Occupational Exposure Science for Nanomaterials

Current State, Challenges, and Future Research

QEEN
Workshop

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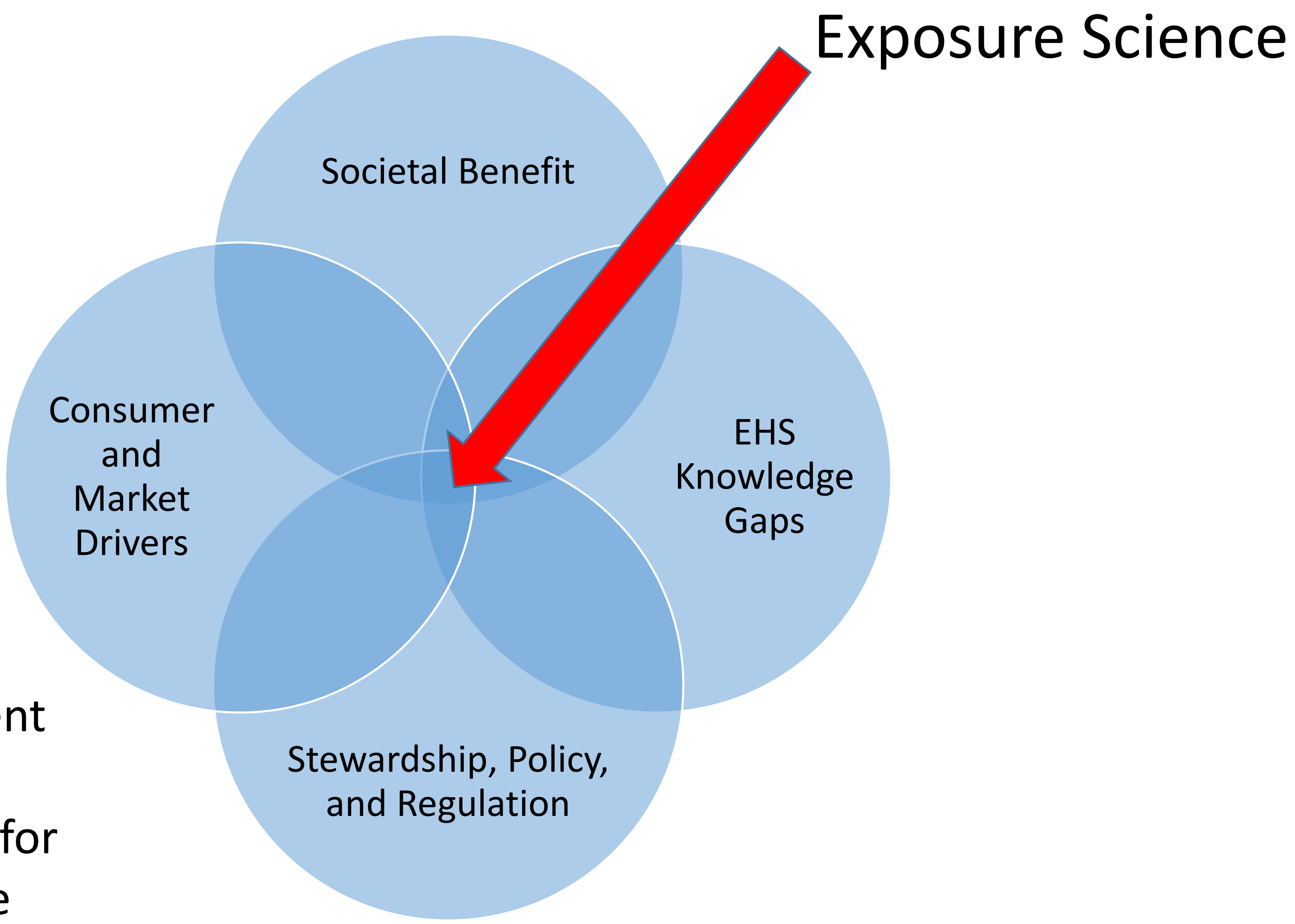
Nanotechnology Research Center
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

Overview

- Context of Exposure Science
- Application to the Occupational Setting
- Evolution of Workplace Assessment
- Future Work

Development of Nanotechnology has multiple drivers



Responsible development of Nanotechnology has created a high demand for robust exposure science

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Why Exposure Science?

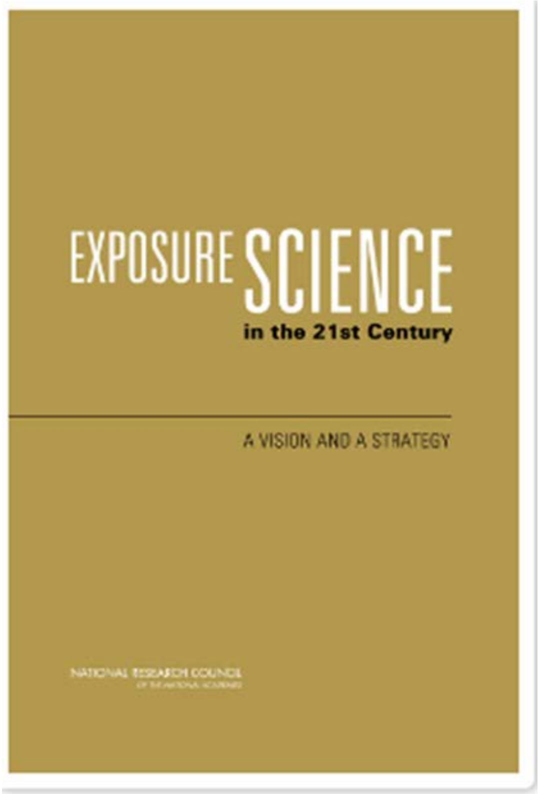
The study of human contact with stressors (for today, Nanomaterials) in their environments (the workplace) and knowledge of the events causing or preventing adverse health outcomes.

Hazard of stressor: toxicology

Anticipate and measure contact: exposure

Risk: predicted, characterized

Prevention: risk management



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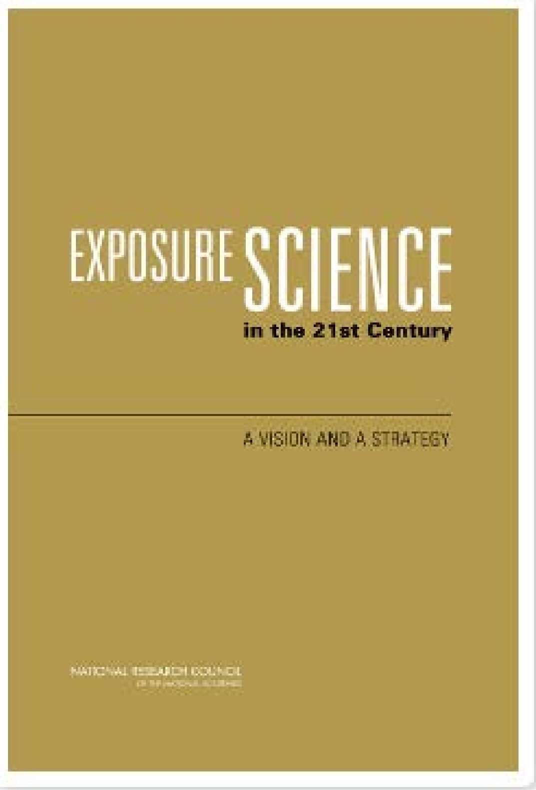
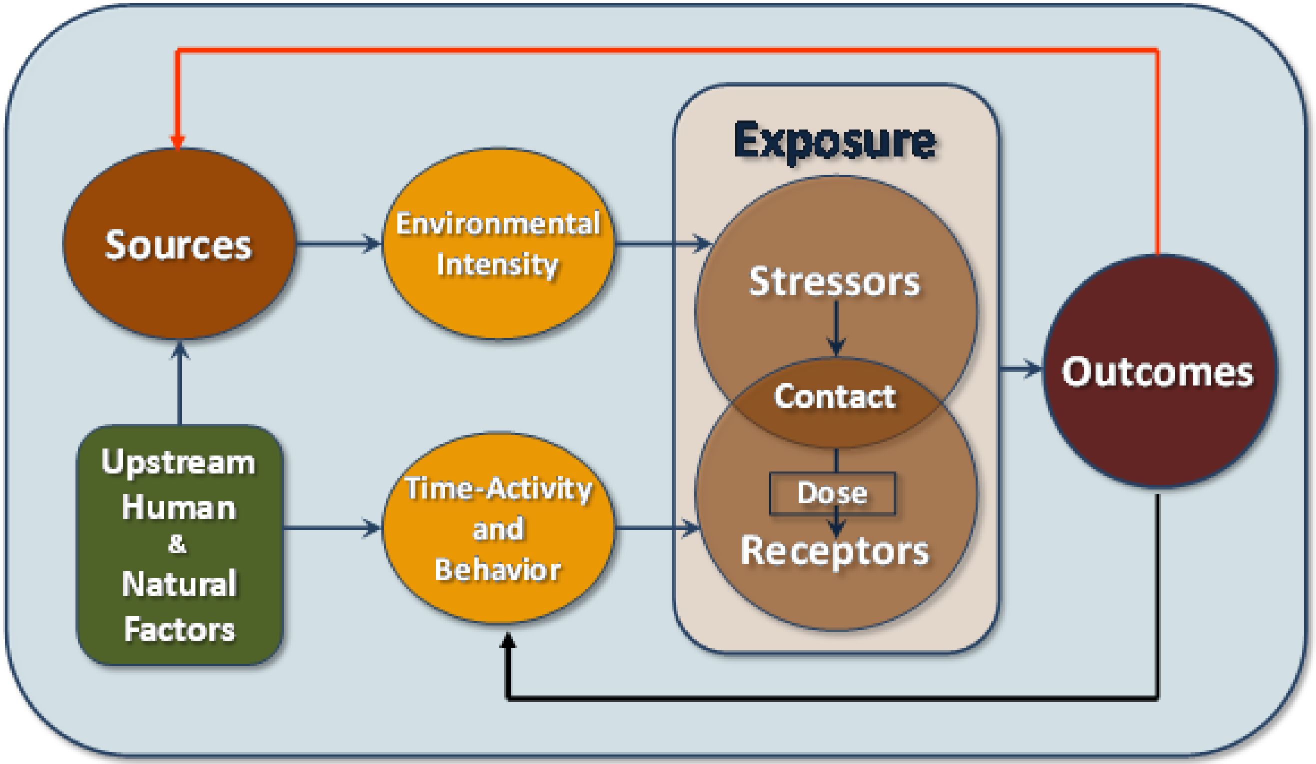
Why Workplace Exposure Assessment?

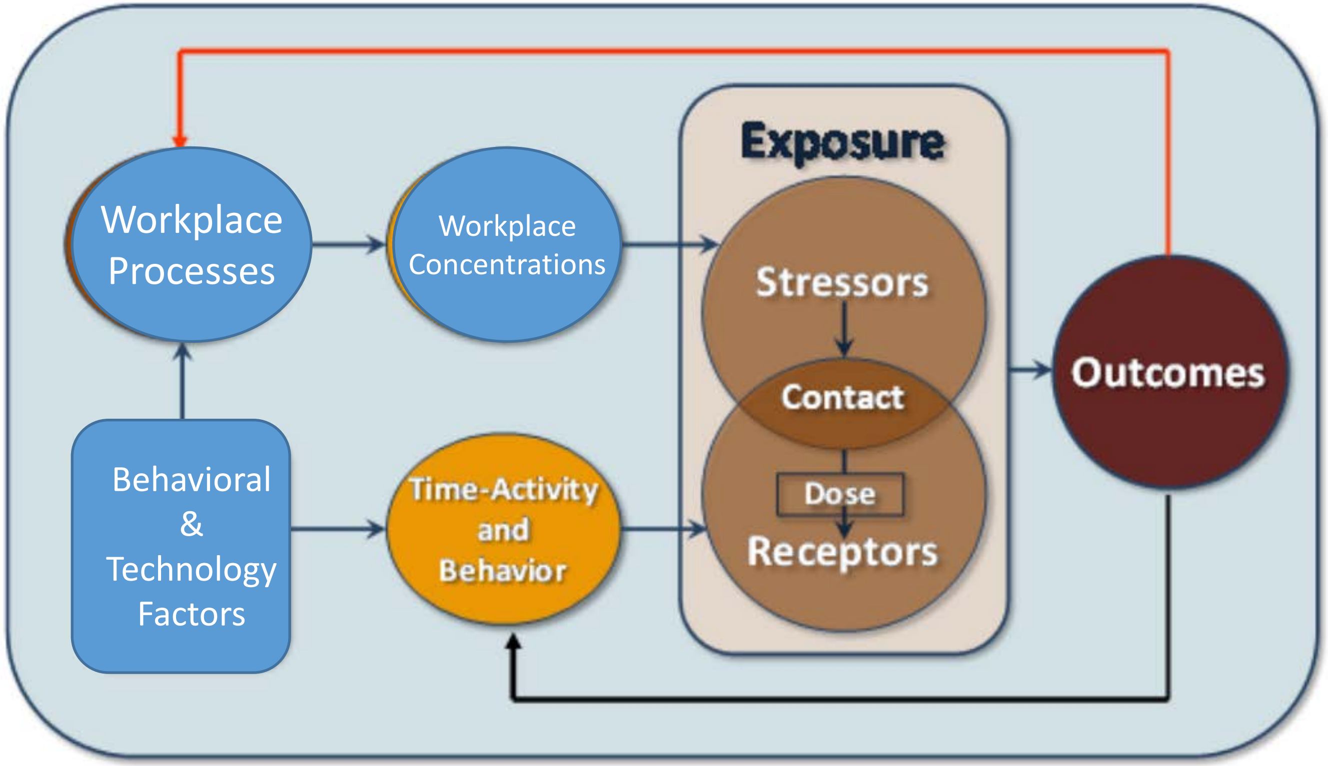
- Workers generally the first people in society exposed to a new technology and its materials
- Nanotechnology is no exception
- More than 1,000 nano-enabled products reportedly in commerce
- Workers make and use them; from R&D labs, to concept testing, to manufacturing.
- First opportunity to develop good stewardship practices

Exposure Science: Key Elements

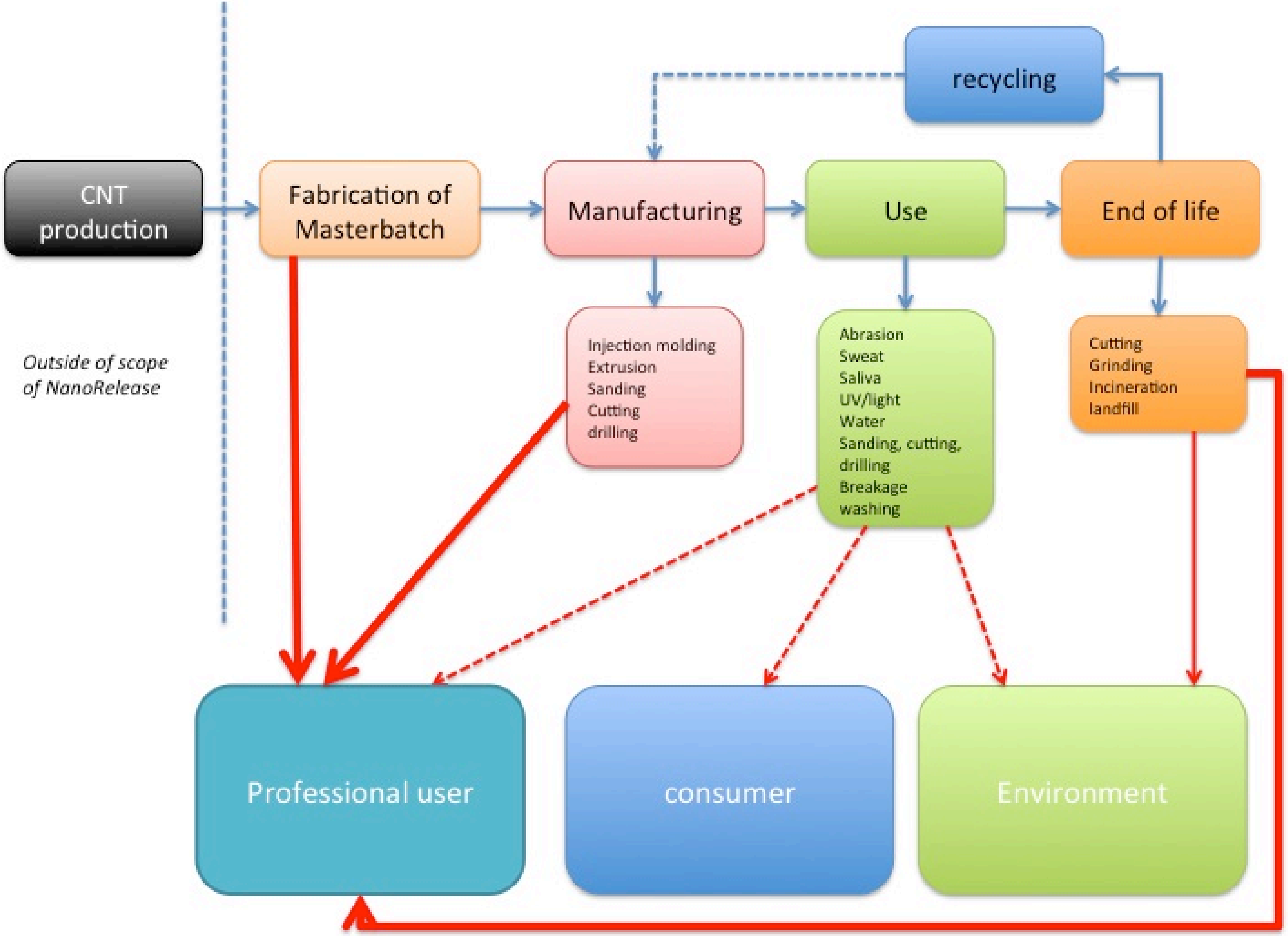




Occupational Focus: Slight Modification

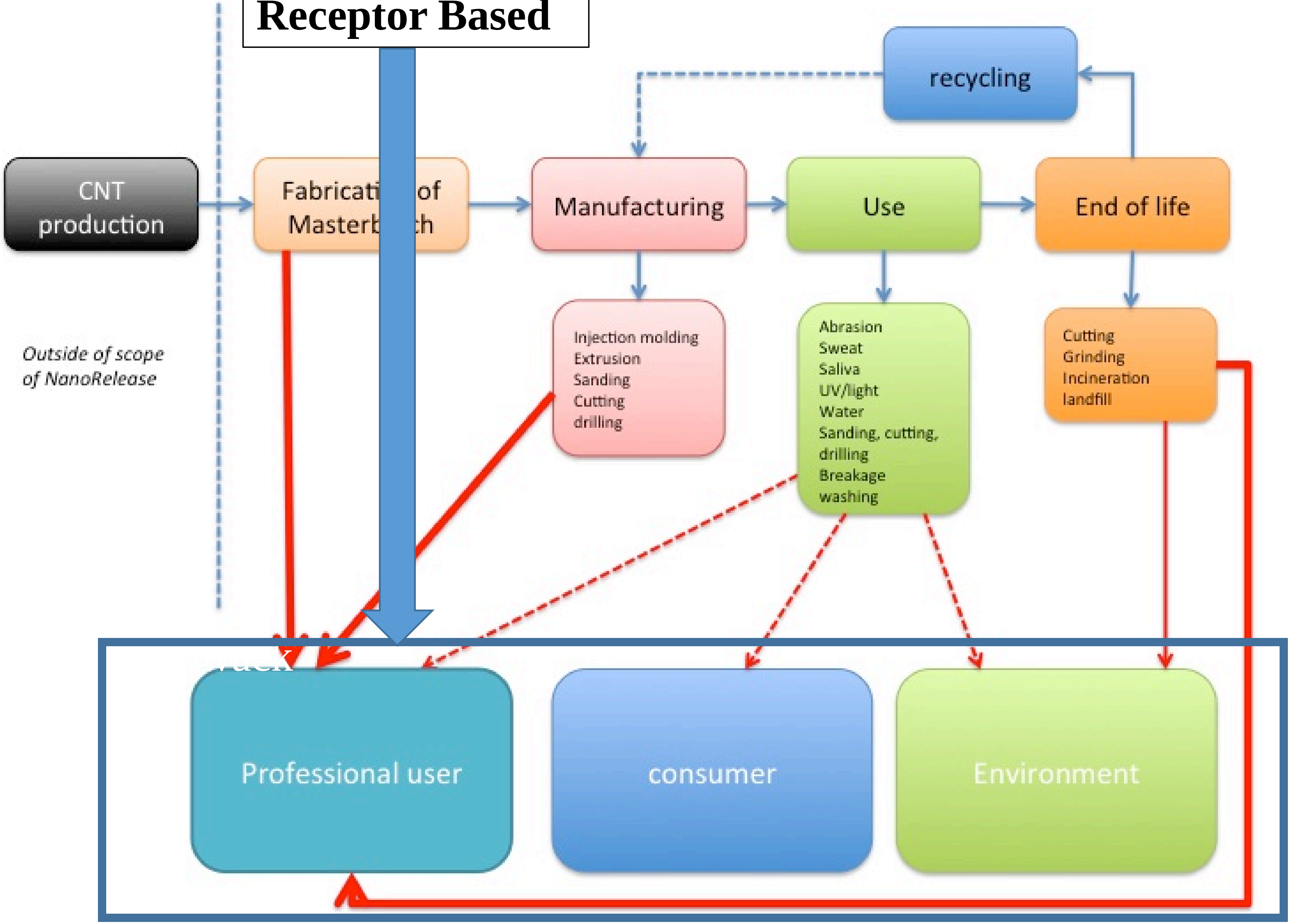


There are many potential sources for initiation of an exposure pathway



Source:
Bernd Nowack

Receptor Based



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Workplace Hazard?

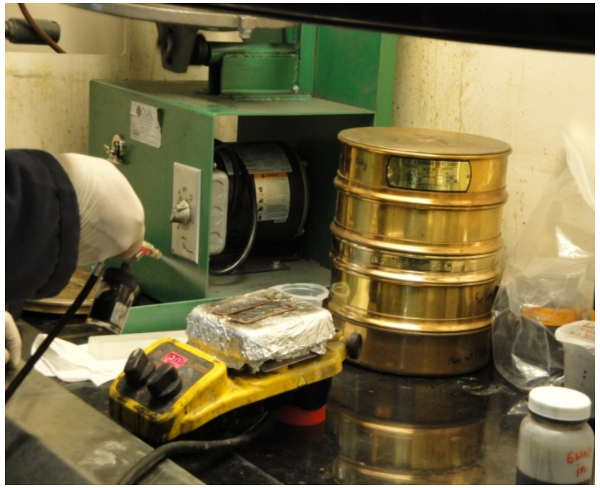
- Dramatic increase in nanomaterial hazard information: Nanotoxicology
- Growing interest in workplace issues
- Small but growing amount of information on actual workplace experience
- Interest and actions by governing bodies

Occupational Exposure Science: Links and Tools

- Toxicology
- Risk Assessment
- Exposure Assessment
  - Strategies
  - Measurement Technology
- Risk Characterization
- Epidemiology
- Predictive Tools

Changing Nanotechnology Workforce

- Trend – from laboratory research to scale-up
- Higher potential exposures



- “Nanotechnology is unquestionably moving toward manufacturing, involving a still very small but increasing component of the labor force.” [Invernizzi N. J Nanopart Res 2011]

Occupational Exposure Assessment

- Critical component of risk management
- Identifies populations at risk
- Characterize the exposure, therefore better understanding of risk
  - Nature of exposure: low vs. high, short vs. long
  - Extent of exposure: few or many
  - Complexity of the exposure
  - Place the exposure on the life cycle
- Verify controls

KEY INDUSTRIES AND WORKER INVOLVMENT

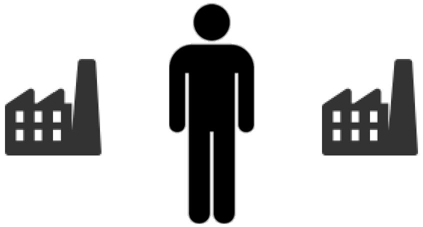
Transportation
transportation.ccs.k12.nc.us

Water
dupont.com

Agriculture
us.123rf.com

Textiles
glogster.com

Building Materials
cinorthwest.com



Paper
openlettersmonthly.com

Cosmetics
dreamstime.com

Medical
theavtimes.com

Electronics
sathiyam.tv

Food
bubblews.com

Energy
acmworldwide.com

Courtesy C. Sayes

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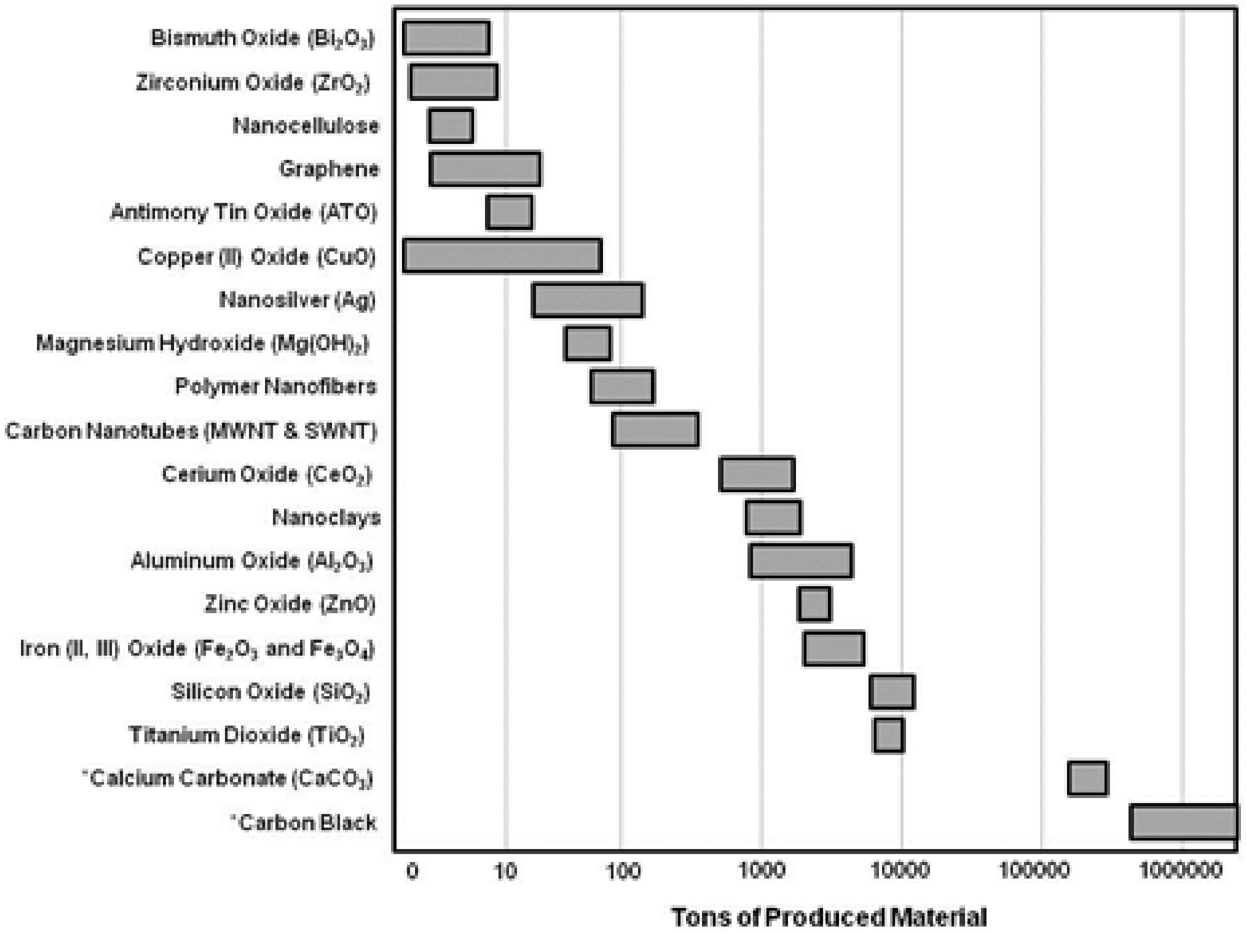
Commonly Produced and Used NM



C. Sayes: NIOSH Contract Report

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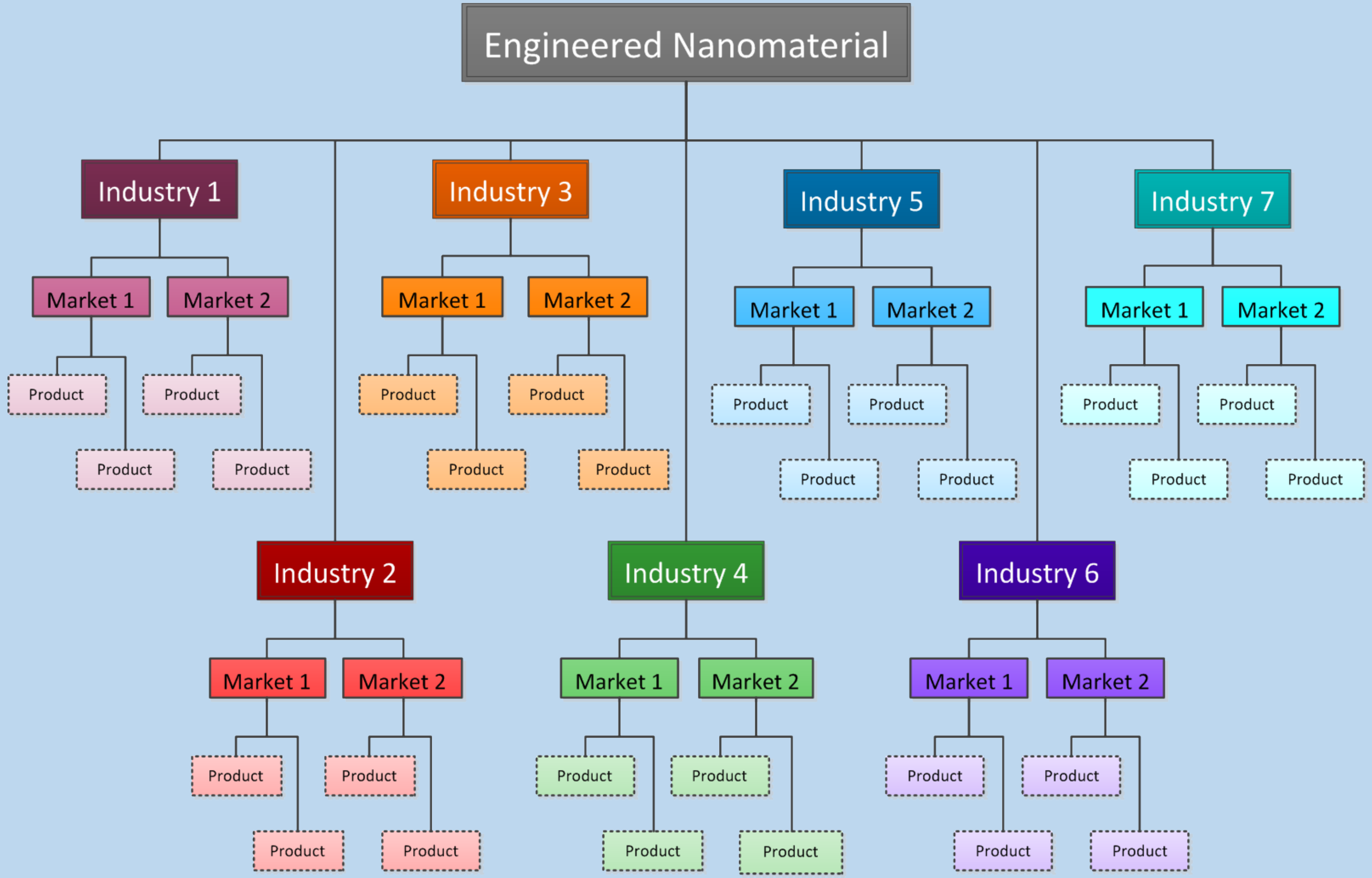
The ENM value chain gets complex quickly and magnifies the challenge



C. Sayes: Contract report to NIOSH

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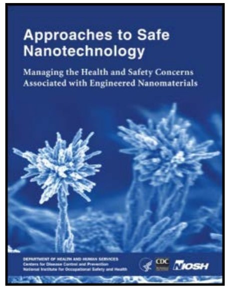
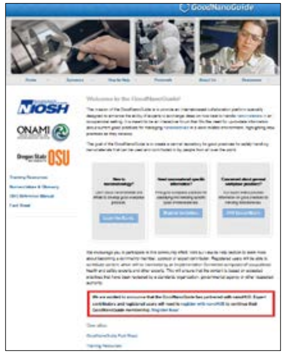
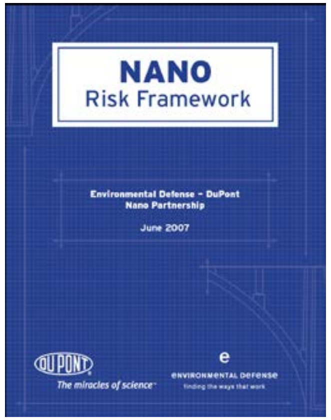
Occupational Exposure Characteristics

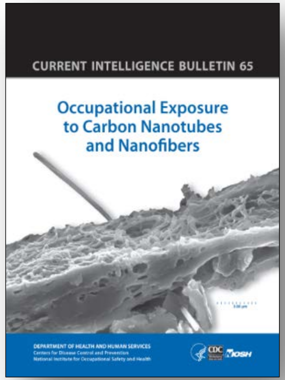
- R&D - Basic: Limited to small volumes but the materials are not well characterized
- R&D – Applied: Proof of concept and prototyping. Volumes and characterization increase, still lab scale
- Pilot systems: first processes, high volumes, greatest potential for human exposure to the free, unbound nanomaterial
- Full commercial deployment

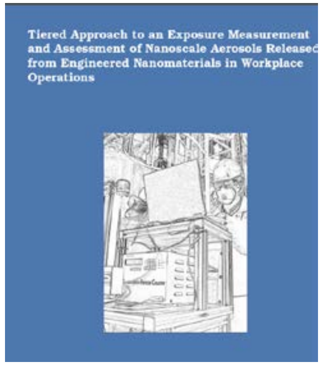
A tiny sample of guidance coming out globally

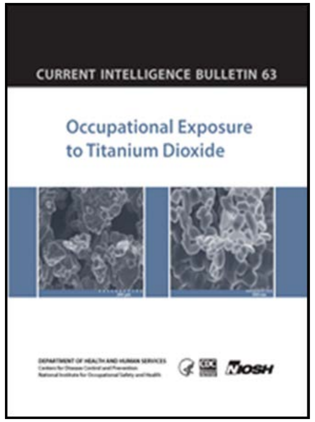


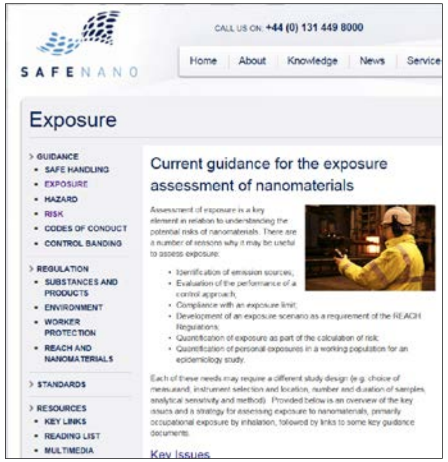


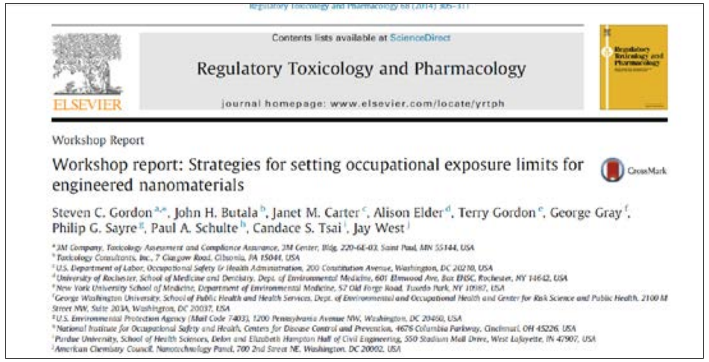












PUBLISHED DOCUMENTS DEVELOPED BY ISO/TC 229

'Exposure Science' Guidance from just one source

ISO/TS 27687:2008 – *Nanotechnologies -- Terminology and definitions for nano-objects -- Nanoparticle, nanofibre and nanoplate*
ISO/TR 12885:2008 – *Nanotechnologies – Health and safety practices in occupational settings relevant to nanotechnologies*
ISO/TR 11360:2010 – *Nanotechnologies – Methodology for the classification and categorization of nanomaterials*
ISO/TS 80004-3:2010 – *Nanotechnologies --Terminology and definitions --Part 3: Carbon nano-objects*
ISO/29701:2010 - *Nanotechnologies --Endotoxin test on nanomaterial samples for in vitro systems -- LAL Assay*
ISO/TS 10867:2010 – *Nanotechnologies -- Characterization of single-wall carbon nanotubes using near infrared photoluminescence spectroscopy*
ISO/TS 80004-1:2010 – *Nanotechnologies – Vocabulary – Part 1: Core terms*
ISO/TR 12802-2010 – *Nanotechnologies – Model taxonomic framework for use in developing vocabularies – Core concepts*
ISO/TS 11251-2010 – *Nanotechnologies – Characterization of volatile components in single-wall carbon nanotube samples using evolved gas analysis/gas chromatograph-mass spectrometry*
ISO 10801:2010 – *Nanotechnologies --Generation of metal nanoparticles for inhalation toxicity testing using the evaporation/condensation method*
ISO 10808:2010 – *Nanotechnologies --Characterization of nanoparticles in inhalation exposure chambers for inhalation toxicity testing*
ISO/TR 13121:2011 – *Nanotechnologies -- Nanomaterial risk evaluation*
ISO/TS 10798:2011 - *Nanotechnologies -- Characterization of single-wall carbon nanotubes using scanning electron microscopy and energy dispersive X-ray spectrometry analysis*
ISO/TS 10868:2011 - *Nanotechnologies -- Characterization of single-wall carbon nanotubes using ultraviolet-visible-near infrared (UV-Vis-NIR) absorption spectroscopy*
ISO/TS 80004-7:2011 - *Nanotechnologies -- Vocabulary -- Part 7: Diagnostics and therapeutics for healthcare*
ISO/TS 13278:2011 – *Nanotechnologies – Determination of metal impurities in samples of carbon nanotubes using inductively coupled plasma mass spectrometry*
ISO/TS 11308:2011 – *Nanotechnologies – Characterization of single-wall carbon nanotubes using thermogravimetric analysis*
ISO/TS 11888:2011 – *Nanotechnologies - Characterization of multiwall carbon nanotubes -- Mesoscopic shape factors*
ISO/TS 12805:2011 – *Nanotechnologies -- Materials specifications -- Guidance on specifying nano-objects*
ISO/TS 80004-4:2011 – *Nanotechnologies – Vocabulary – Part 4: Nanostructured materials*
ISO/TS 80004-5:2011 – *Nanotechnologies – Vocabulary – Part 5: Bionano interface*
ISO/TR 10929:2012 - *Nanotechnologies -- Characterization of multiwall carbon nanotube (MWCNT) samples*
ISO/TR 13014:2012 - *Nanotechnologies - Guidance on physicochemical characterization of engineered nanoscale materials for toxicologic assessment*
ISO/TS 10797:2012 – *Nanotechnologies -- Characterization of single-wall carbon nanotubes using transmission electron microscopy (TEM)*
ISO/TR 11811-2012 – *Nanotechnologies -- Guidance on methods for nano- and microtribology instruments*
IEC/ISO TS 62622 - *Nanotechnologies – Description, measurement and dimensional quality parameters of artificial gratings*
ISO/TS 12025:2012 - *Nanomaterials -- Quantification of nano-object release from powders by generation of aerosols*
ISO/TS 14101:2012 - *Surface characterization of gold nanoparticles for nanomaterial specific toxicity screening: FT-IR method*
ISO/TS 12901-1:2012 - *Nanotechnologies – Occupational risk management applied to engineered nanomaterials Part 1: Principles and approaches*
ISO/TR 13329:2012 - *Nanomaterials -- Preparation of material safety data sheet (MSDS)*
ISO/TS 11931:2012 - *Nanotechnologies -- Nanoscale calcium carbonate in powder form -- Characteristics and measurement*
ISO/TS 11937:2012 - *Nanotechnologies -- Nanoscale titanium dioxide in powder form -- Characteristics and measurement*
ISO/TS 16195:2013 - *Nanotechnologies -Generic requirements for reference materials for development of methods for characteristic testing, performance testing and safety testing of nano-particle and nano-fiber powders*
ISO/TS 17200:2013 - *Nanotechnology -- Nanoparticles in powder form -- Characteristics and measurements*
ISO/TS 80004-6:2013 - *Nanotechnologies -- Vocabulary -- Part 6: Nano-object characterization*
ISO/TS 13830:2013 – *Nanotechnologies – Guidance on voluntary labelling for consumer products containing manufactured nano-objects*
ISO/TS 80004-8:2013 - *Nanotechnologies -- Vocabulary -- Part 8: Nanomanufacturing*
ISO/TR 14786:2014 - *Nanotechnologies — Considerations for the development of chemical nomenclature for selected nano-objects*
ISO/TS 12901-2:2014 – *Nanotechnologies – Occupational risk management applied to engineered nanomaterials – Part 2: Use of the control banding approach*
ISO/TR 16197:2014 - *Nanotechnologies -- Compilation and description of toxicological screening methods for manufactured nanomaterials*
ISO/TS 16550:2014 - *Nanotechnologies -- Determination of silver nanoparticles potency by release of muramic acid from Staphylococcus aureus*
ISO/TS 80004-2:2015 - *Nanotechnologies -- Vocabulary -- Part 2: Nano-objects* [**Replaces ISO/TS 27687**]

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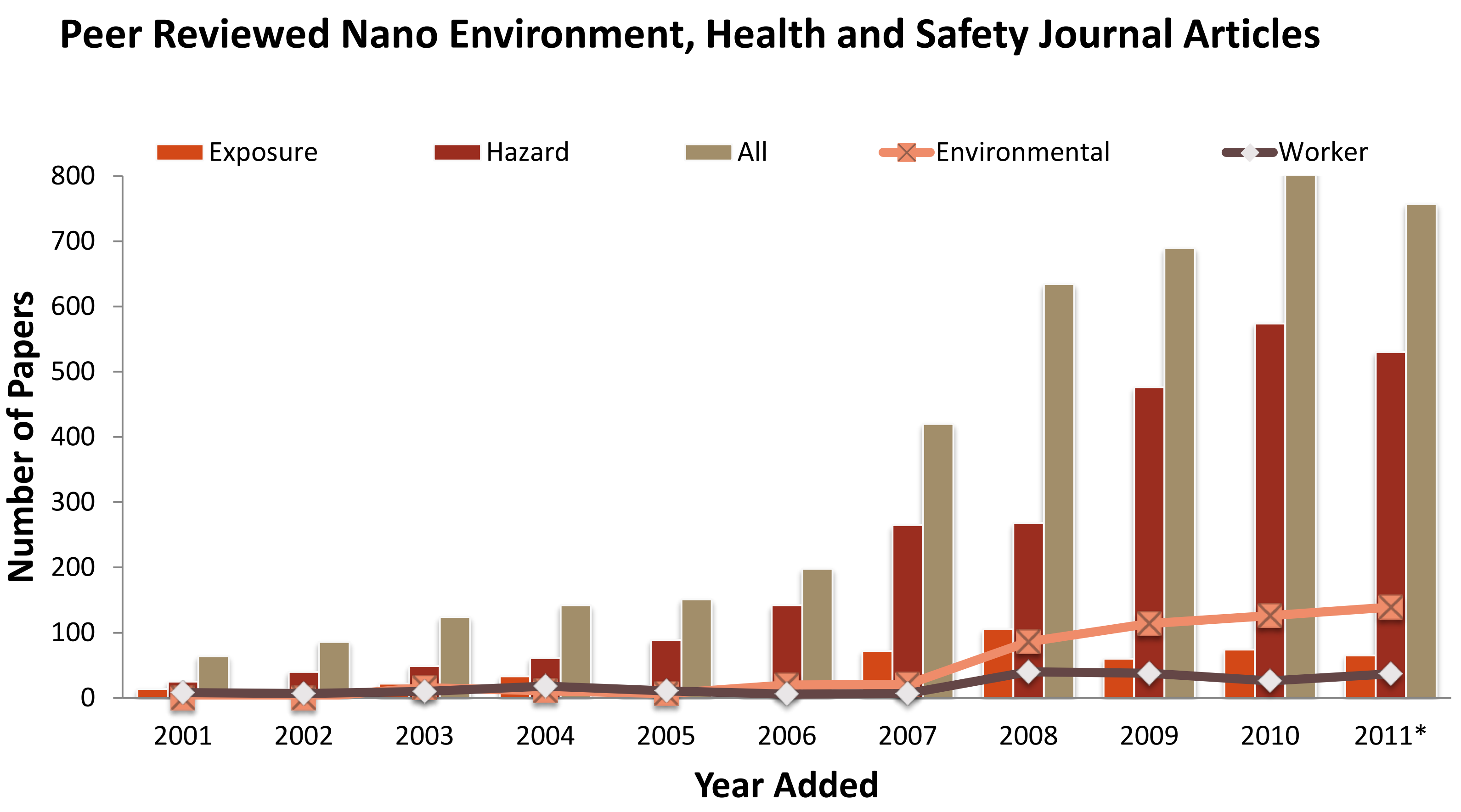
What Does the Nano-EHS Research Tell Us?



http://icon.rice.edu/research.cfm

Meeting the Exposure Science Challenge: An Example from one Agency

The NIOSH Research Program Flow

Follow the Risk Model → Identify Critical Research Areas

Hazard Identification
"Is there reason to believe this could be harmful?"

Exposure Assessment
"Will there be exposure in real-world conditions?"

Risk Characterization
"Is substance hazardous *and* will there be exposure?"

Risk Management
"Develop procedures to minimize exposures."

A concurrent approach to match the pace of innovation.

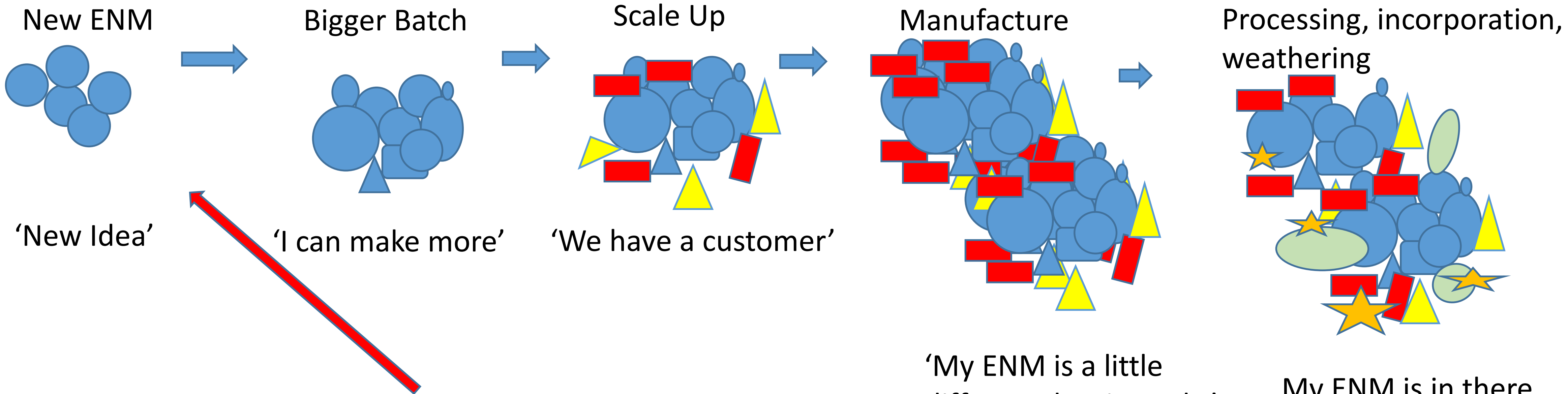
1. Toxicology and internal dose
2. Measurement methods
3. Exposure assessment
4. Epidemiology and surveillance
5. Risk assessment
6. Engineering controls and PPE
7. Fire and explosion safety
8. Recommendations and guidance
9. Communication and information
10. Applications

Contributions to Exposure Science in every area!

“ Nanoparticle” Exposure Assessment Challenges

- Definition of nanoparticle or nanomaterial
- Heterogeneity of nanomaterials
- Agreement on the most appropriate metric
- Lack of evaluation criteria: OELs
- Lack of ruggedized methods to measure and characterize

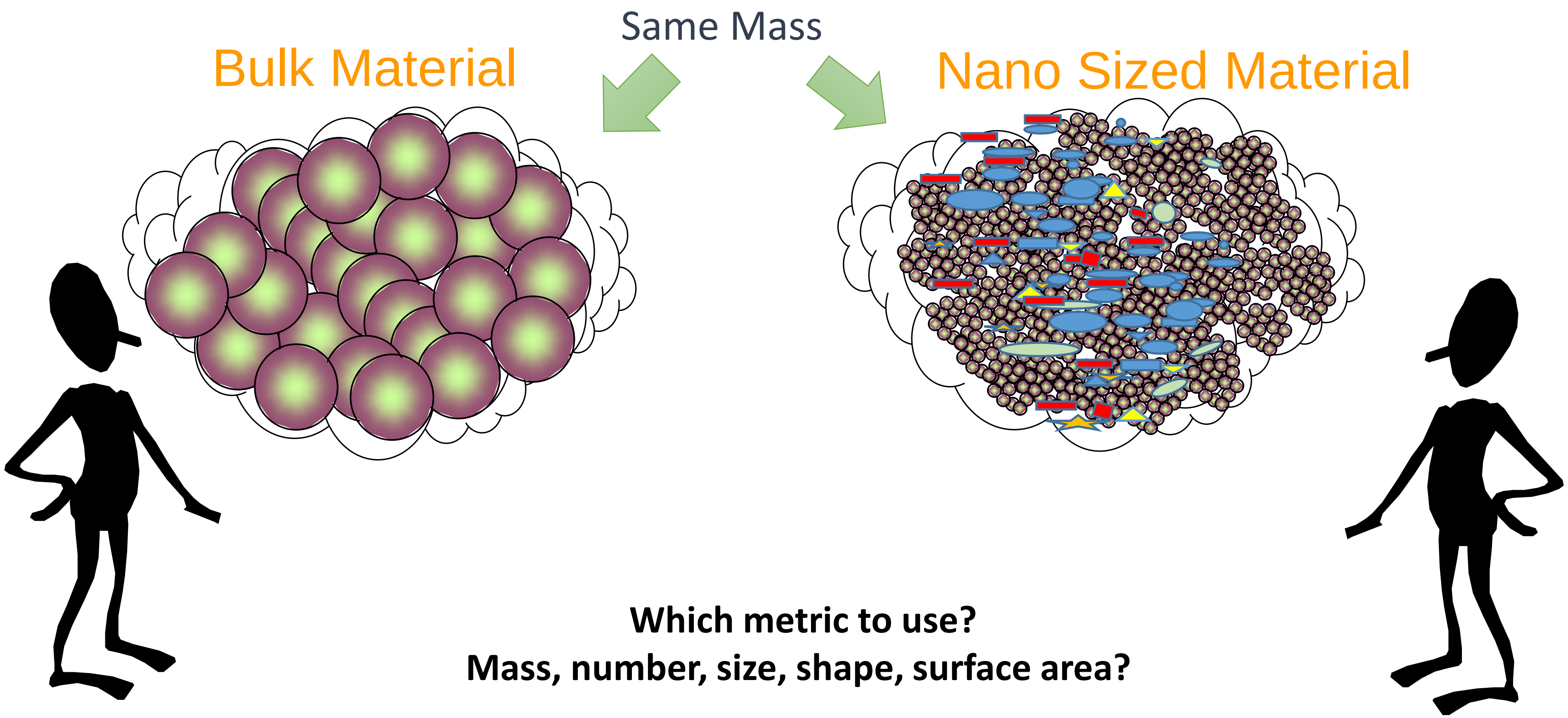
Simple View of a Complex Life Cycle Reality



To measure the presence of <u>this</u>, we have to deal with the realities of change: weathering, transformation, aggregation, etc.

Evaluating the exposure dose

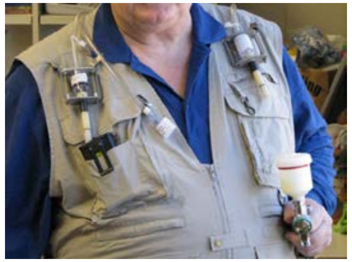
Based on what we know so far, how do we evaluate exposure and risk?

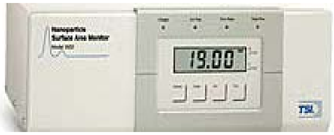


Which metric to use?
Mass, number, size, shape, surface area?

Exposure and Emission Measurements

- Qualitative and Quantitative
  - Confirmation: e.g. TEM with elemental analysis
- Mass concentration
  - Elemental mass, mass by size
- Particle number
  - Total and by size
- Size distribution
  - Count or mass by size
- Surface area





Occupational Exposures:
What metric to use?

Metric	Qualification
Mass	Standard (NIOSH CNT and TiO_2 CIB)
Surface Area	Advantage for low solubility particles
Surface Chemistry	Toxicological studies
Particle Number	Relevance
Particle Size	Translocation
Particle Shape	HAR versus spheres



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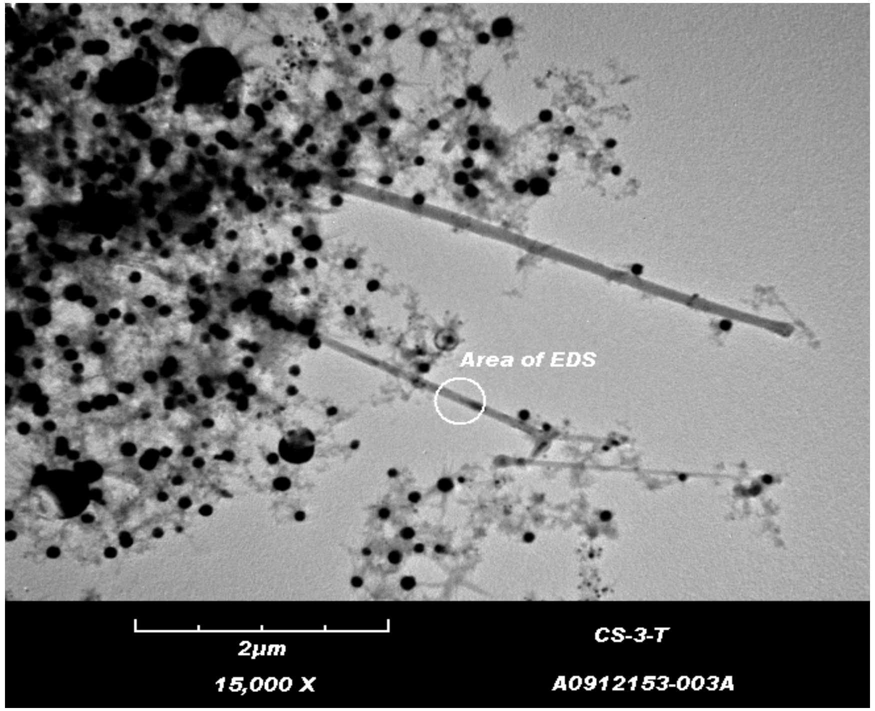
Harvesting SWCNTs from a Carbon Arc Reactor

Task-based PBZ air sample analyzed via TEM w/ EDS



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Initial Focus on 'First Generation Products'

Paint containing silver and titanium dioxide acts as a biocide

Commercial and Consumer Potential

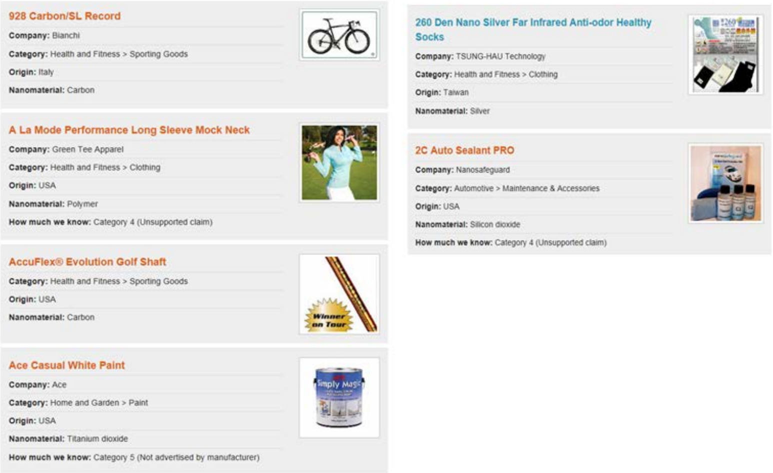
Mixing and applying Nanocrete mortar

Applying glass coating

PCI Nanosilent combines leveling, isolating and sound reduction in one step

BASF: "Special polymers and rubber granules"

Examples of consumer products that contain nanomaterials



928 Carbon/SL Record
Company: Bianchi
Category: Health and Fitness > Sporting Goods
Origin: Italy
Nanomaterial: Carbon

A La Mode Performance Long Sleeve Mock Neck
Company: Green Tee Apparel
Category: Health and Fitness > Clothing
Origin: USA
Nanomaterial: Polymer
How much we know: Category 4 (Unsupported claim)

AccuFlex® Evolution Golf Shaft
Category: Health and Fitness > Sporting Goods
Origin: USA
Nanomaterial: Carbon

Ace Casual White Paint
Company: Ace
Category: Home and Garden > Paint
Origin: USA
Nanomaterial: Titanium dioxide
How much we know: Category 5 (Not advertised by manufacturer)

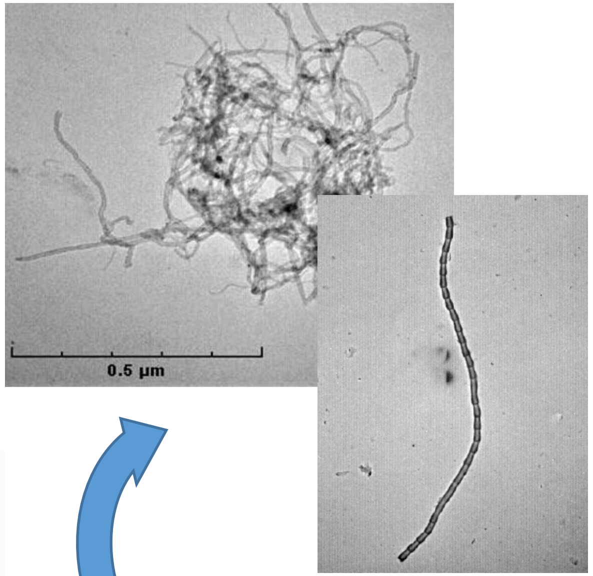
260 Den Nano Silver Far Infrared Anti-odor Healthy Socks
Company: TSUNG-HAU Technology
Category: Health and Fitness > Clothing
Origin: Taiwan
Nanomaterial: Silver

2C Auto Sealant PRO
Company: Nanosafeguard
Category: Automotive > Maintenance & Accessories
Origin: USA
Nanomaterial: Silicon dioxide
How much we know: Category 4 (Unsupported claim)

Nano TiO2 Based Smog Eating Roof Tiles

Field Challenge: A mix of Simple and Complex Measurements

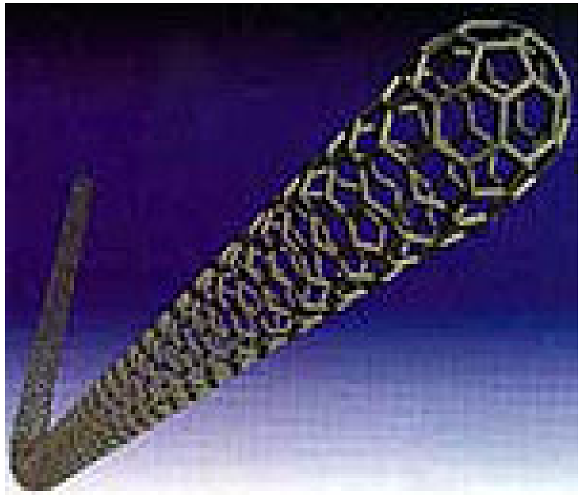
Electron microscopy



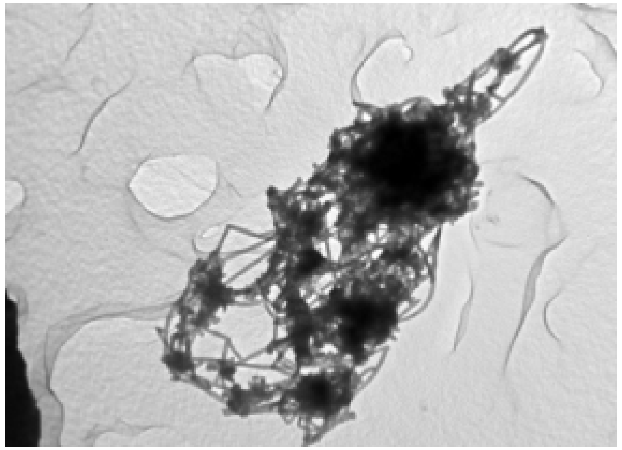
Elemental Analysis

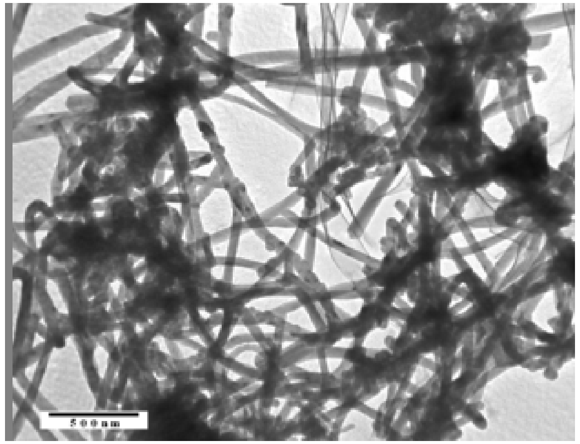
Particle Counters and Size Analyzers

Facing the reality of airborne CNT: A Mini Case Study



Single-walled CNT





MWCNT air samples

Artist's rendering versus real world

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CNT Exposure Metrics

- Mass of CNT
  - Current metric in toxicology
  - Difficult to be specific
  - Markers or surrogates?
  - Sensitive enough?
- Particle number and size
- Fiber or structure count
- Surface area

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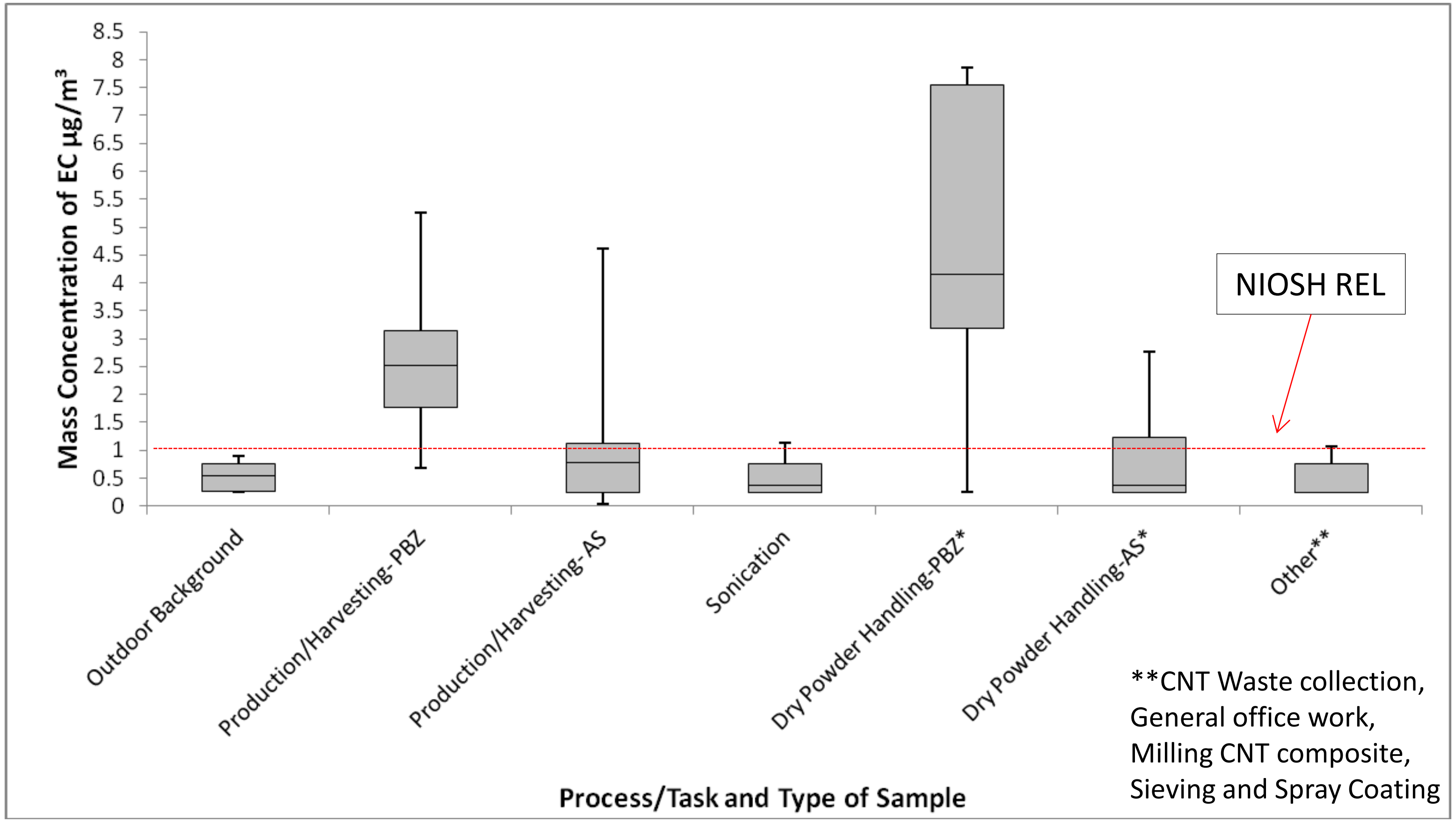
Variation in elemental carbon exposure by task
(Dahm et al., J Occ Environ Hyg)



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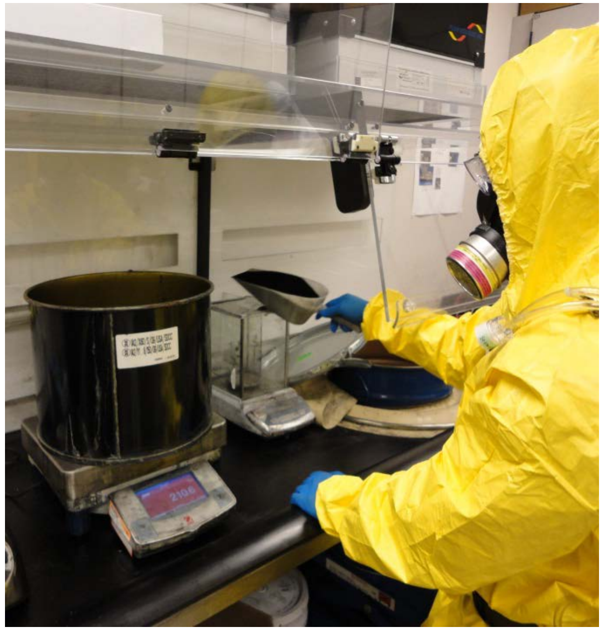
Specific Task Evaluation: Dry Powder Handling

Process: Extrusion
Task: Weighing MWCNT
Volume: 1 kg
Duration of Sample: 112 min
Exposure Concentration=
3.19 µg/m³



Process: Wet Shipping
Task: Weighing MWCNT
Volume: 7.7 kg
Duration of Sample: 269 min
Exposure Concentration=
0.3 µg/m³

Process: Resin Formulation
Task: Weighing CNF/MWCNT
Volume: 100-200 g
Duration of Sample: 178 min
Exposure Concentration=
7.54 µg/m³

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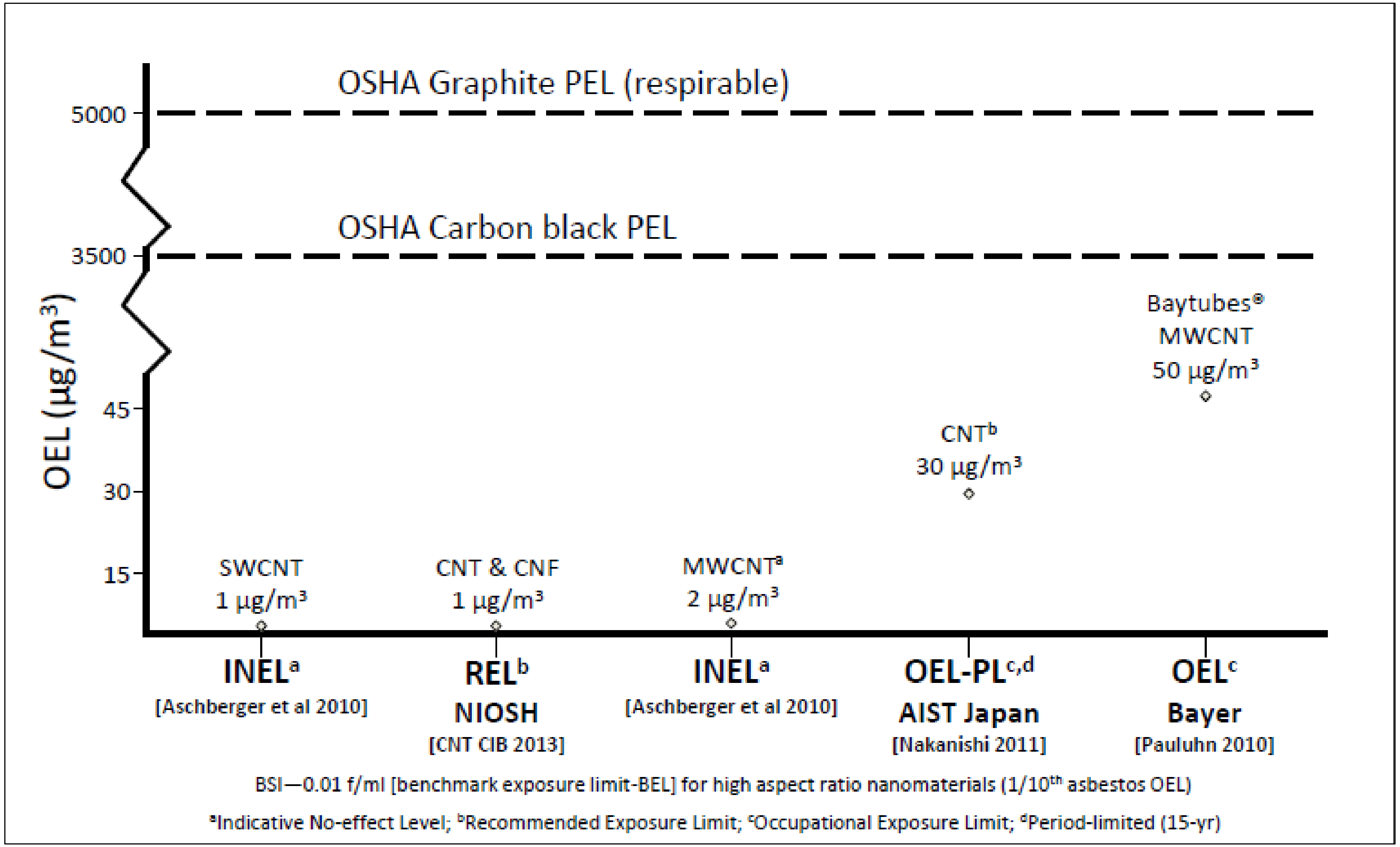
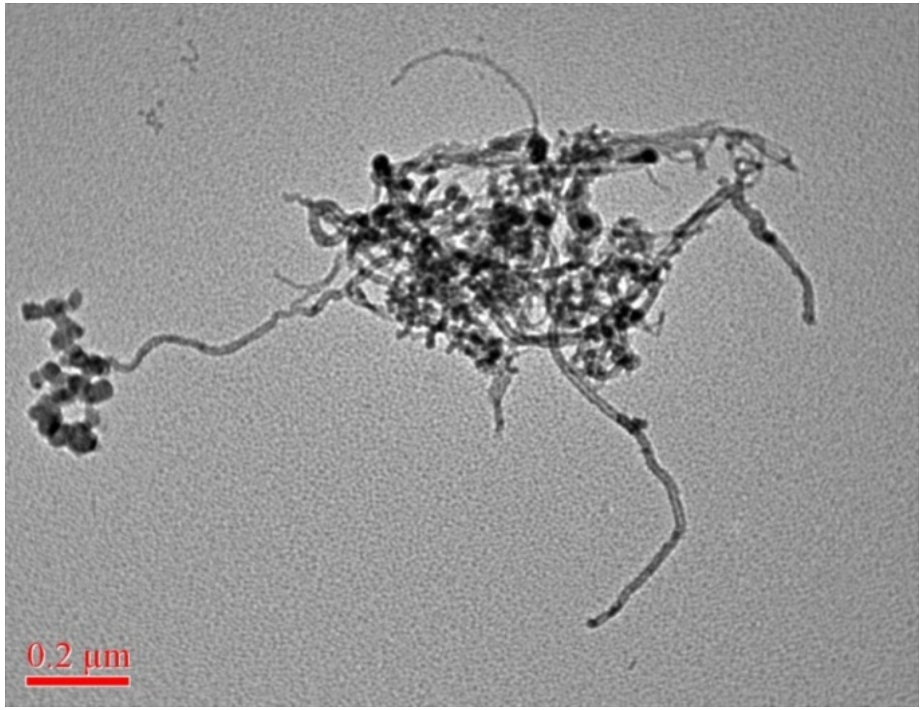
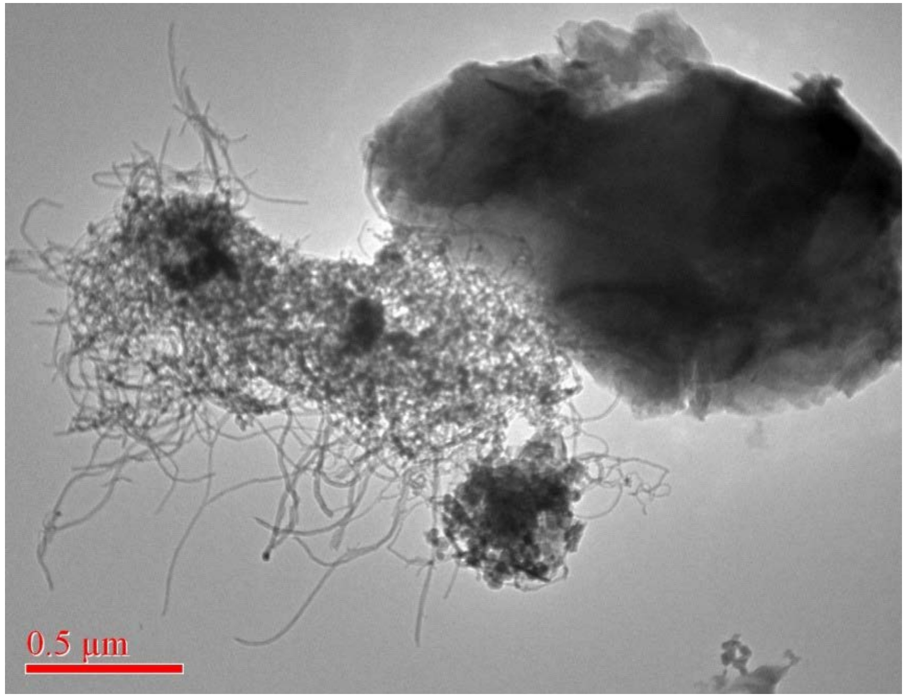
Evidence of Activity: OELs for CNT



Exposure Assessment/Tox Challenges

- Two structures measured as EC. Same hazard?





Images from personal breathing zone samples from CNT manufacturing (Dahm et al. 2012)

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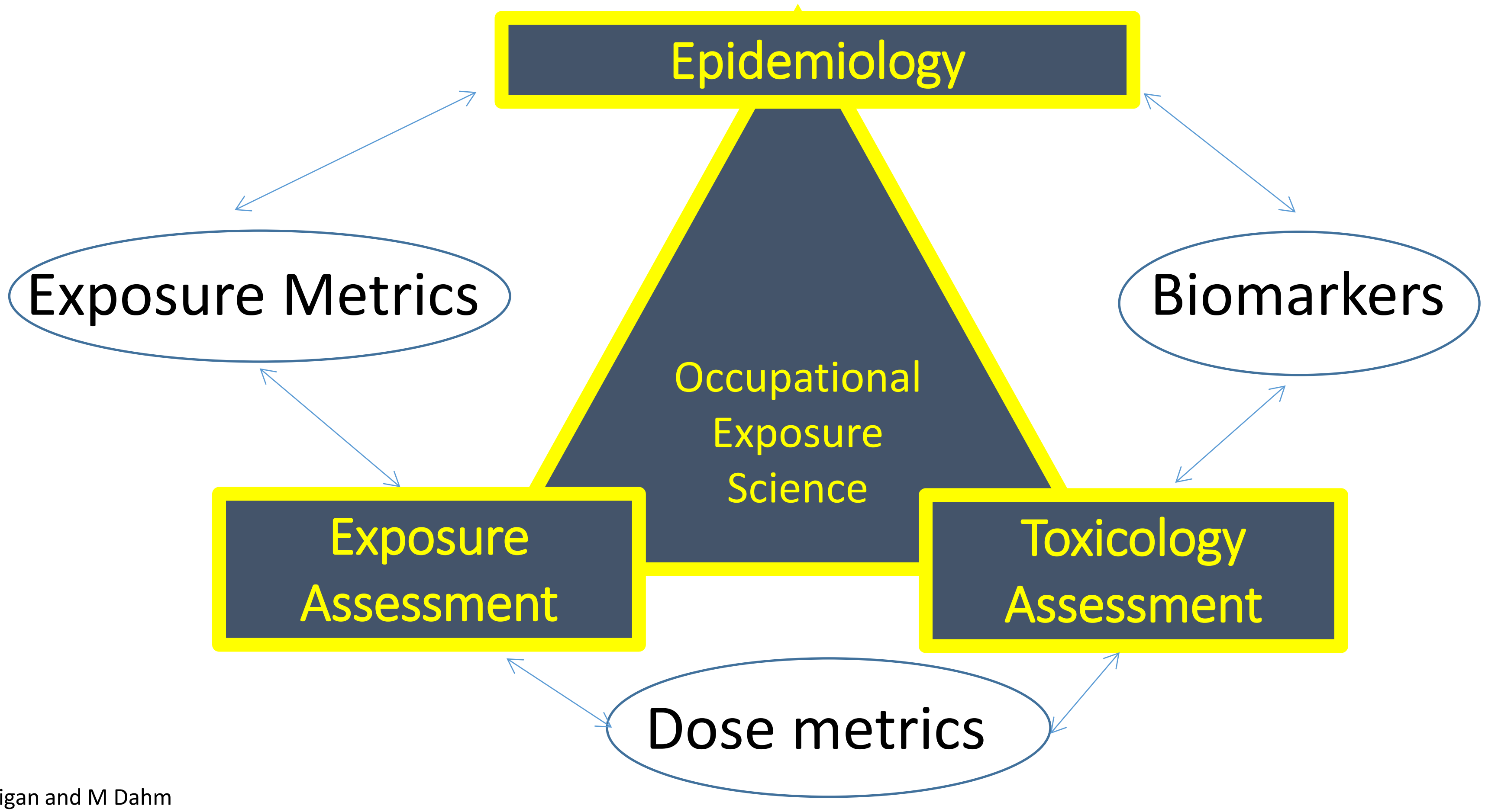
Connecting the Key Exposure Assessment Elements



Courtesy of M Schubauer-Berigan and M Dahm

Key Elements of the NIOSH Approach

Pre-Assessment Prioritization	Field Measurements	Risk Management	Routine Monitoring
Gather Information • Work flows, staffing and tasks • Anticipated and recognized hazards • Nanomaterials used • Safety data sheets • Literature review • Other indicators of potential hazards and exposure situations	• Full-shift and task-based • Integrated filter sampling for elemental mass and microscopy • Direct reading instruments • Evaluation of ventilation and engineering controls • Advanced techniques or developmental methods as needed	• Evaluation of data for exposure-informed hazard assessment • Strategies to mitigate hazard and exposure potential based on results and utilizing the hierarchy of controls • Communications regarding potential occupational risks	• Confirmation of continued risk control • May indicate need for additional measurements or controls

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Exposure Measurements Take a lot of Planning and Effort

Photos courtesy A Eastlake and L Hodson, NIOSH

Exposure Data: Conclusions/Challenges

- New thinking needed
- Exposures do occur in the workplace
- Exposure limits are being developed
- Mass is still the primary metric reported in hazard studies
- Direct-reading approaches have a growing role
- Additional metrics need to be explored: e.g. fiber count for CNT?
- Confirmatory methods are needed
- Controls can be effective

Thank you, and thanks to all of my co-workers!

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

The NIOSH Nanotechnology Research Center

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