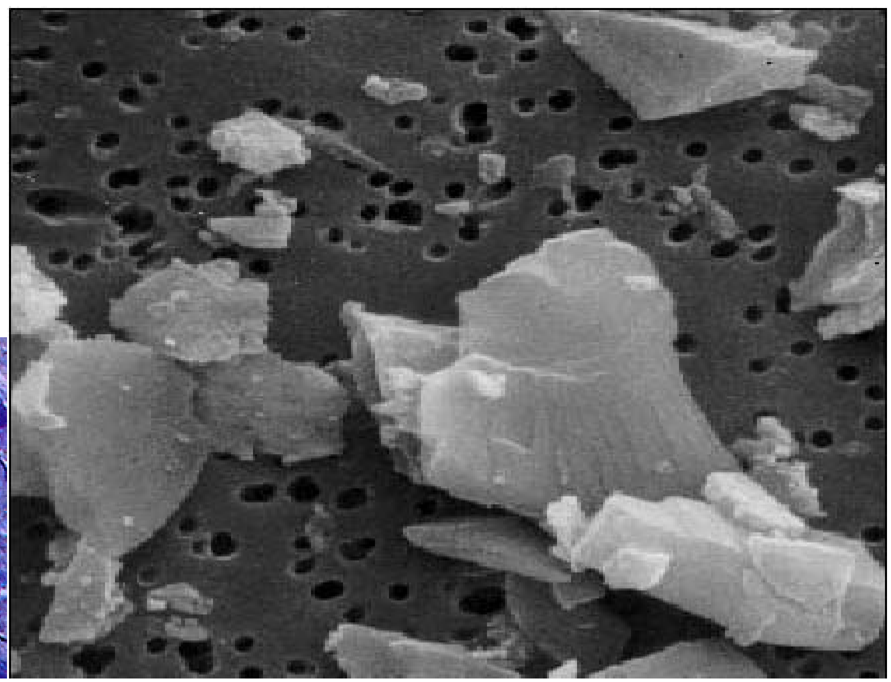




Alpha Quartz.
Crystal Structure:
hexagonal

Molecules arranged in a repetitive pattern that has a unique spacing, lattice structure and angular relationship of the atoms



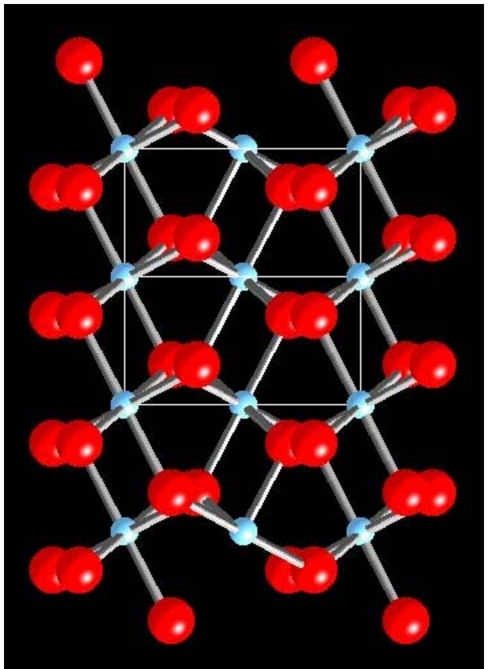


SEM of Crystalline Silica on filter. Source: NIOSH

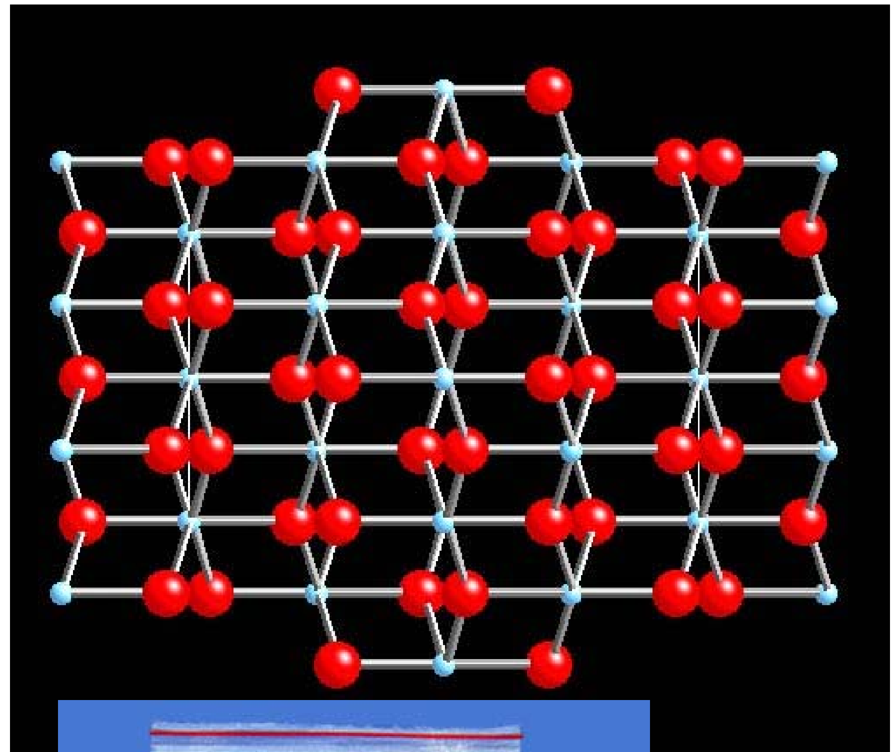
No discrete molecular units. Atoms are held together by covalent bonds with neighboring atoms.

Crystalline Form

TiO_2 Rutile Polymorph
Crystal Structure: tetragonal



TiO_2 Anatase Polymorph:
Crystal Structure: tetragonal



Solubility

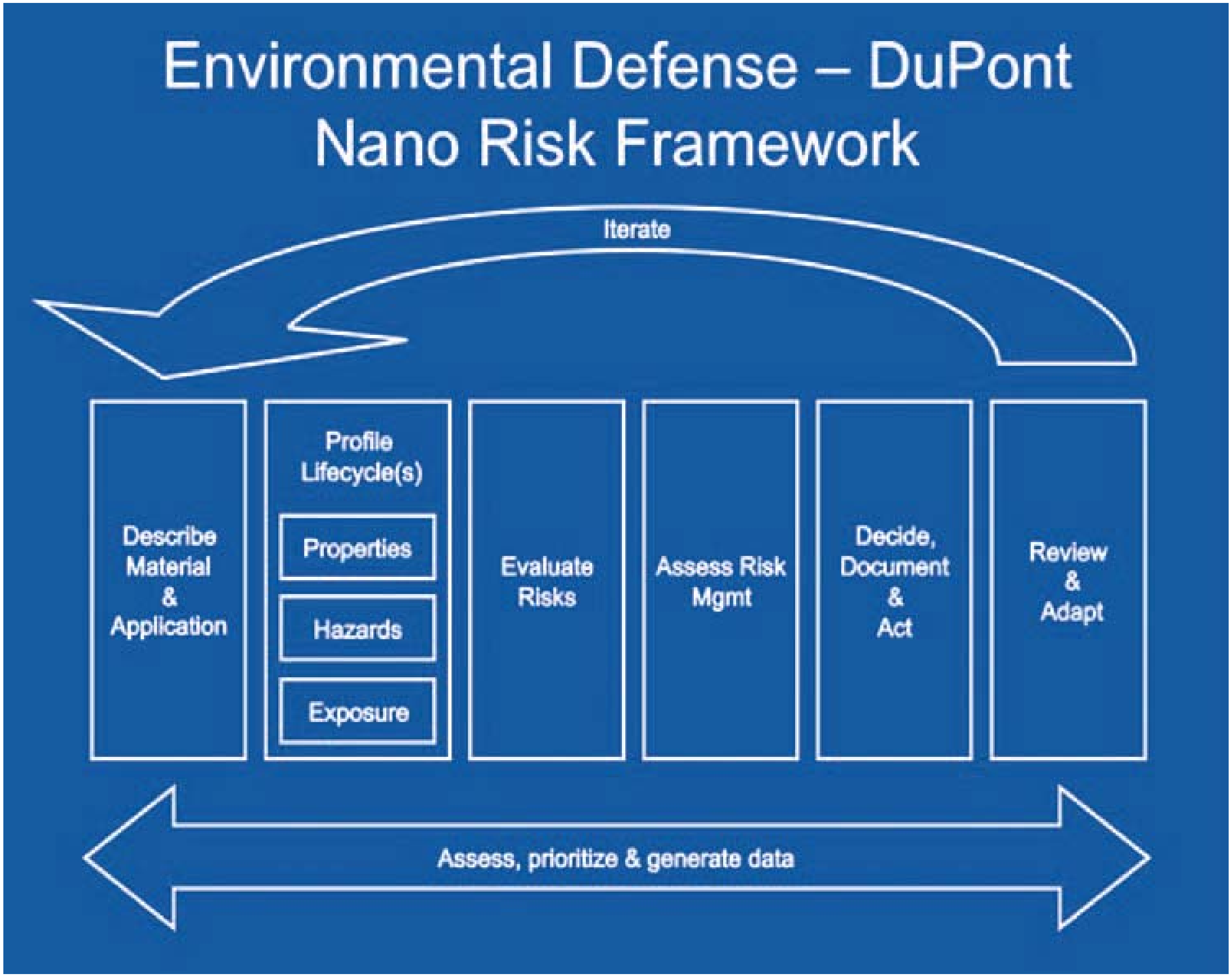
- The maximum equilibrium amount of solute which can normally dissolve per amount of solvent, e.g., **g/100 cc or moles/100 cc**
- If supersaturated, the solution becomes unstable and a precipitate will form
- Solubility affected by:

*__temperature__ (37 deg C normal body temperature)

*__pH__ (saliva, lung fluids, stomach fluids, small intestine fluids, subcellular compartments such as lysosomes)

*__proteins and other solutes in body fluids__

Environmental Defense – DuPont Nano Risk Framework (June 2007)



Material Characterization for Toxicology Studies

- **Warheit (2008):**
  - **How Meaningful are the Results of Nanotoxicology Studies in the Absence of Adequate Material Characterization?**,
  - Toxicological Sciences 101(2), 183-185, 2008

Material Characterization for Toxicology Studies

- **Warheit (2008)**
- At a minimum, recommends the following **(prioritized)** prior to conducting toxicology studies:
  - **Particle size and size distribution (wet state)**
  - **Surface area (dry state)**
  - **In the relevant media being used-depending on route of exposure**

Material Characterization for Toxicology Studies

- **Warheit (2008)**
  - **Crystal structure/crystallinity**
  - **Aggregation status in the relevant media**
  - **Composition/surface coatings**
  - **Surface reactivity**
  - **Method of nanomaterial synthesis and/or preparation** including postsynthetic modifications (e.g., neutralization of ultrafine TiO_2 particle-types)
  - **Purity of sample**

Material Characterization for Toxicology Studies

- **Murdock et. al. (2008):**
  - Characterization of Nanomaterials Dispersion in Solution Prior to In Vitro Exposure Using Dynamic Light Scattering Technique
  - Toxicological Sciences 101(2), 239-253

Material Characterization for Toxicology Studies

- **Murdock et. al. (2008):**
  - Characterized wide range of nanomaterials using DLS and TEM
  - Metals, metal oxides, carbon-based materials
  - In water and cell culture, w/ and w/o serum
  - Cell viability and cell morphology studies conducted in conjunction w/ DLS experiments
  - Evaluated toxicological effects from observed agglomeration changes in presence and absence of serum in cell culture media

ASTM E56 Nanotechnology New Toxicology Assessment Standards

- Three National Institutes of Health (NIH)/National Cancer Institute (NCI) Nanotechnology Characterization Laboratory (NCL)-championed ASTM nanomaterial toxicity testing standards were passed by the ASTM on 31 December, 2007:
  - Standard Practice for Assessment of Hemolytic Properties of Materials
  - Standard Practice for Evaluation of the Effect of Nanoparticulate Materials on the Formation of Mouse Granulocyte-Macrophage Colonies
  - Standard Practice for Evaluation of Cytotoxicity of Nanoparticulate Materials on Porcine Kidney Cells

ASTM E56 Nanotechnology New Toxicology Assessment Standards

- The three ASTM standards are part of a currently-underway inter-laboratory study (ILS)
  - using a nanoscale colloidal gold reference material (RM) supported by the NCL and developed by the National Institute of Standards and Technology

- RM is described here: http://ncl.cancer.gov/resources_news_06292007.asp

Penetration (Inhalable/Thoracic/Respirable) and Deposition

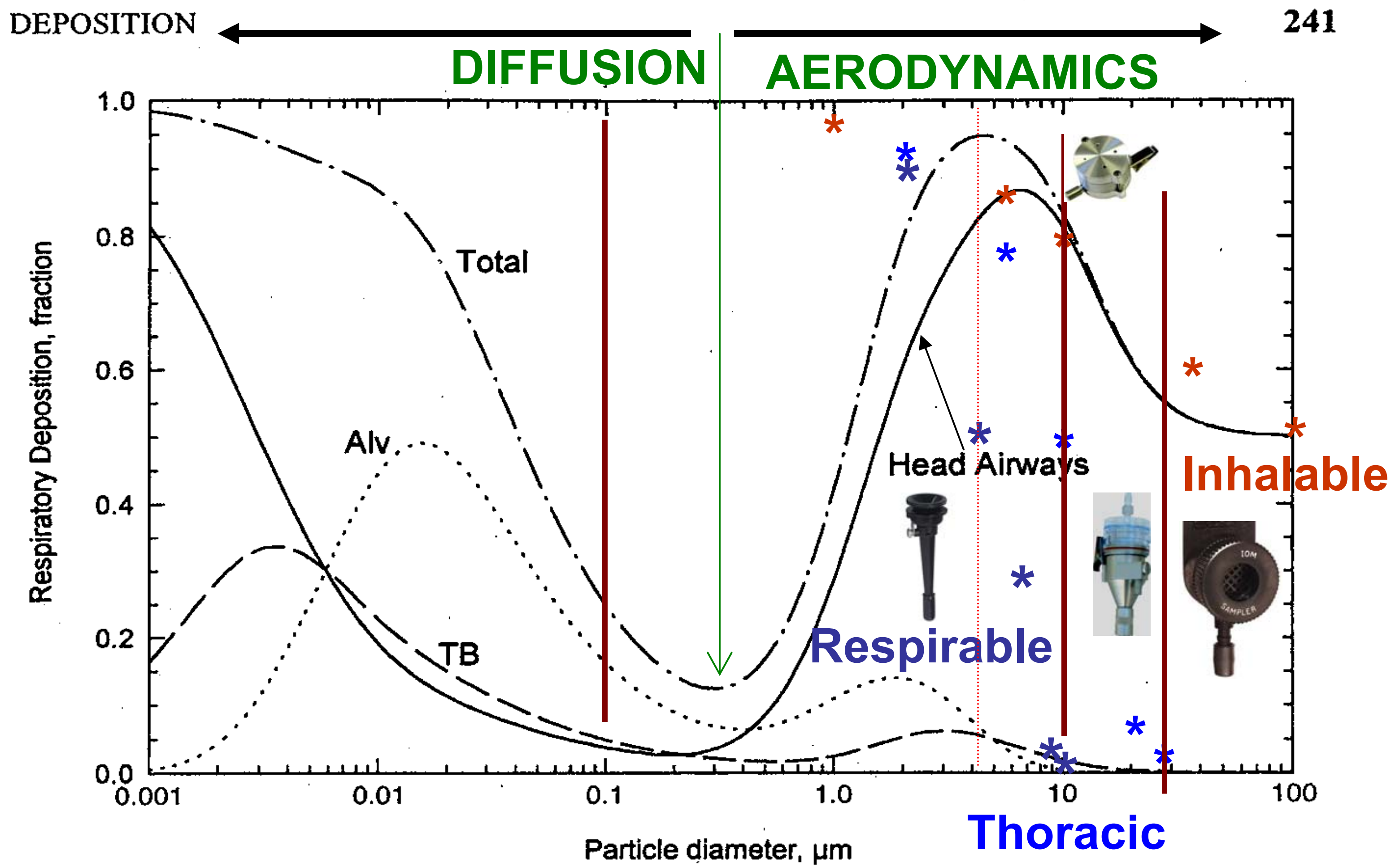


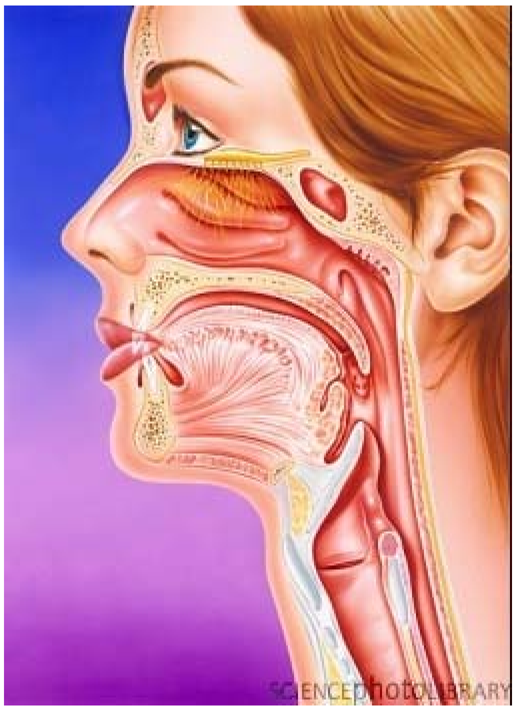
FIGURE 11.3 Predicted total and regional deposition for light exercise (nose breathing) based on ICRP deposition model. Average data for males and females.

Adapted from Hinds, W.C., Aerosol Technology, 2nd Edition, 1999

Colored information is NOT from Hinds.

Will Nanoparticles Travel Along Sensory Nerves in Respiratory Tract to Ganglionic and CNS Structures (e.g., brain)?

Olfactory Nerves



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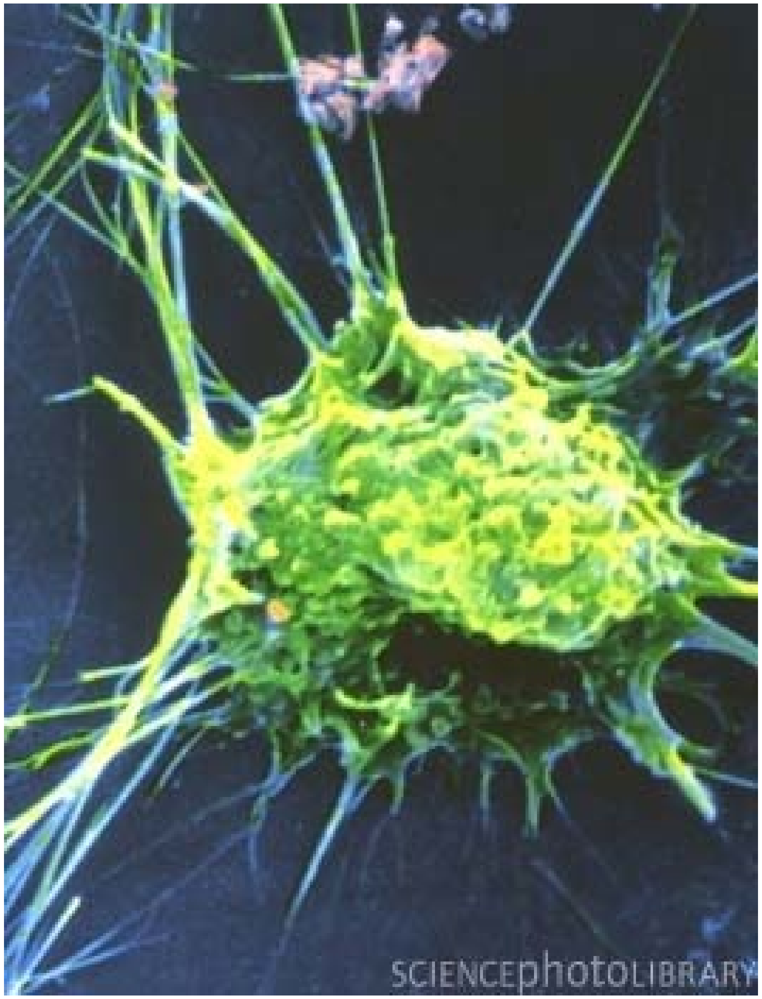
Trigeminal Nerve

D. ROBERTS / SCIENCE PHOTO LIBRARY

Tracheobronchial

Alveolar Macrophages Capture Larger Particles, but Nanoparticles Evade Them



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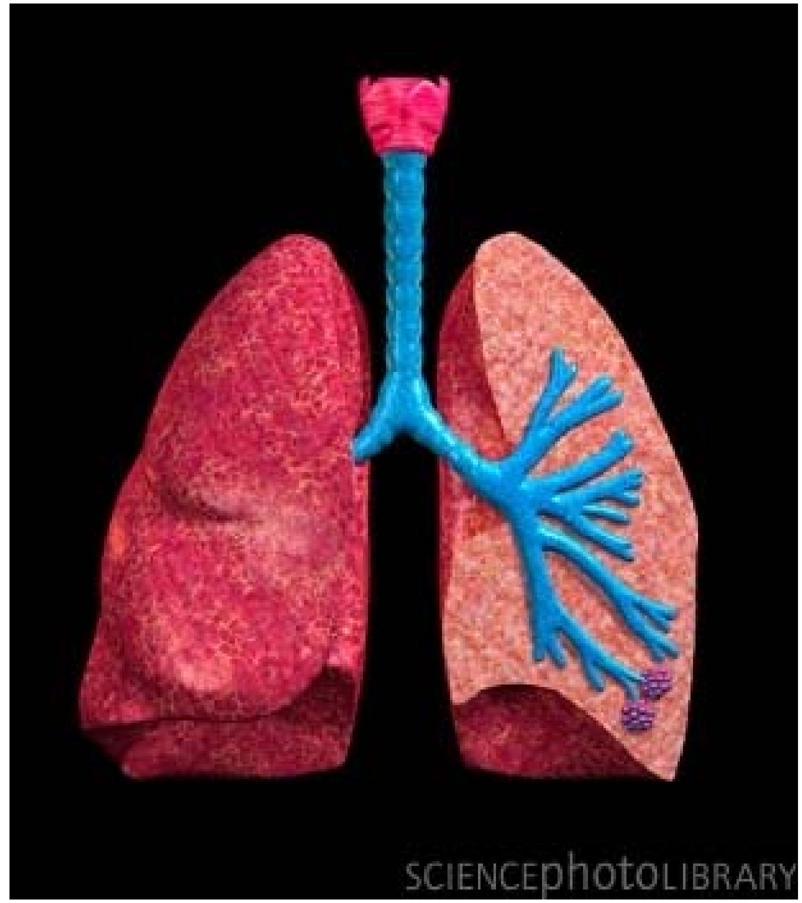

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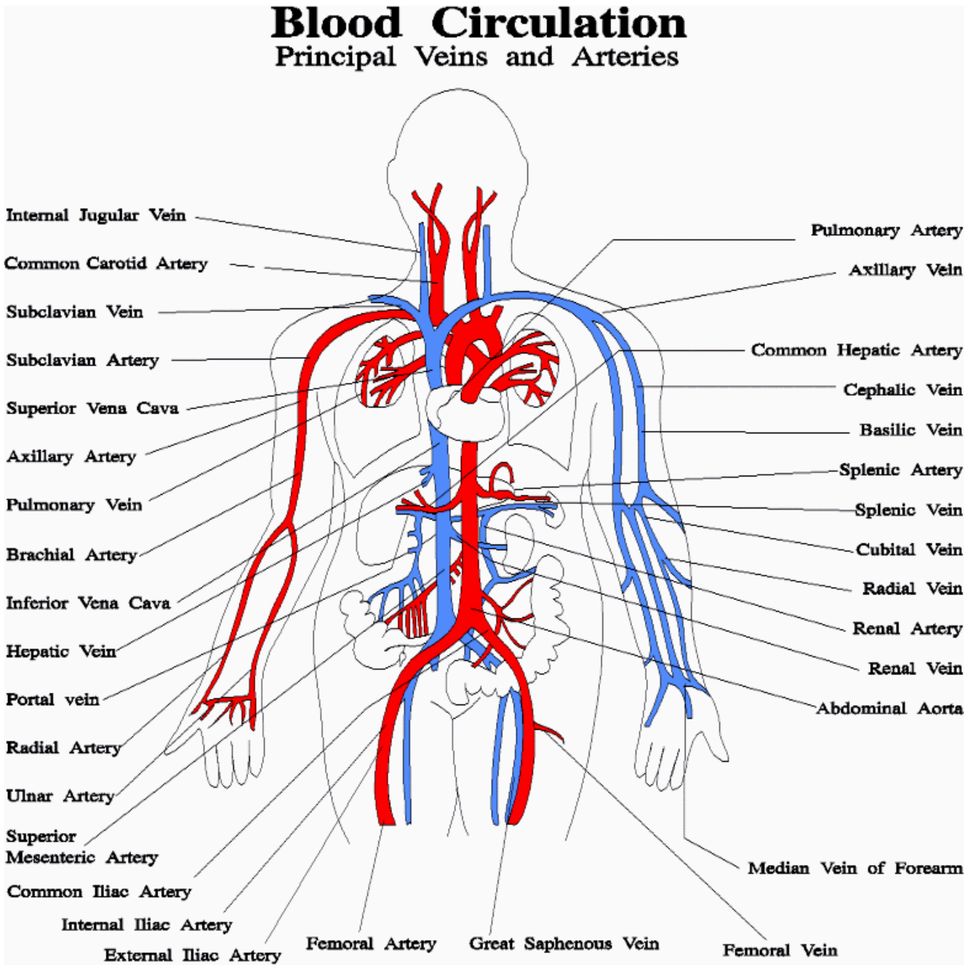
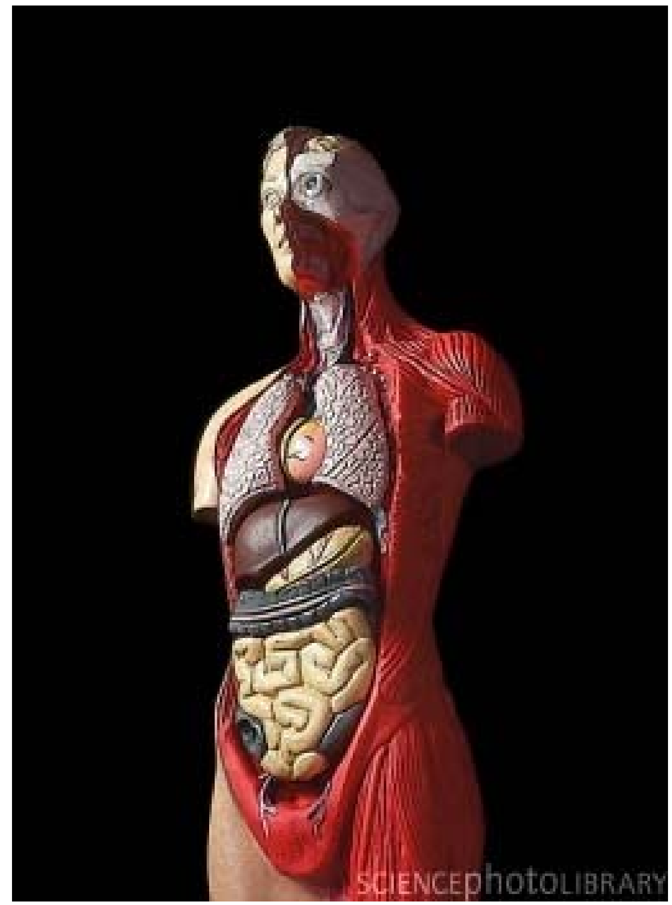
Nanoparticles May Translocate from Lungs to other Organs





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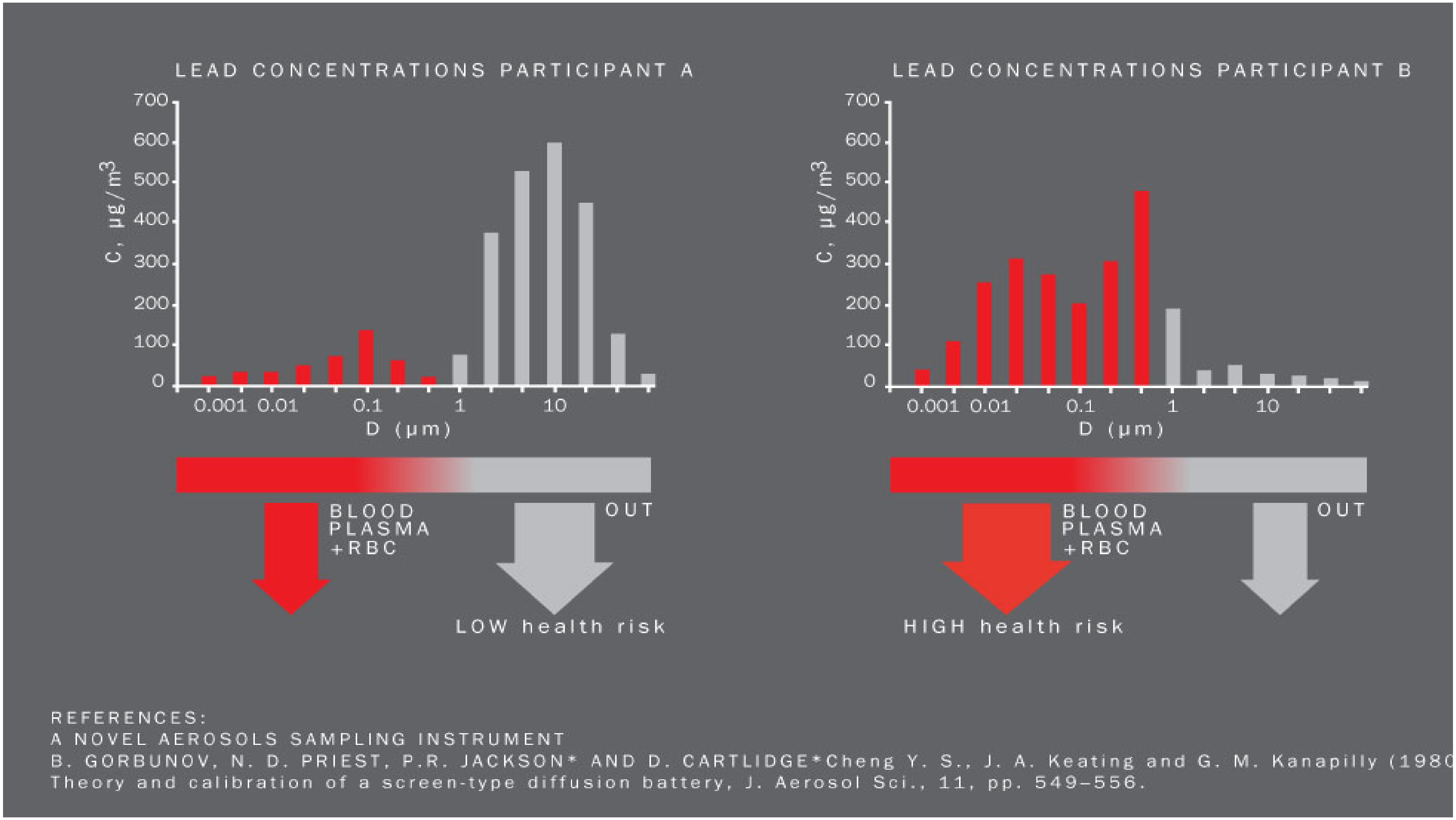
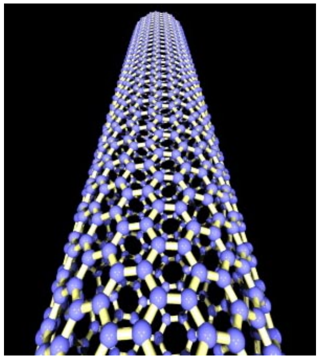
European Crystal Glass Industry Studies of Lead Concentration, Particle Size, and Lead in Blood



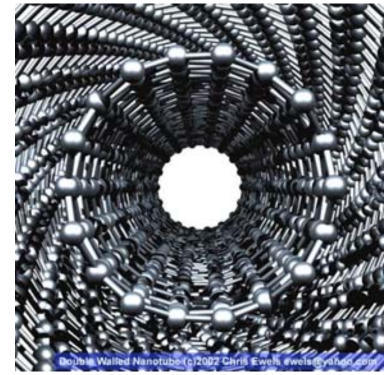
Highly correlated (R^2 = 0.95) blood lead with particles < 200 nm but not as total dust (R^2 = 0.58), PM10 (R^2 = 0.61), or respirable fraction (R^2 = 0.59).

Exposure Limits and Nanomaterials

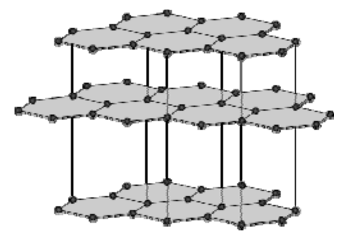
- Nanoscale particles of existing materials **(Ag, Al, Au, ZnO, TiO_2, C, Fe, MgO, etc.)** are being manufactured or researched
- TLVs, PELs, WEELs, IDLHs, ERPGs, may not be relevant, adequate for poorly-soluble or insoluble nanoscale particles
- Consult PEL, TLV, and IDLH documentation for basis!



Carbon Nanotubes



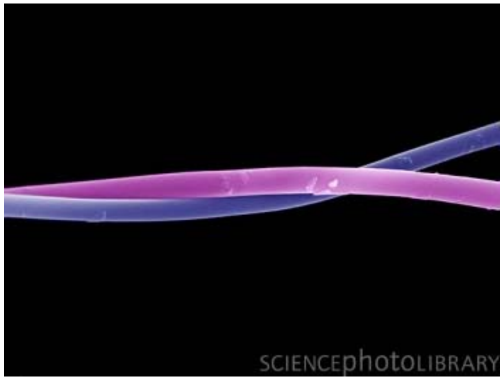
- **Carbon black** (disordered graphite sheets)
  - ACGIH: 3.5 mg/m^3, 8-hr TWA, as “total dust”
- **Graphite**
  - ACGIH: 2 mg/m^3, 8-hr TWA, respirable fraction



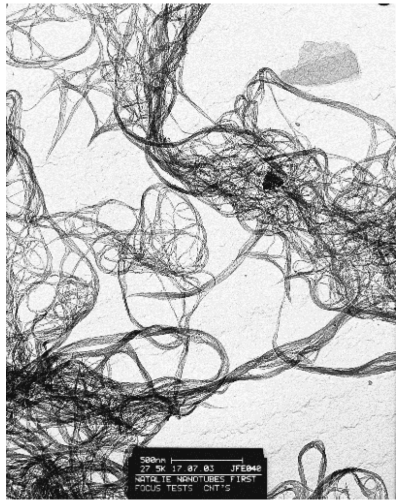
- **Crystalline silica**
  - ACGIH: 0.025 mg/m^3, 8-hr TWA, respirable
- **Graphite/carbon fibers** (strands of layered graphite): 1 f/cc, 8-hr. TWA, respirable, NIOSH 7400 Method, “B” Rules
- **Chrysotile asbestos**: 0.1 f/cc, 8-hr. TWA, NIOSH 7400 Method, “A” Rules (> 5 um length, ≥ 3:1 aspect ratio, etc.)

Carbon Nanotube Toxicity Factors?

Structure, Shape



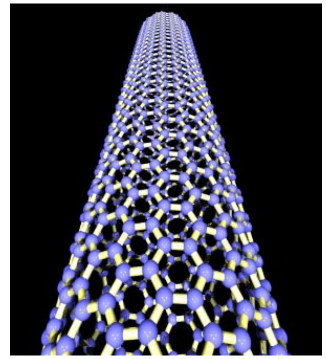
SEM Image. DR KOSTAS KOSTARELOS & DAVID MCCARTHY/ SCIENCE PHOTO LIBRARY



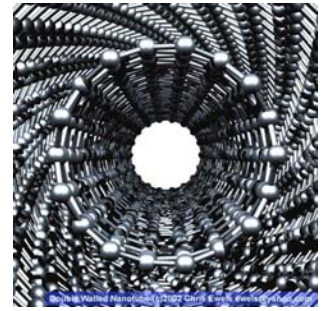
Institute for Integrated Micro and Nanosystems

Diameter, SW, MW

0.7-3 nm

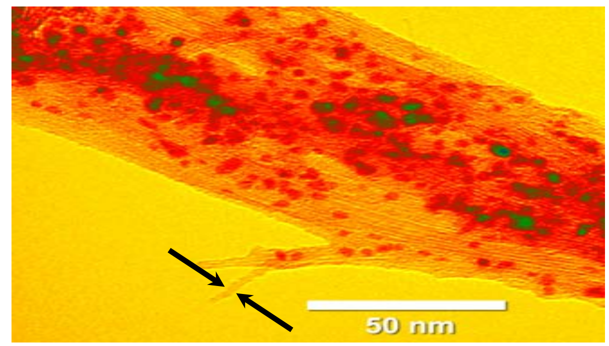


10 to 200 nm



Aspect Ratio: length to width

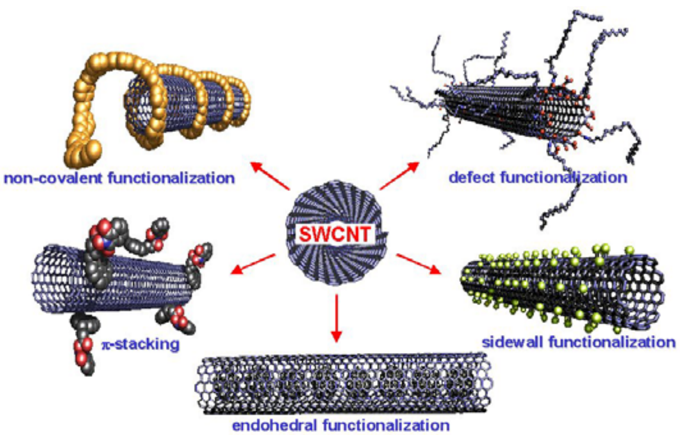
Trace Contaminants



1.4 nm

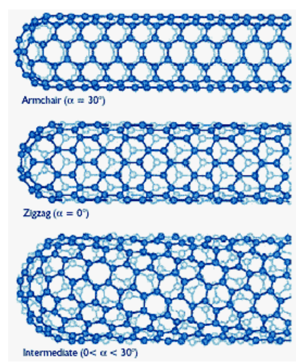
Source: Maynard, NIOSH

Functionalization



Computer Chemistry Center
University of Erlangen-Nuremberg

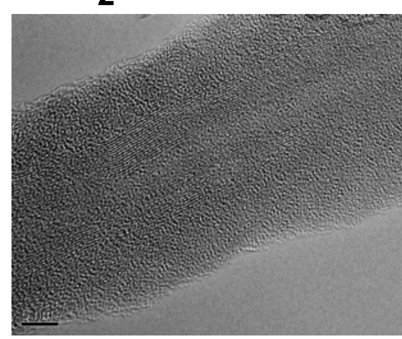
Chirality



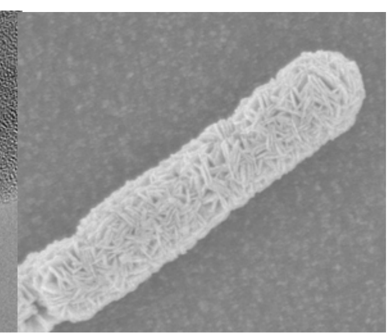
American Institute of Physics

Surface Coatings

SiO_2 Coated



Ag Coated



Titanium Dioxide

- **ACGIH**
  - 10 mg/m^3, 8-hour TWA, total dust
- **NIOSH** 11/05 Draft Recommendations **(NIOSH 0600, Respirable Particles)**: Up to 45-year working lifetime
  - Potency associated with surface area
  - Fine: 1.5 mg/m^3, 10-hour TWA
    - (based on 6.68 m^2/g)
  - Ultrafine (and respirable agglomerates of ultrafine): 0.1 mg/m^3, 10-hour TWA, 40-hr/wk
    - (based on 48 m^2/g)

Titanium Dioxide

- **National Research Council** (1999), Military Smokes and Obscurants:

- Respirable: 2 mg/m^3, 8-hour TWA, 5 d/week

- Ultrafine: 0.25 mg/m^3 8-hour TWA, i.e., 2/8
  - ** SA for UF TiO_2 reported to be about 50 m^2/g
  - ** SA for Fine TiO_2 typically 6-8 m^2/g
  - ** 50 divided by 6-8 = about 8

NIOSH National Institute for Occupational Safety and Health

Exposure Management Control Banding Concept

Schulte et. al., NIOSH, Occupational Risk Management of Engineered Nanoparticles, JOEH, 2:4, Apr 08

- **Amount used**:
  - gram
  - kilogram
  - greater than kilogram
- **Dustiness – potential to become airborne**:
  - Low: liquid suspension
  - Medium: sticky powders
  - High: finely divided powders

Exposure Management Control Banding Concept

Schulte et. al., NIOSH, Occupational Risk Management of Engineered Nanoparticles, JOEH, 2:4, Apr 08

- **Hazard Group:**
  - **A:** skin, eye, or unclassified irritants
  - **B:** harmful on single exposure
  - **C:** toxic, corrosive, etc.
  - **D:** very toxic or toxic to reproduction
  - **E:** capable of causing asthma, cancer, or genetic damage

Exposure management

Control banding - concept

	Low Dustiness	Medium Dustiness	High Dustiness
Hazard Group A			
Small	1	1	1
Medium	1	1	2
Large	1	2	2
Hazard Group B			
Small	1	1	1
Medium	1	2	2
Large	1	3	3
Hazard Group C			
Small	1	1	2
Medium	2	3	3
Large	2	4	4
Hazard Group D			
Small	2	2	3
Medium	3	4	4
Large	3	4	4
Hazard Group E			
For all hazard group E substances, choose control approach 4			

Parameters

Amount Used

Dustiness

Hazard Group (R-Phrase)

Control Approach

1. General Ventilation
2. Engineering Control
3. Containment
4. Specialist Advice

NIOSH: TJ Lentz

www.ilo.org

DRAFT Possible Target Ranges for Exposure Control of NPs in the Workplace, NIOSH

Hazard Class	Type or Degree of Hazard	General Character of Control Band	Target Range for Exposure Control
A	Slight and reversible ?	Good industrial hygiene practice with open handling or local exhaust ventilation	100 to 500 µg/m³ dust *? Other criteria ?*
B	Moderate and reversible ?	Local exhaust ventilation or enclosed processes	10 to 100 µg/m³ dust *? Other criteria ?*
C	Severe and reversible or moderate and irreversible ?	Enclosed processes	1 to 10 µg/m³ dust *? Other criteria ?*
D	Severe and irreversible ?	Isolated or remote handling	<1 µg/m³ dust *? Other criteria ?*

Draft for discussion

BSI, Nanotechnologies – Part 2: Guide to safe handling and disposal of manufactured nanomaterials, December 2007

- **"Benchmark levels"** proposed for four nanoparticle hazard types in the Selection of Controls
- **FIBROUS nanomaterial:** a high aspect ratio insoluble nanomaterial:
  - clearance limit in UK asbestos removal activities,
    - **0.01 f/cc as assessed by SEM or TEM.**

BSI, Nanotechnologies – Part 2: Guide to safe handling and disposal of manufactured nanomaterials, December 2007

- **CMAR nanomaterial:** any nanomaterial which is already classified in its larger particle form as carcinogenetic (C), mutagenic (M), asthmagenic (A) or a reproductive toxin (R):
  - Due to potential for increased solubility in nanoparticle form:
    - **0.1 x British Workplace Exposure Limit (WEL)**

BSI, Nanotechnologies – Part 2: Guide to safe handling and disposal of manufactured nanomaterials, December 2007

- **INSOLUBLE nanomaterial:** Insoluble insoluble or poorly soluble nanomaterials not in the fibrous or CMAR category
  - NIOSH Draft Recommendation for Ultrafine TiO_2 is 0.1 mg/m^3, Fine TiO_2 is 1.5 mg/m3
  - Based on the ratio 0.1/1.5 = 0.066, apply to other nanomaterials:
    - **0.066 x WEL**

BSI, Nanotechnologies – Part 2: Guide to safe handling and disposal of manufactured nanomaterials, December 2007

- **INSOLUBLE nanomaterial:** Insoluble insoluble or poorly soluble nanomaterials not in the fibrous or CMAR category
  - **Alternative benchmark based particle number concentration.** In the UK, current urban pollution ranges from 20,000 p/cc to 50,000 p/cc
  - Suggested benchmark for insoluble nanomaterial:
    - **20,000 p/cc**

BSI, Nanotechnologies – Part 2: Guide to safe handling and disposal of manufactured nanomaterials, December 2007

- **SOLUBLE nanomaterial:** Soluble nanomaterials not in fibrous or CMAR category
  - For materials that are highly soluble in any case, nanoparticle forms are unlikely to lead to greater bioavailability
  - Types of effects associated with insoluble particles are NOT likely to occur
  - Suggested benchmark:
    - **0.5 x WEL**

Exposure Assessment Metrics for Engineered Nanoparticles

- Concentration
  Example:
  - Surface area concentration
  - Particle number concentration
  - Mass concentration

- Other physicochemical parameters
  - Particle size distribution
  - Particle chemistry
  - Aggregation/Agglomeration state of particles

Surface Area Concentration Monitors, Diffusion Charger – Direct-Reading, Non-Specific

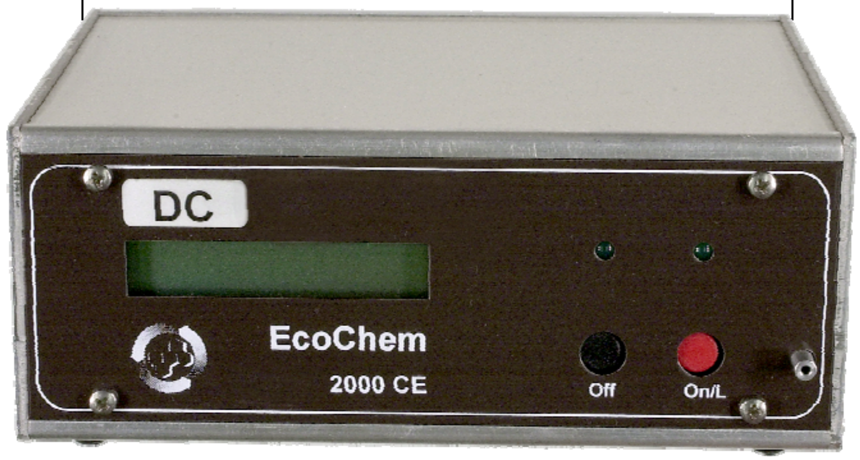
Measures
active surface area,
External Surface Area

Generally insensitive to particle porosity

< 100 nm mobility diameter: correlates well with TEM-derived surface area

> 100 nm, surface area is underestimated

Charge on Aerosol $\propto$ Surface Area



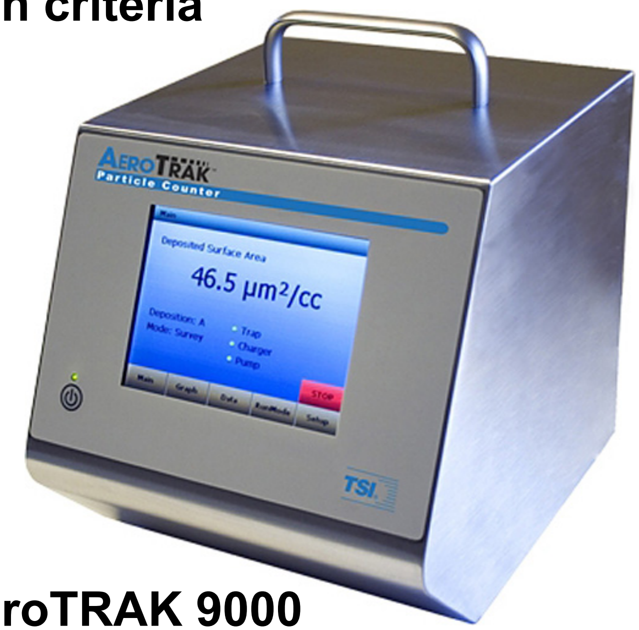
DC2000 CE Diffusion Charger ***EcoChem***

Particle size range: 10 nm to 1,000 nm

Cost: $10,000

Surface Area Concentration Monitors, Diffusion Charger, Direct-Reading, Non-Specific

User selectable response modes indicate lung deposited surface area of nanoparticles deposited in the tracheobronchial (TB) and alveolar (A) regions of the lung, corresponding to the ICRP lung deposition criteria



TSI Model 3550 **Cost; $16,000**

Concentration range:
TB:1 to 2,500 µm²/cc
A: 1 to 10,000 µm²/cc

Size range: 10 to 1000 nm (with 1µm cyclone on inlet)

TSI AeroTRAK 9000
Battery-Operated
Cost: $10,000

Generally insensitive to particle porosity

Measures active DEPOSITED surface area in the TB or A regions of the lung

Measures Deposited External Surface Area Within the Lung

Nanoparticle Surface Area and Pore Size

Laboratory Bench Top:

BET-Accelerated Surface Area and Porosimetry System -

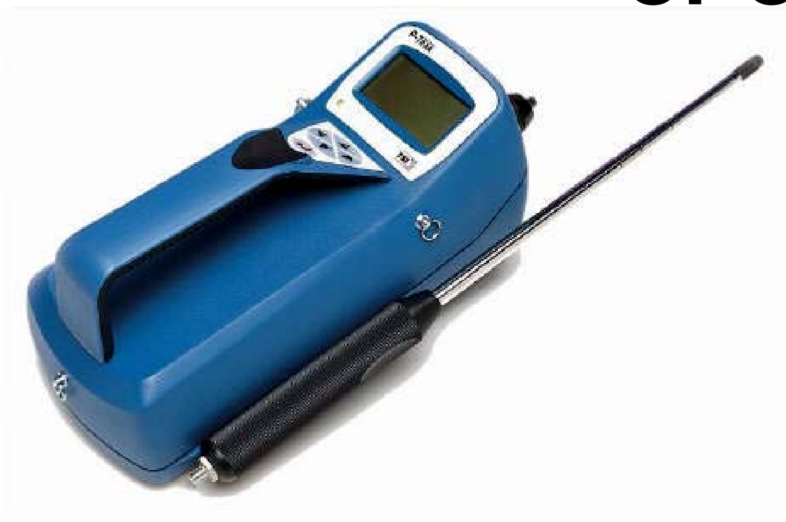
Requires large amounts of material

Measurements influenced by particle porosity

Source: Rice University

Provides a tool to quantify the size of surface area (minerals, powders, etc.) and pores

Particle Number Concentration,
Particles 10 or 20 nm to 300 nm
CPC minus OPC



p/cc 20 to 1,000 nm

p/cc 10 to 1,000 nm

SUBTRACT

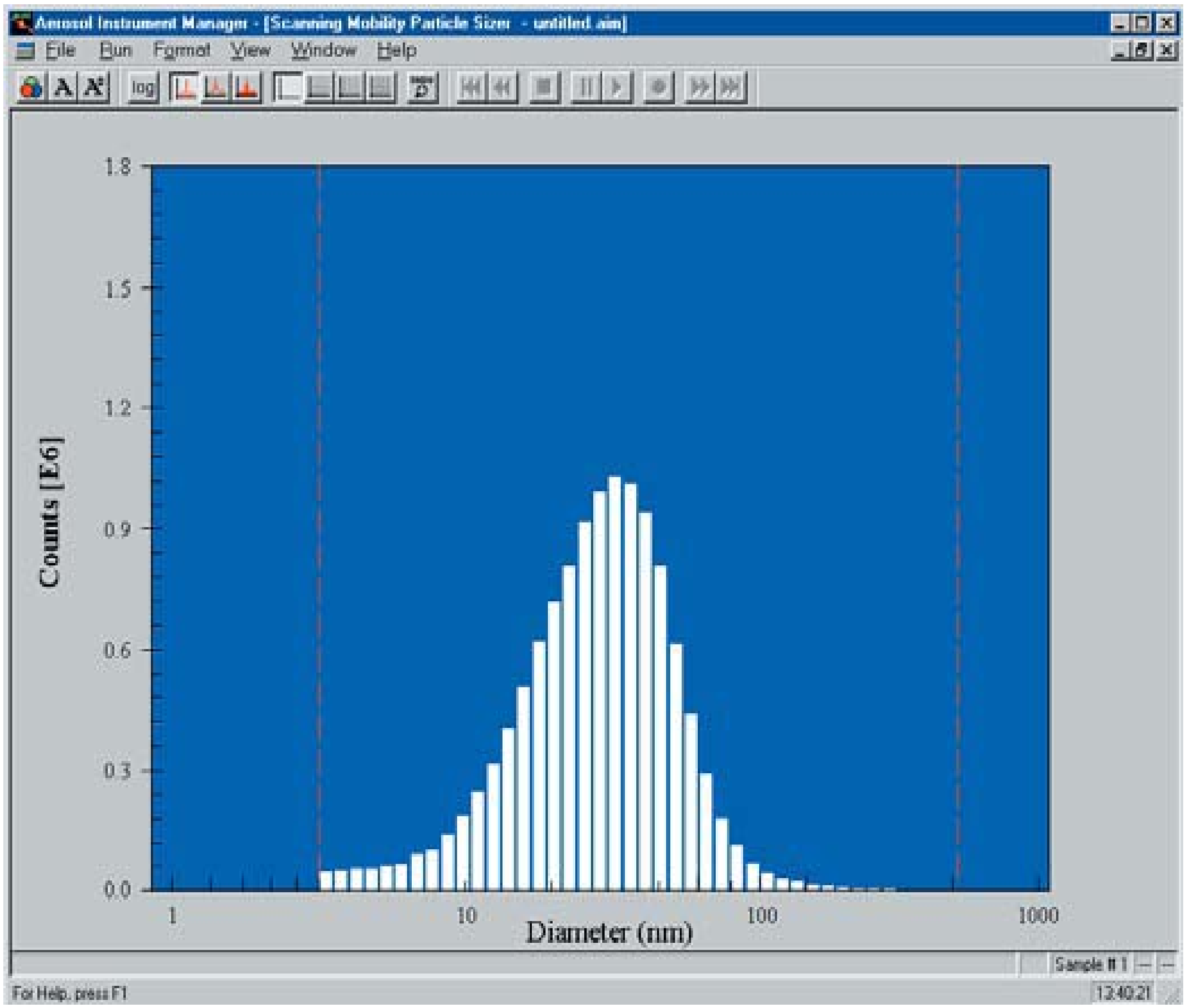
p/cc > 300 nm

NIOSH monitoring of a worker during a nanomaterial powder production and collection operation

NIOSH National Institute for Occupational Safety and Health

Source: NIOSH

Size and Size Distribution



Portable Particle Detector/monitor

Naneum Selector and Counter (SAC) Model 1

$38,500

www.naneum.com

Specification:

- **9V (x7) battery operated**
- hand-held, 2.7 kg
- on-line measurement
- Response time: from 3 minutes, depending on conc., resolut
- **Size range covered 3 - 500 nm**
- USP output to PC (requires Naneum SAC Software)

Properties measured:

Particle concentration (10 to 10^7 p/cc)
Particle size distribution

Applications

- Particle distribution mapping
- Identify "hot spots"
- Background from engineered particles
- Continuous monitoring
- Identify "events"
- Exposure/dose

Intellectual property

- EU Application
- Patents in preparation but not yet filed

Naneum Remote Monitor Particle Detector/Monitor

- Expected to be available in mid-2009
- Specification:
  - **Battery operated**
  - Continuous unintended operation
  - Single digit read-outs
  - Wireless network, or alarm
  - **20 nm – 1 micron**
  - **Up to 5 bin sizes**
- Cost based on volume:
  - **1 ea. ($8,000)**
  - **10 or more ($4,000 ea.)**
  - **Larger orders ($2,000 to $3,000 ea.)**

Technical Principles:
****Inertial deposition and diffusion**
****Miniature CPC/counter**

Naneum Personal Size Unit based On Remote Monitor (Particle Detector/Monitor)

- Expected to be launched/available in late 2008
- FIRST direct-reading particle number concentration sampler that can be used as a PERSONAL sampler
- Particle Size Range:
  - **5/10 nm up to 10 microns**
  - **Up to 7 size bins**

Mass Concentration (mg/m^3), Photometers Non-Specific, Personal Sampling

PHOTOMETERS: Calibration only valid for the specific calibration aerosol and can differ as much as a factor of ten when used with an aerosol from a different source, different composition, and size distribution

Built-in impactors: “none,” 1.0, 2.5 or 10-micron cut off

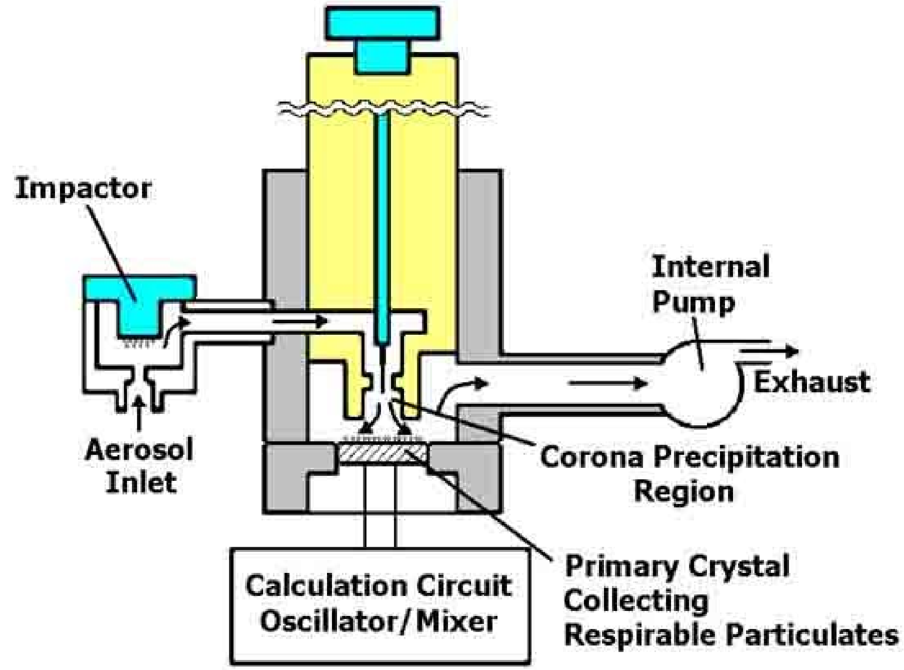
Light Scattering, 670 nm Laser Diode

Size range: 100 nm to 10 micron

Concentration Range: 0.001 to 20 mg/m3

Mass Concentration (mg/m^3), Piezobalance Dust Monitor, Non-Specific, General Area

KANOMAX USA, INC.



Size range: < 10 microns

Concentration: 0.02-10 mg/m3

Accuracy: +/-10% of reading +/-1 digit

Mass Concentration (mg/m^3), Filter for Collecting Particles, Personal Sampling

Utility for carbon nanotubes, fullerenes, carbon nanofibers, etc.??

< 1 µm: 1.7 lpm
< 400 nm: about 3 lpm

Theoretical:
< 200 nm: about 6 lpm
< 100 nm: about 10 lpm

SKC: Diesel Particulate Matter (DPM) Cassette

At 1.7 to 2.0 LPM, particles less than 1.0 µm aerodynamic diameter are collected on heat-treated low carbon quartz filters. Samples are analyzed for organic and elemental carbon content using a highly sensitive Evolved Gas Analysis (EGA) technique with thermal-optical analyzer as specified in NIOSH Method 5040.
Meets specs for NIOSH 5040 for analysis of elemental carbon (EC) to determine total carbon (organic and elemental) in a sample. Total carbon represents more than 80% of diesel particulate emissions.

Size Distribution
Mass, Chemistry, Personal Sampling

Size Distribution

> 2.5 µm

1 µm – 2.5 µm

500 nm – 1 µm

250 nm – 500 nm

< 250 nm

50% cut-points:

2.5 µm
1.0 µm

500 nm
250 nm

<250 nm (after filter)

Aerodynamic diameter

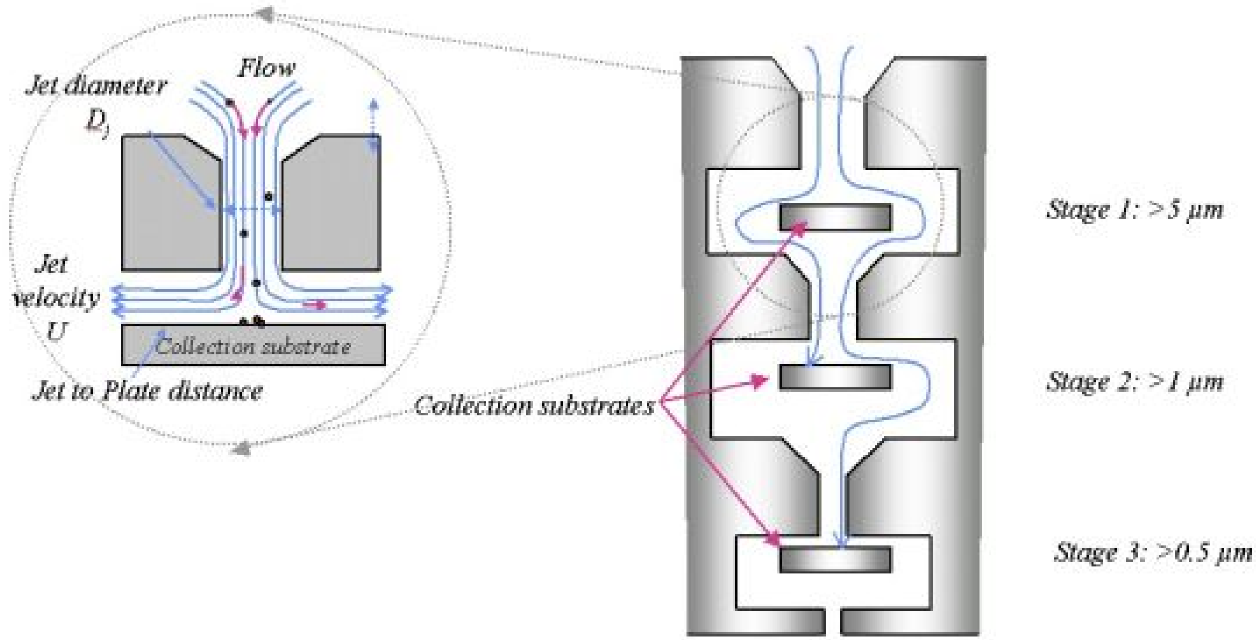
Sioutas Cascade Impactor; teflon filters recommended

Analysis: gravimetrically, chemically, and microscopically

Size Distribution, Mass Concentration, Chemistry,

Dekati Low Pressure Impactor

$20,000



Aerodynamic diameter from 30 nm up to 10 µm. With the filter stage accessory, particles below 30 nm can be collected on a 47 mm filter.

Naneum Wide range Aerosol sampler (WRAS)

- Specification:
  - Mains operated portable sampler weighing approx 10kg
  - Continuous collection of size resolved samples on custom substrate
  - **Up to 15 size “bins” from 2/3nm-20µm**
  - Flow rates from 5lpm-1000lpm
  - Samples suitable for off-line analysis using SEM/TEM, MS, Atomic Adsorption,HPLC etc.
- Properties measured:
  - **Size resolved chemical composition**
  - **Size resolved morphology**
- Technical Principles
  - **Inertial deposition (300 nm to 20 µm)and Diffusion (2 -300 nm)**
  - Integrated to give seamless size resolution across aerosol range
- Intellectual property
  - 2 granted UK patents
  - USA application

$38,000

Naneum Personal Sampler

- Would be based on same principles as WRAS, except:
  - **2/3 nm to 10 microns**
  - **Up to 10 size bins**
- Not available yet and currently no plans by Naneum to make:
  - Can be made by Naneum in 2009 IF there is a “clear, large attractive opportunity” given a market demand

Naneum Personal Sampler

- Cost based on volume:
  - **1 ea. ($5,000)**
  - **10 or more (about $3,000 ea.)**
  - **large orders (between about $1,000 and $2,000)**

Transmission Electron Microscopy

- **Size:** projected area of particles
- **Shape and structure**
- **Number distribution**
- **Surface area:** projected area may be related to geometric area for some particle shapes
- **Aggregation/agglomeration state**
- **Chemistry:** Combined with Energy Dispersive X-Ray Analysis (EDX), can provide spatially resolved information on particle elemental composition and compositional heterogeneity

Detection of Carbon Nanotubes

- Ratna Tantra and Peter Cumpson (Dec 07)
  – The Detection of Airborne Carbon Nanotubes in Relation to Toxicology and Workplace Safety
  – Nanotoxicology, 1:4, 251-265, December 2007
- Spectroscopy Methods:
  – **Raman spectroscopy shows most promise**
- Microscopic Methods:
  – **Scanning Electron Microscopy (SEM)** more suitable than Transmission Electron Microscopy (TEM)
  – Atomic Force Microscope (AFM) more suitable than Scanning Tunneling Microscope (STM)

ISO TC 229 Nanotechnologies

International Organization for Standardization

Technical Specifications for Carbon Nanotubes Under Development

- Use of **Raman spectroscopy** in the characterization of single-walled carbon nanotubes (SWCNTs)
- Scanning electron microscopy **(SEM)** and energy dispersive X-ray analysis **(EDXA)** in the characterization of single walled carbon nanotubes (SWCNTs)
- Use of transmission electron microscopy **(TEM)** in walled carbon nanotubes (SWCNTs)

Engineering Controls

Local exhaust ventilation controlling fugitive emissions during precursor mixing at a primary nanoscale metal oxide Production facility

Source: NIOSH

Engineering Controls

Enclosing hood with HEPA exhaust constructed to control possible emission of nylon nanofibers during destructive testing

Source: NIOSH

Sampling and data collection during a mixing operation

Source: NIOSH

How Effective Are Respirators?

A flat plate test system for measuring respirator filter penetration of 3 to 20 nm silver particles

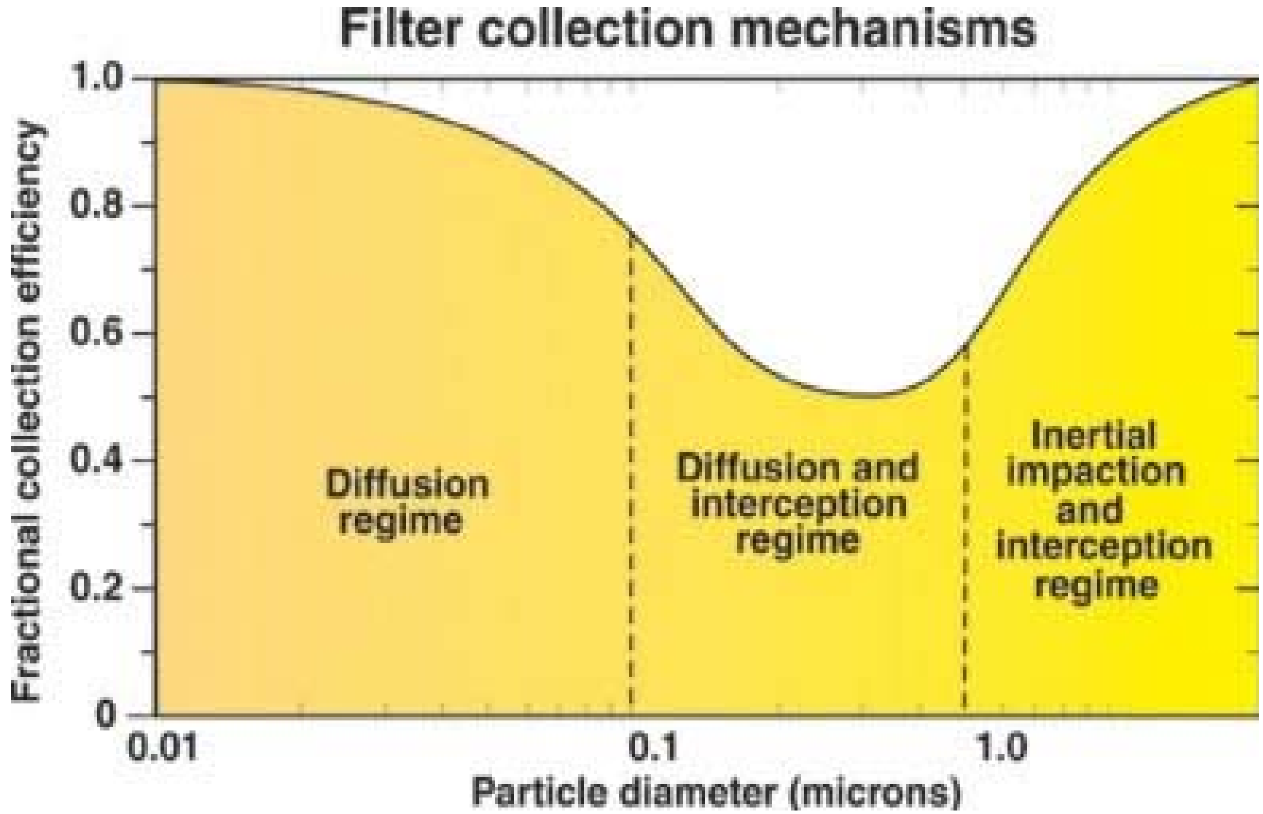
Source: NIOSH

NIOSH National Institute for Occupational Safety and Health

Filter Efficiency

Most Penetrating Size for many filters:
300 nm

HEPA filters:
Most penetrating
Size **100-300 nm**



N95 Electrostatically Charged. Most Penetrating Size:
30-70 nm
50-100 nm
40 nm

How Effective is Personal Protective Clothing Against Nanoparticles?

ASTM F1671-03
Standard test method for resistance of materials used in protective clothing to penetration by blood-borne pathogens using Phi—X174 bacteriophage penetration as a test system

- Specifies use of a 27 nm bacteriophage

Controls

- Controls may have to be more stringent for nanomaterial than for the insoluble/poorly-soluble micro- or macro-scale material of same chemical composition

- For instance, if 10-x above a TLV or PEL, and you use a ½ facepiece APR to get down to the TLV or PEL, consider ratcheting up to a full-face APR with HEPA

Medical Surveillance

- Questionnaire administration
- Physical administration
- Medical testing/screening
- The most basic medical surveillance – periodic collection of medical history or symptom information

DOE Nanoscale Science Research Centers

Approach to Nanomaterial ES&H, Rev 2, June 07

- Basic worker health and environmental monitoring recommended:
  - Identify "nanoparticle workers" exposed to engineered nanoparticles of unknown health effects.
    - Handles engineered nanoscale particulates that have the potential to become dispersed in the air
    - Routinely spends (significant amounts of) time in an area in which engineered nanoparticles have the potential to become dispersed in the air
    - Works on equipment that might be contaminated with materials that could foreseeably release engineered nanoparticles during servicing or maintenance

DOE Nanoscale Science Research Centers Approach to Nanomaterial ES&H, Rev 2, June 07

– Conduct workplace characterization and worker exposure assessments

Medical Screening and Surveillance DOE Nanoscale Science Research Centers

– Provide nanoparticle workers with “baseline” medical evaluations and including them in a nonspecific routine health monitoring program

– Ensure that engineered nanoparticle workers are offered periodic medical evaluations that may include routine tests such as

  - Pulmonary function testing
  - Renal function
  - Liver function
  - Hematopoietic function

ASTM E2535-07 Standard Guide for Handling Unbound Engineered Nanoscale Particles in Occupational Settings, November 2007

- Scope:
  - unbound engineered nanoparticles nanoscale particles or their respirable agglomerates or aggregates thereof

ASTM E2535-07 Standard Guide, 2007
MEDICAL SURVEILLANCE

- Whether a medical surveillance program is warranted is a management decision to be made in consideration of a number of factors including:
  - whether there is good reason to believe that adverse health effects may occur as a result of the contemplated exposure
  - the invasiveness of the surveillance procedures
  - the benefits, risks and costs of the surveillance method
  - and the utility of the information reasonably expected to be generated by the surveillance program

ASTM E2535-07 Standard Guide, 2007 MEDICAL SURVEILLANCE

- Medical surveillance program should be developed and implemented only with
  - medical
  - industrial hygiene and legal professional consultation, and
  - under the direction of a physician experienced in medical surveillance programs with a high level understanding of the available information concerning the UNP and potential exposure circumstances

ASTM E2535-07 Standard Guide, 2007
MEDICAL SURVEILLANCE

- **Responding to Accidental or Unanticipated Releases of UNP**

  – Provide medical examinations to significantly exposed individuals

ASTM **E2535-07** Standard Guide, 2007
MEDICAL SURVEILLANCE

- *Periodic Review of Program.*
  - *Program may need to be amended based upon* the results of medical surveillance

- For guidance on medical surveillance of UNP workers consult the NIOSH Nanotechnology homepage

NIOSH Interim Guidance for Medical Screening of Workers Potentially Exposed to Engineered Nanoparticles DRAFT

- Issued 15 December 2007 for public review and comment on the NIOSH web page
- Public meeting held January 30, 2008
- Public comment period ended February 15, 2008
- Document will then be peer reviewed
  - the peer reviewers will be provided all substantive public comments received

NIOSH Draft Interim Guidance for Medical Screening of Workers Potentially Exposed to Engineered Nanoparticles

- **Purpose:**
  - provide interim guidance concerning whether specific **medical screening/monitoring** (i.e., medical tests for asymptomatic workers) is appropriate

NIOSH Interim Guidance for Medical Screening of Workers Potentially Exposed to Engineered Nanoparticles

- **Purpose of Medical Screening:**
  - to **detect preclinical changes** in organ function or changes that occur in the very early stages of disease—**before a person would normally seek medical care and when intervention is beneficial**

NIOSH Interim Guidance for Medical Screening of Workers Potentially Exposed to Engineered Nanoparticles

- Feasibility and appropriateness of conducting medical screening can be judged according to established criteria

- Inherent in all criteria for medical screening is that the
  - **specific disease endpoint(s) must be known to allow for test selection**

NIOSH Interim Guidance for Medical Screening of Workers Potentially Exposed to Engineered Nanoparticles

- **Conclusion:**
  - Insufficient scientific and medical evidence exists to recommend the specific medical screening of workers potentially exposed to engineered nanoparticles

NIOSH National Institute for Occupational Safety and Health

NIOSH Interim Guidance for Medical Screening of Workers Potentially Exposed to Engineered Nanoparticles

- **Conclusion:**
  - No substantial link has been established between occupational exposure to engineered nanoparticles and adverse health effects
  - Toxicological research to date is insufficient to recommend such monitoring, the appropriate triggers for it, or components of it

NIOSH Interim Guidance for Medical Screening of Workers Potentially Exposed to Engineered Nanoparticles

- Research needed to assess candidate biological markers for use in medical screening, including molecular markers
- Research needed to assess
  - sensitivity, specificity, and predictive value of biomarkers
  - and clinical tests that could be used in the screening of workers health

NIOSH Interim Guidance for Medical Screening – **Nanoscale Metal Oxides**

- Pulmonary exposure to nanoscale metal oxides:
  - Pulmonary inflammation in rats
  - Inhibit the ability of the systemic microvasculature to respond to dilators
- Nanoscale TiO_2 more potent than fine TiO_2 on an equivalent mass basis
- Effects have been associated with oxidant stress and induction of inflammatory mediators

NIOSH National Institute for Occupational Safety and Health

NIOSH Interim Guidance for Medical Screening – **Nanoscale Metal Oxides**

- Potential biological markers:
  - **Nitrous oxide or isoprostanes**
    - **in exhaled breath**
  - **Blood markers of oxidant stress**
- Problem – utility of these markers for screening workers exposed to engineered nanoparticles has not been demonstrated

NIOSH Interim Guidance for Medical Screening of Workers Potentially Exposed to Engineered Nanoparticles

- Lack of evidence for recommending medical screening should not preclude its use if employees want to take additional precautions
- Warning - negative consequences of nonspecific medical testing could include adverse effects:
  - **Radiation from chest radiographs**
  - **Unnecessary anxiety from false positive screening tests**
  - **Cost of additional diagnostic evaluations**

NIOSH National Institute for Occupational Safety and Health

NIOSH Interim Guidance for Medical Screening

- Medical screening is typically triggered by
  - **airborne** **“action level”** **concentration**,
    - e.g., 50%, of an OEL

- Not known if the action level concentration recommended for a chemical substance **(e.g., Cd, etc.)** is adequate for nanoscale form of the same chemical

NIOSH Interim Guidance for Medical Screening

- **Consider established medical surveillance approaches**
  - to help assess whether controls are effective
  - to identify new or unrecognized problems and health effects
    - increased frequency of adverse respiratory and cardiovascular effects

NIOSH Interim Guidance for Medical Screening

- NIOSH is not recommending that **medical surveillance** **(questionnaires, physicals, medical testing/screening/monitoring)** be done for workers exposed to engineered nanoparticle

  – **not enough evidence to recommend mandating medical surveillance**

NIOSH Interim Guidance for Medical Screening

- **However, OSHA regulations may require medical clearance or surveillance if**
  - **respirators are used**
  - **exposures are within a laboratory**
  - **HAZWOPER applies**
  - **if there is a substance specific standard for the substance (e.g., Cd, Pb, As, Cr+6, etc.)**

- **If there is already a medical surveillance program in place, then continue on and**
  - **watch for sentinel events**

NIOSH Interim Guidance for Medical Screening

- **Conduct hazard surveillance as the basis for implementing controls**
  - **Identify and document jobs/tasks or processes involving production or use of engineered nanoparticles**
  - Information serves as basis for applying various control measures

NIOSH Interim Guidance for Medical Screening

- **Consider precautionary management approaches**
  - Concerns raised from toxicology studies on certain engineered NPs and from epidemiological studies regarding incidental nanoparticles
- **Take prudent measures to control exposures to engineered nanoparticles**
  - NIOSH draft document *Approaches to Safe Nanotechnology: An Information Exchange with NIOSH, 2006*

ISO TC 229 Nanotechnologies Draft Technical Report: Health and Safety Practices in Occupational Settings Relevant to Nanotechnologies

- Expected publishing date 2008
- Will have recommendations on **Health Surveillance**

Biological Monitoring

- Biological Fluids (e.g., blood, urine)
- Schulte et. al., NIOSH, Occupational Risk Management of Engineered Nanoparticles, JOEH, 2:4, Apr 08
  - Assessing NP (or metabolite) levels could show extent of exposures
  - However, limited information to define parameters of a biological monitoring program for NP
  - Presence of NP in biological fluids in animal studies influenced by particle surface chemistry, coating, size, etc.

Biological Monitoring

- Biological Fluids (e.g., blood, urine)
- OSHA and ACGIH (BEI) have recommended biological exposure levels for some chemicals:
  - As
  - Cd
  - Co
  - Cr+6
  - Pb
  - V_2O_5

Questions?

Please consult the following slides for important related documents and resources

GENERAL INTRODUCTION TO NANOTECHNOLOGY

- **Booker, R. and Boysen, E, Nanotechnology for Dummies,** Wiley Publishing, Inc., 2005, http://www.wiley.com/WileyCDA/WileyTitle/productCd-0764583689.html

- **Luther, Wolfgang (Ed.), Industrial Application of Nanomaterials - chances and risks,** Future Technologies Division of VDI Technologiezentrum GmbH, Germany, 2004

Top Documents of Relevance for the Practicing Industrial Hygienist

- **ASTM, E2535-07 Standard Guide for Handling Unbound Engineered Nanoscale particles in Occupational Settings,** November 2007. **Available at:** http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/SUBCOMMIT/E5603.htm?L+mystore+cprk8709+1177117315

- **Brouwer, et. al., Personal Exposure to Ultrafine Particles in the Workplace: Exploring Sampling Techniques and Strategies,** Ann. Occup. Hyg. Vol. 48, No. 5, pp. 439-453, 2004

Top Documents of Relevance for the Practicing Industrial Hygienist

- **BSI, Nanotechnologies – Part 2: Guide to safe handling and disposal of manufactured nanomaterials,** December 2007. Available at: http://www.bsi-global.com/en/Standards-and-Publications/Industry-Sectors/Nanotechnologies/Nano-Downloads/
- **Chen, Da-Ren, and Pui, D., Nanoparticles and Ultrafine Aerosol Measurements,** ACGIH, 2008, http://www.acgih.org/store/ProductDetail.cfm?id=2008
- **Department of Energy Nanoscale Science Research Centers, Approach to Nanomaterial ES&H,** Revision 2 – June 2007. Available at: http://www.sc.doe.gov/bes/DOE_NSRC_Approach_to_Nanomaterial_ESH.pdf

Top Documents of Relevance for the Practicing Industrial Hygienist

- **Environmental Defense – DuPont Nano Risk Framework,** June 2007: Available at: http://www.nanoriskframework.com/page.cfm?tagID=1095
- **Hoover, M., Geraci, C., and Maher, T., WEBINAR CD-ROM – Nanotechnology Health and Safety: Case Studies in the Occupational Setting, ACGIH, 2007, http://www.acgih.org/store/ProductDetail.cfm?id=1978**
- **ISO TC 229 Nanotechnologies Draft Technical Report: Health and Safety Practices in Occupational Settings Relevant to Nanotechnologies. Under development. Available at: http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_tc_browse.htm?commid=381983**

Top Documents of Relevance for the Practicing Industrial Hygienist

- **ISO**, **Workplace Atmospheres - Ultrafine, nanoparticle and nano-structured aerosols - Exposure characterization and assessment.** Geneva: Switzerland: International Standards Organization. Document no. ISO/TR 27628, 2007. Available for purchase from ANSI, http://www.ansi.org/

- **Maynard, A.D. and Aitken, R.J.**, **Assessing exposure to airborne nanomaterials: Current abilities and future requirements**, Nanotoxicology, Volume 1:1, 26-41, March 2007. Available at: http://www.informaworld.com/smpp/title~content=t716100760

- **NIOSH, Approaches to Safe Nanotechnology -- An Information Exchange with NIOSH,** 2006. Available at: http://www.cdc.gov/niosh/topics/nanotech/safenano/

Top Documents of Relevance for the Practicing Industrial Hygienist

- **NIOSH, Evaluation of Health Hazard and Recommendations for Occupational Exposure to Titanium Dioxide, DRAFT Current Intelligence Bulletin"** November 2005. Online, available: http://www.cdc.gov/niosh/review/public/TIo2/

- **NIOSH, Interim Guidance for Medical Screening of Workers Potentially Exposed to Engineered Nanoparticles**, DRAFT, November 2007. Available at: http://www.cdc.gov/niosh/updates/upd-12-13-07.html

- **NIOSH, Progress Toward Safe Nanotechnology in the Workplace,** February 2007. Available at: http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf

Top Documents of Relevance for the Practicing Industrial Hygienist

- **NIOSH Health Hazard Evaluation Report, HETA #2005-0291-3025,** [Carbon Nanofibers], University of Dayton Research Institute, Dayton, Ohio, October 2006, http://www.cdc.gov/niosh/hhe/reports/pdfs/2005-0291-3025.pdf

- **Schulte et. al., NIOSH, Occupational Risk Management of Engineered Nanoparticles, Journal of Occupational and Environmental Hygiene, 2:4, Apr 08**

General Aerosol-Related Resources

- **Baron, P.A., and Willeke, K., Aerosol Measurement – Principles, Techniques, and Applications, 2nd ed.,** John Wiley & Sons, Inc., 2001
- **Hinds, W.C., Aerosol Technology – Properties, Behavior, and Measurement of Airborne Particles, 2nd ed.,** John Wiley & Sons, Inc.,1999.
- **NIOSH Safety and Health Topic: Aerosols,** http://www.cdc.gov/niosh/topics/aerosols/
- **Vincent, J.H., Particle Size-Selective Sampling for Particulate Air Contaminants,** ACGIH, 1999, http://www.acgih.org/Store/ProductDetail.cfm?id=367

On-line databases of relevance

- **ICON, Online EHS journal and database:** http://icon.rice.edu/virtualjournal.cfm
- **NIOSH, Nanoparticle Information Library: http://www2a.cdc.gov/niosh-nil/index.asp**
- **Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars, Health and Environmental Implications: an inventory of current research: http://www.nanotechproject.org/inventories/ehs/**

Websites

- **American Industrial Hygiene Association (AIHA):** http://www.aiha.org/Content/Topics/nano/

- **ASTM E56 Nanotechnologies**: http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/COMMITTEE/E56.htm?L+mystore+cprk8709+1179181259

- **BSI, British Standards, Nanotechnology:** http://www.bsi-global.com/en/Standards-and-Publications/Industry-Sectors/Nanotechnologies/Nano-Downloads/

Websites

- **Defense Nanotechnology Research and Development Programs, May 17, 2005:** http://www.nano.gov/html/res/DefenseNano2005.pdf

- **DoD laboratory research and development:** http://www.nanosra.nrl.navy.mil/

- **DoD NNI Centers, Networks, and Facilities:** http://www.nano.gov/html/centers/nnicenters.html

Websites

- **Environmental Protection Agency (EPA):** http://es.epa.gov/ncer/nano/
- **EPA Draft Nanomaterial Research Strategy**, 24 January 2008, http://es.epa.gov/ncer/nano/publications/nano_strategy_012408.pdf
- **Food and Drug Administration (FDA):** http://www.fda.gov/nanotechnology/

Websites

- **International Conference on Nanotechnology: Occupational and Environmental Health & Safety, 4-7 December 2006, Cincinnati, OH. Slide presentations online, available:** http://www.uc.edu/noehs/conference_program.asp.

- **International Council on Nanotechnology (ICON):** http://cohesion.rice.edu/centersandinst/cben/industry.cfm?doc_id=5023

- **International Organization for Standardization (ISO) TC 229 Nanotechnologies:** http://www.iso.org/iso/en/CatalogueListPage.CatalogueList?COMMID=5932&scopelist=PROGRAMME

Websites

- **National Institute for Occupational Safety and Health (NIOSH):** http://www.cdc.gov/niosh/topics/nanotech/
- **Occupational Safety and Health Administration (OSHA):** http://www.osha.gov/
- **Organization for Economic Co-operation and Development (OECD):** http://www.oecd.org/department/0,2688,en_2649_37015404_1_1_1_1_1,00.html

Websites

- **National Nanotechnology Initiative (NNI):** http://www.nano.gov/
- **NNI, Research and Development Leading to a Revolution in Technology and Industry (Supplement to the President's FY 2007 Budget), July 2006: http://www.nano.gov/NNI_07Budget.pdf**
- **NNI, EHS research needs for Engineered nanoscale materials: http://www.nano.gov/NNI_EHS_research_needs.pdf)**

Websites

- **NNI, Strategy for Nanotechnology-Related Environmental, Health, and Safety Research, February 2008:** http://www.nano.gov/NNI_EHS_Research_Strategy.pdf

- **Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies:** http://www.nanotechproject.org/

- **National Cancer Institute (NCI):** http://nano.cancer.gov/

Websites

- **Defense Information Resources:**
  - DoD Directive 4715.1E, "Environment, Safety, and Occupational Health", March 19, 2005: http://www.dtic.mil/whs/directives/corres/html/471501.htm
  - DoD Directive 5000.1, “The Defense Acquisition System”, May 12, 2003: http://www.dtic.mil/whs/directives/corres/pdf/500001p.pdf
  - DoD Instruction 5000.2, "Operation of the Defense Acquisition System," May 12, 2003: http://www.dtic.mil/whs/directives/corres/html/500002.htm
  - DoD Instruction 6050.05, "DoD Hazard Communication (HAZCOM) Program", 08/15/2006: http://www.dtic.mil/whs/directives/corres/html/605005.htm

Websites

- **Defense Information Resources:**
  - DoD Instruction 6055.1, "DoD Safety and Occupational Health (SOH) Program", August 19, 1998: http://www.dtic.mil/whs/directives/corres/html/605501.htm
  - DoDI 6055.5 DoD Instruction 6055.5, "Industrial Hygiene and Occupational Health", January 10, 1989: http://www.dtic.mil/whs/directives/corres/html/605505.htm
  - DoD 6055.05-M, "Occupational Medical Examinations and Surveillance Manual", May 2, 2007: http://www.dtic.mil/whs/directives/corres/html/605505m.htm
  - DoD 4160.21-M-1, “Defense Demilitarization Manual”, October 21, 1991; Incorporating Change 1 – February 14, 1995: http://www.dtic.mil/whs/directives/corres/html/416021m1.htm

Websites

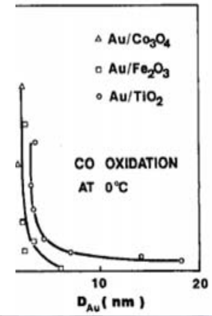
- **Defense Information Resources:**
  - MIL-STD-882D, “Standard Practice for Systems Safety”, February 10, 2000: http://assist.daps.dla.mil/quicksearch/basic_profile.cfm?ident_number=36027
  - Acquisition Community Connection: https://acc.dau.mil/CommunityBrowser.aspx?id=17996
  - Defense Environmental Information Exchange (DENIX): https://www.denix.osd.mil/portal/page/portal/denix

Websites

- **Note: The NIOSH, ASTM, ISO, and OSHA links should be regularly consulted for the latest developments related to occupational health and safety**

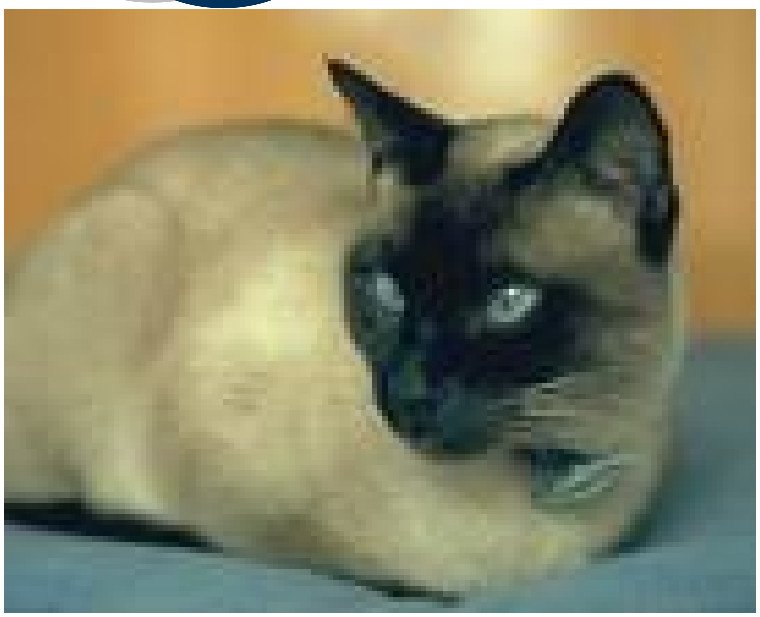
Cat becomes/behaves like a Dog

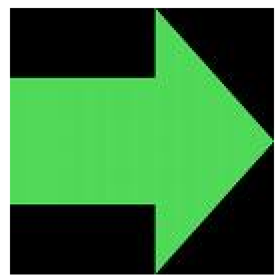
TRANSITIVE NANOPARTICLE



Quantum-Tagged Prostate Cancer Cells

Shuming Nie, Ph.D., Georgia Institute of Technology.





Exhibits size-related intensive property that differs significantly from larger particles

Behavior that is not smoothly or simply extrapolated from the larger particles

Environmental Defense – DuPont Nano Risk Framework (June 2007)

- **Base Set of Physicochemical Properties:**
  - Technical Name
  - Commercial Name
  - Common Form
  - Chemical Composition (including surface coating)
  - Molecular Structure
  - Crystal Structure

Environmental Defense – DuPont Nano Risk Framework (June 2007)

- **Base Set of Physicochemical Properties:**
  - Physical Form/Shape (at room temp & pressure)
  - Particle Size and Size Distribution
  - Particle Surface Area
  - Particle Density
  - Solubility (in water and biologically relevant fluids)

Environmental Defense – DuPont Nano Risk Framework (June 2007)

- **Base Set of Physicochemical Properties:**
  - Dispersability
  - Bulk Density
  - Agglomeration/Aggregation State Porosity
  - Surface Charge
  - Surface Reactivity

Incident Investigations

- **Think out of the box** if investigating reasons for adverse signs and symptoms!

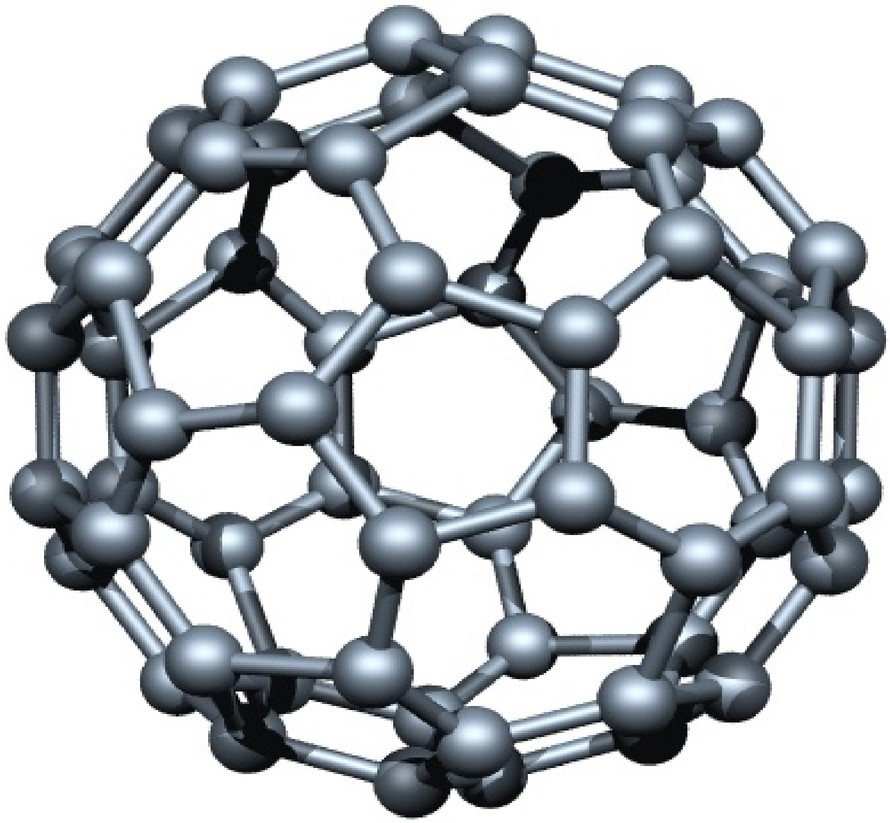
- Current mass-based TLVs for poorly-soluble or insoluble particles may not necessarily be a good means for predicting health effect for nanoscale particles!

Smaller Diameter Fibers

- Nanowires (e.g., Co, Au, Cu, silicon)

- Carbon nanofibers

C_{60} Fullerene



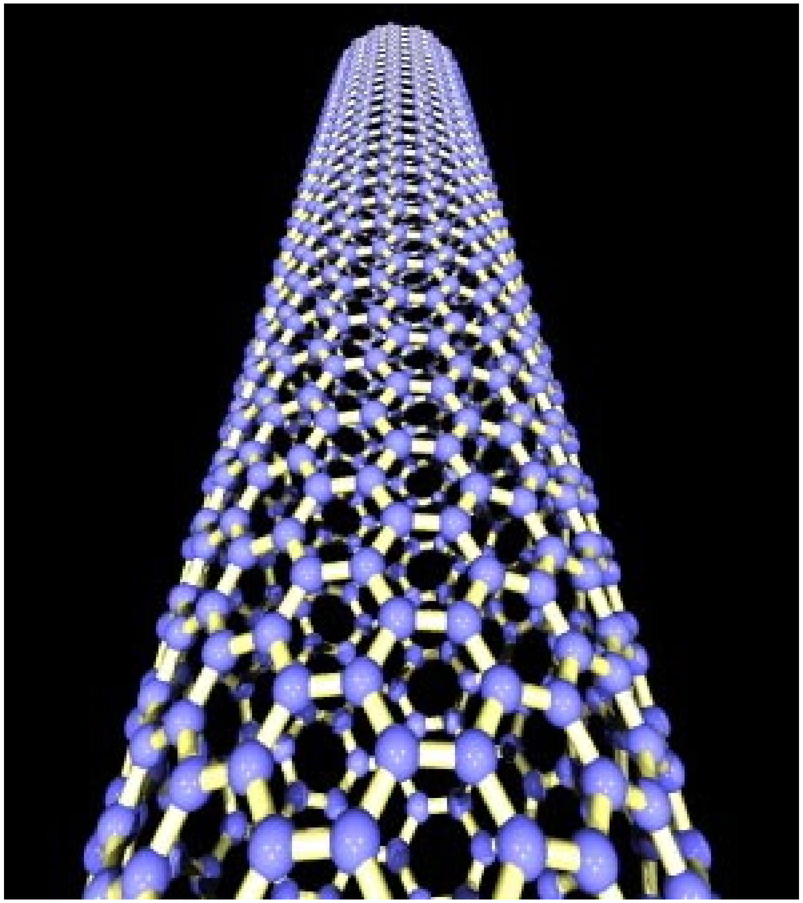
About 1 nm diameter

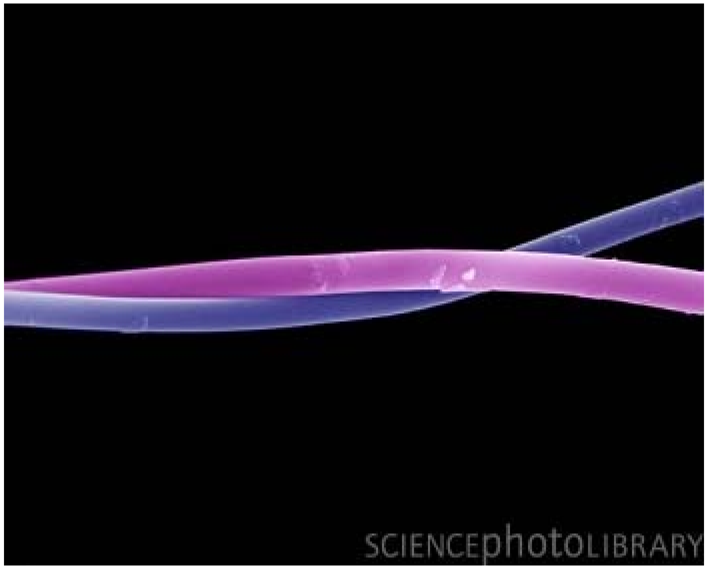
Fullerene C_{60} molecules seen with a scanning tunneling microscope *(Image: Swiss Re)*

Single-Walled Carbon Nanotubes (SWCNT)

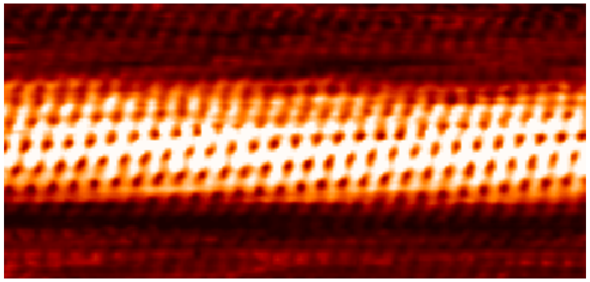
0.7-3 nm diameter
Length: widely variable, up to tens of microns

10-times as strong as steel, 1.2 times as stiff as diamond





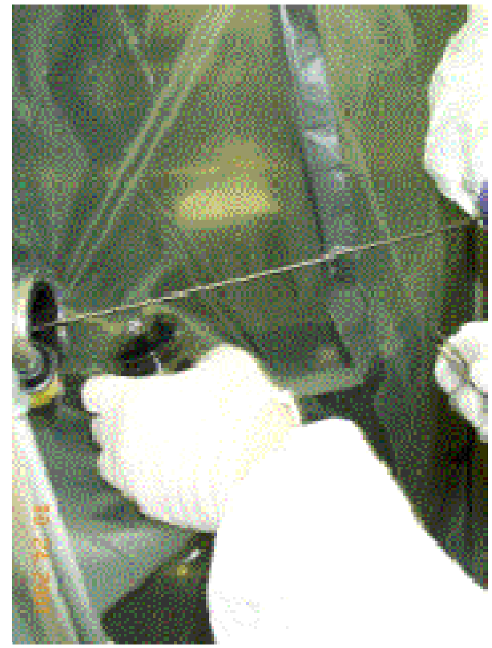
SEM Image. DR KOSTAS KOSTARELOS & DAVID MCCARTHY/ SCIENCE PHOTO LIBRARY



STM Image, American Institute of Physics

Carbon Nanotube Manufacture

Material removal
from HiPCO reactor



Removing material from
laser ablation reactor

Source: A. Maynard

Multi-Walled Carbon Nanotube (MWCNT)

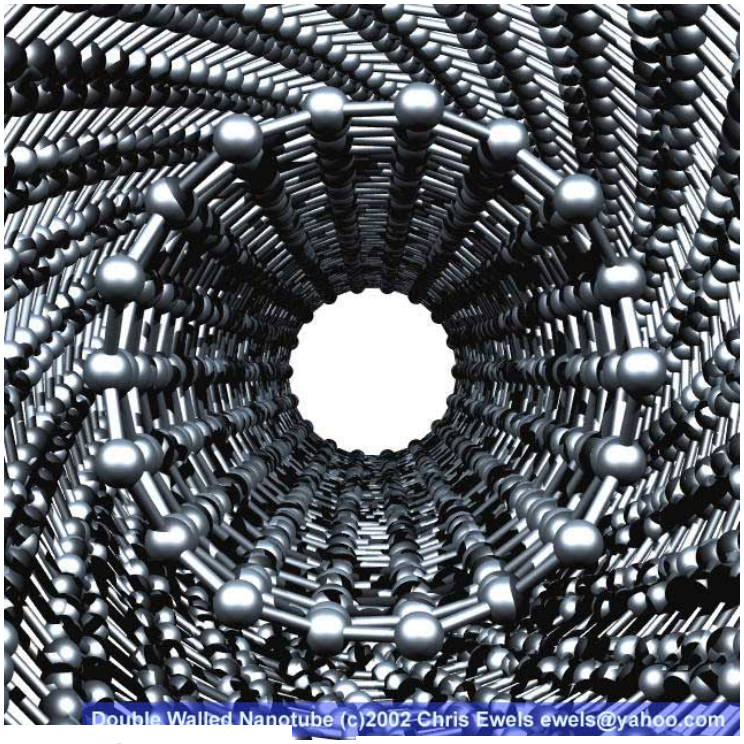
10 to 200 nm diameter
Length: widely variable, up to tens of microns

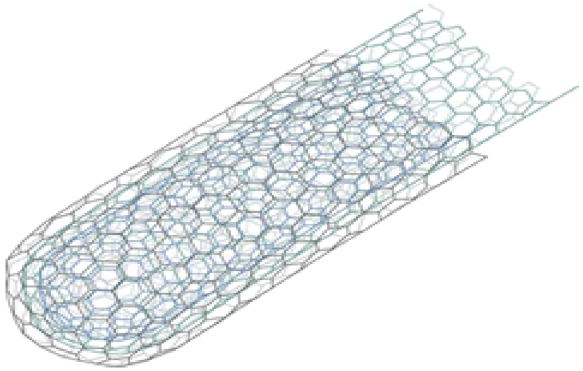
Test tube

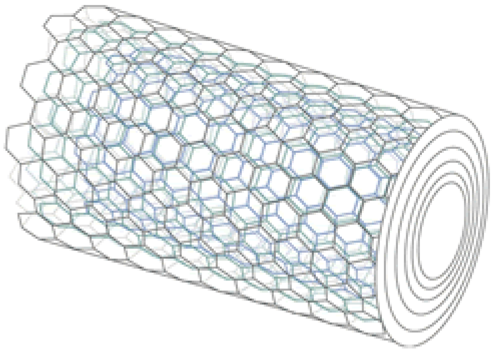
Automobile plastics (i.e.. fenders, door handles, mirror housings)

Automobile fuel systems (i.e.. fuel lines, quick connects, O-rings, filter housings, pump modules)

Potential use:
1. flame retardant
2. flat-panel displays, advanced batteries and fuel cells

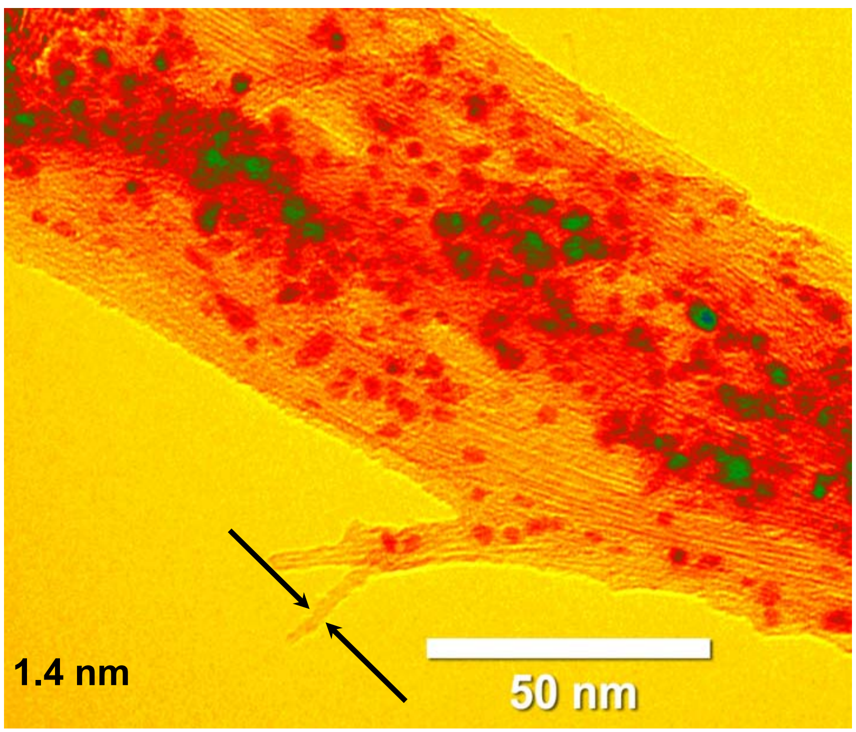






Trace Contaminants/Impurities

- **Metals used in carbon nanotube synthesis: Co, Fe, Ni, Mo**
- **Carbon nanotube organic trace contaminants: carbon black, PAHs**



Source: Maynard, NIOSH

Titanium Dioxide

- **Is it possible to have one ultrafine exposure limit that applies to all polymorphs, shapes, sizes, etc?**
- Different Crystalline Polymorphs (anatase, rutile),
- Coatings (e.g., Ag)
- Particle Size Distributions, Shapes
  - Different Surface areas
  - Different Deposition Probabilities in Respiratory Tract
  - Different Translocation Potentials?

Exposure Management Control Banding Concept

Schulte et. al., NIOSH, Occupational Risk Management of Engineered Nanoparticles, JOEH, 2:4, Apr 08

- **Control Approach:**
  - **Band 1:** Use good IH practice and general ventilation
  - **Band 2:** Use engineering control, e.g., LEV
  - **Band 3:** Enclose the process
  - **Band 4:** Seek expert advice

Nanosilver

- Apply TLV-TWA for “metal” or soluble compounds (as Ag)?
  - **TLV-TWA of 0.1 mg/m^3, metal, “total”**
    - ?? 0.066 x TLV = 0.007 mg/m^3
  - **TLV-TWA of 0.01 mg/m^3, soluble compounds, as Ag, “total”**
    - ?? 0.5 x TLV = 0.005 mg/m^3

Nanoaluminum

- Is TLV-TWA (2008) adequate?
  - **1 mg/m^3, metal and insoluble compounds; respirable**
    - ?? $0.066 \times 1\ mg/m^3 = 0.07\ mg/m^3$

Particle Number Concentration, Direct-Reading Hand-Held Condensation Particle Counters (CPC), Non-Specific, < 1,000 nm

Cost: $6,000

TSI P-Trak

20 nm to 1,000 nm

0 to 500,000 particles/cc

Cost: $8,000

TSI Model 3007

10 nm to 1,000 nm

0 to 100,000 particles/cc

Without a nanoparticle pre-separator, they are not specific to the nanometer size range.
(no suitable pre-separators are currently available)

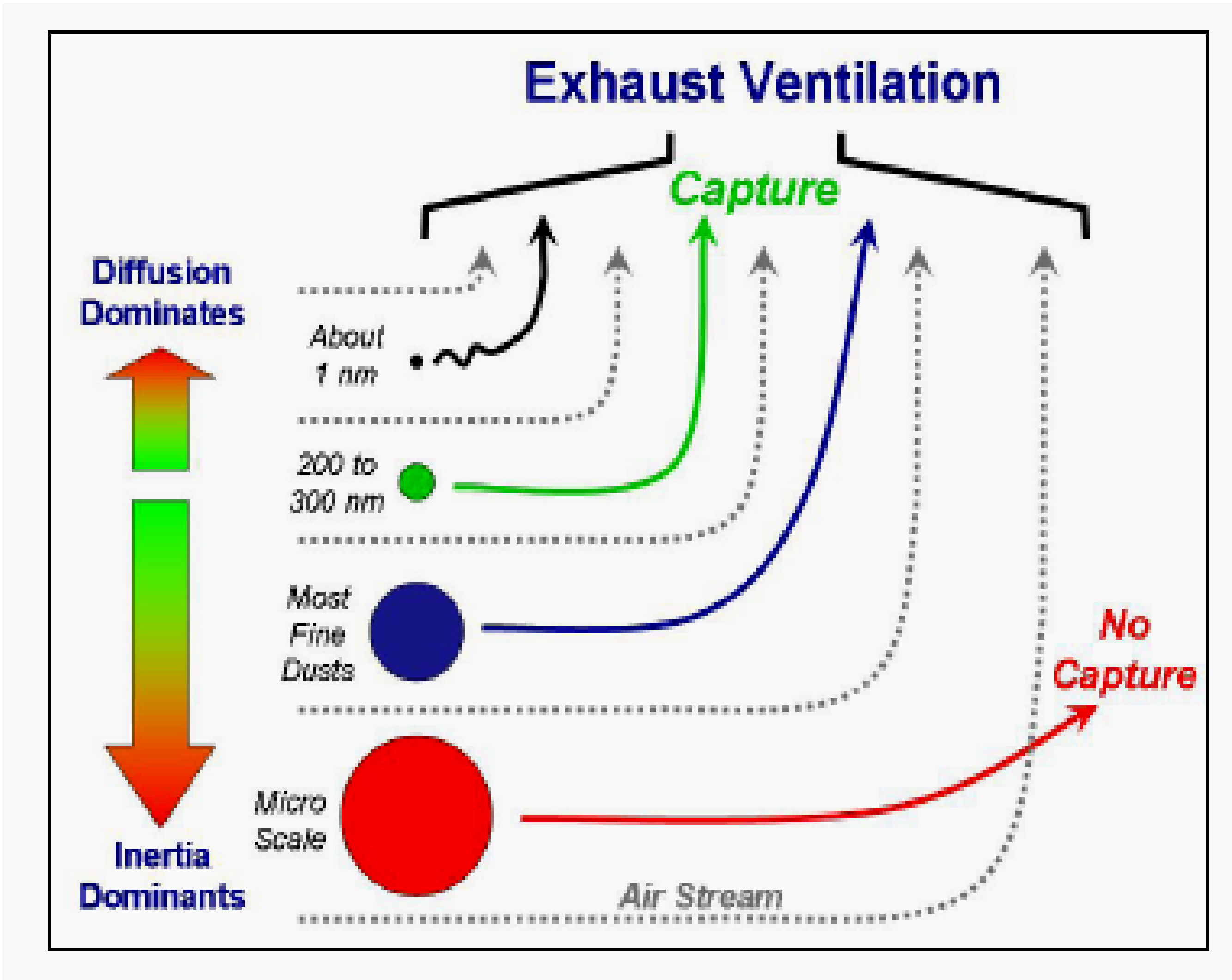
Particle Number Concentration,

Optical Particle Counter (OPC):

> 300 nm diameter

Counts in 1 to 6 user-adjustable bin sizes from 0.3 to 10 microns

Ventilation and NP Source: NIOSH



Peer Reviewers for NIOSH Interim Guidance for Medical Screening

- **Robert J. McCunney, Ph.D.**
  Department of Biological Engineering
  MIT
- **Michael Kosnett, MD, MPH**
  University of Colorado at Denver
- **Prof. Ken Donaldson, Ph.D.**
  ELEGI Colt Laboratory
  Wilkie Laboratory
  MRC Centre for Inflammation Research
  University of Edinburgh Medical School

Schulte et. al., NIOSH, Occupational Risk Management of Engineered Nanoparticles, JOEH, 2:4, Apr 08

- **Increased potential for NP exposure:**
  - – Generating NP in **gas phase** in nonenclosed systems
  - – Handling nanostructured **powders**
  - – Working with NPs in **liquid suspension**:
    - w/o adequate PPE (e.g., gloves, etc.)
    - pouring or mixing operations
    - or where high degree of agitation is involved

Schulte et. al., NIOSH, Occupational Risk Management of Engineered Nanoparticles, JOEH, 2:4, Apr 08

- **Increased potential for NP exposure:**
  - Machining, sanding, drilling, or other mechanical disruptions of materials containing nanoparticles
  - Maintenance
    - On equipment and processes used to produce or fabricate nanomaterials
    - Cleanup of spills or waste material
    - Cleanup of dust collection systems used to capture nanoparticles

Schulte et. al., NIOSH, Occupational Risk Management of Engineered Nanoparticles, JOEH, 2:4, Apr 08

- **Reducing potential for inhalation:**
  - Pelletizing nanoparticles
  - Prilling to encapsulate nanoparticles
  - Using slurries or suspensions instead of powders
- **Reducing toxicity of nanoparticles:**
  - Coating the particles w/ less hazardous material that does not interfere w/ commercial properties