

NIOSH - Nanotechnology Research Center

Active in the lab and in the field

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Nanotechnology Research Center

Education and Information Division

National Institute for Occupational Safety and Health

The findings and conclusions in this presentation have not been formally reviewed by the National Institute for Occupational Safety and Health and should not be construed to represent any agency determination or policy.



Nanotechnology

- Illustrates the challenges to society of a new technology
 - Beneficial properties
 - Potential hazard
 - What to do when information is lacking or uncertain

NIOSH

- NIOSH headquarters : Washington, D.C. and Atlanta, GA
- Professionally diverse staff of 1,200 scientists from the fields of epidemiology, medicine, industrial hygiene, safety, psychology, engineering, chemistry, statistics, economics and administration
- Budget: \$316 Million



NIOSH Mission

- Generate new knowledge in the field of occupational safety and health and to transfer that knowledge into practice for the betterment of workers.

This is done by:

- Being a world leader in conducting scientific research, developing guidance and authoritative recommendations, disseminating information, and responding to requests for workplace health hazard evaluations.



NIOSH's Role in Nanotechnology

- Legislative mandate to investigate new hazards
 - Section 20 (a) (4) of the Occupational Safety and Health Act of 1970:
 - ..Conduct special research necessary to explore new problems, including those created by new technology.....and develop new solutions
- Major scientific contributor to National Nanotechnology Initiative (NNI): NSET, NEHI, Signature Initiatives
- Collaborations with other agencies and international community
- One of the first agencies to identify that exposures to engineered nanoparticles could cause health effects in laboratory animals
- Pioneered techniques to generate aerosols of engineered nanoparticles for animal testing
- Demonstrated that certified respirators, engineering controls, and good practices can protect workers



Nanotechnology Research Center

NTRC chartered in 2004

- Vision
 - Safe nanotechnology by providing national and world leadership for research and guidance on the implications and applications of nanotechnology .
- Mission
 - Evaluate potential hazards of new and emerging nanomaterials
 - Develop authoritative recommendations and effective risk management approaches
 - Explore innovative methods for understanding and mitigating risk



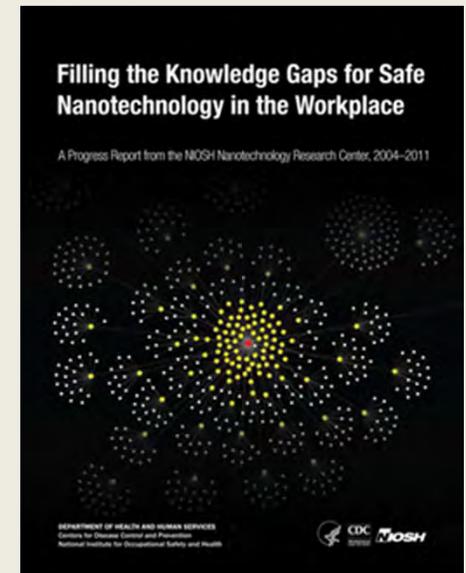
Director's Vision



- General Duty Clause
 - Is the hazard recognized, are injuries linked to the recognized hazard, and is it feasible to eliminate the hazard?
- National Nanotechnology Partnership
 - Encouraging implementation of prudent exposure mitigation measures
 - Promoting nanotechnology risk assessment
 - Collecting and sharing exposure information among nanotechnology workplaces
 - Identifying and studying the use of various candidate occupational risk management practices
 - Developing evidence base to provide protection for workers now and in the future

NTRC Program Overview

- Institute-wide portfolio of 69 projects that are >50% nanotechnology
- Involves over 50 scientists
- Cross-Institute matrix for greatest efficiency
- Published over 400 nanomaterial papers in scientific journals
- Developed public-private partnerships with nanotechnology companies for greatest research impact
- Provides strong guidance to protect the nanotechnology workforce
- Leverages collaborations with other government agencies



NIOSH NTRC Researchers



<http://www.cdc.gov/niosh/topics/nanotech/>



NTRC Program Coordination

Paul Schulte, PhD - Manager

Chuck Geraci, PhD, CIH - Coordinator

Laura Hodson MSPH, CIH – Assistant Coordinator

Ken Martinez, MS, CIH- Field Team Leader

- Strategic planning
- Progress reporting (FY10 had 52 active projects)
- Program council of critical area coordinators
- Regular communication
 - Bi-weekly calls
 - Annual program review
 - Biannual scientific meeting
- Representation to external organizations
- Alignment with NNI NEHI EHS Strategy



Objective: Fill knowledge gaps related to nanotechnology health

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

Approaches to Safe Nanotechnology (DHHS (NIOSH) Publication 2009-125)



NTRC Strategic Plan

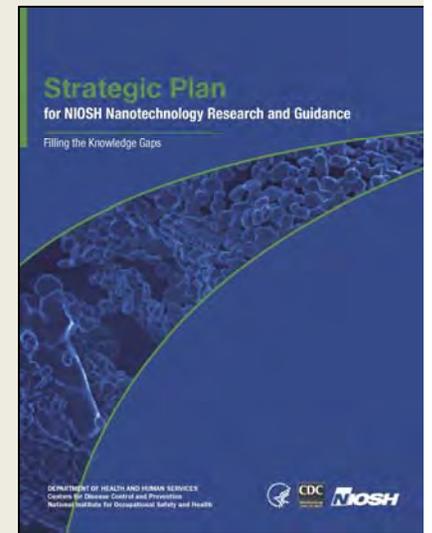
Filling the knowledge gaps

Four overarching goals

Ten critical areas of research

- **Overarching Goals**

- Determine the potential hazards of nanomaterials
- Research possible applications of nanotechnology
- Develop recommendations and interventions
- Enhance global nanomaterial health and safety



10 Critical Areas of Research

- Toxicology
- Measurements
- Exposure Assessment
- Risk Assessment
- Controls & PPE
- Safety
- Recommendations & Guidance
- Communication & Information
- Epidemiology & Surveillance
- Applications



Linked to NNI EHS Priority Research Needs

Hazard Identification

Is there reason to believe this could be harmful?

NTRC Toxicology Research

- Studying carbon black, fullerenes, single-walled carbon nanotubes (SWCNT), multi-walled carbon nanotubes (MWCNT), carbon nanofibers, TiO₂ spheres and wires, silicon nanowires, silver, nickel, quantum dots, ZnO, WC-Co, cerium oxide, etc.
- Evaluating
 - Exposure routes: pulmonary and dermal
 - Biological endpoints: pulmonary, cardiovascular, CNS and dermal
- Determining the relationship between given physicochemical properties of a nanoparticle and its bioactivity
- Developing in vitro screening tests for rapid prediction of the bioactivity of a given nanoparticle

Nanotoxicology Key Findings

- Pulmonary exposure to SWCNT
 - Transient pulmonary inflammation, rapid and persistent granulomas, progressive interstitial fibrosis
 - Oxidant stress in aortic and coronary tissue
 - Increased susceptibility to pulmonary infection
 - Increased atherosclerosis
- Pulmonary exposure to TiO₂ nanoparticles (short term exposure)
 - Transient pulmonary inflammation
 - Nanowires are more potent than nanospheres
 - TiO₂ nanowires induce inflammatory signals in certain areas of the brain
 - TiO₂ nanospheres cause dysfunction of systemic and coronary microvessels (failure to dilate properly)

Nanotoxicology Key Findings (cont)

- Pulmonary exposure to MWCNT (short term exposure with evaluation 0-3 months post-exposure)
 - Transient pulmonary inflammation, rapid and persistent granulomas, rapid and progressive interstitial fibrosis
 - Induction of inflammatory and damage markers in certain areas of the brain
 - MWCNT have been shown to pierce the outer surface of the lung and enter the intrapleural space
 - Pulmonary exposure to MWCNT decreases the ability of coronary arterioles to respond to dilators

Nanotoxicology Key Findings (cont)

- *In vitro* exposure of bronchial epithelial cells to SWCNT or MWCNT disrupts normal mitosis and results in aneuploidy (cells with an incorrect number of chromosomes)
- *In vitro* exposure of bronchial epithelial cells to low doses of SWCNT or MWCNT for 28 weeks causes transformation of cells
- Injection of these transformed cells into the abdomen of a mouse results in tumor formation
- Topical application of raw SWCNT (containing contaminating metal catalysts) to mice results in dermal inflammation

Key Toxicology Updates: Following Pharyngeal Aspiration

- Quantitative microscopy: fibrotic potency of SWCNT greater than MWCNT on a mass basis
- SWCNT more fibrotic than CNF, which was similar to asbestos
- COOH-functionalized MWCNT less fibrotic than non-functionalized MWCNT

Exposure Assessment

Will there be exposure in real-world conditions?

NIOSH Performs On-Site Research

- First (and so far only) U.S. government agency to conduct on-site research
- Evaluate worker exposures, and develop and deploy safe practices and controls
- Focused efforts: carbon nanotubes and nanofibers and new nanomaterials
- State-of-the-art instruments and methods focusing on exposure
- Key partnerships with the private sector
- Employers receive guidance and summary results published in peer reviewed journals
- Over 40 visits to 36 individual sites since mid-2006



Workplace Exposure Assessments

- NTRC field research team (NFRT)
 - Responsible for initial exposure assessments
- Activities
 - Evaluates the entire material flow of a process and identifies points of potential material emission that can result in worker exposure
 - Uses an array of instruments and conventional air sampling methods to characterize exposures
 - Evaluates engineering controls and their effectiveness in reducing emissions and exposures.
 - Evaluates work practices used during the production or use of nanomaterials
 - Evaluates the use of Personal Protective Equipment in use, if any, including respiratory protection
- One of the most successful programs in the NTRC
- Key partnerships with the private sector
- Summary results published

NFRT Site Selection

Exposure Assessment

- Pre-2010
 - Laboratories
 - Pilot facilities
 - Focus on detecting *emissions*
 - Types of nanomaterials: TiO₂, CNT, CNF, Ag, Fe, Ni, Quantum Dots, Graphene
- Post-2010
 - Scale-up: near-production to production
 - Re-visits
 - Focus on *exposure* assessment and characterization
 - Types of nanomaterials: TiO₂, CNT, CNF, Ag, Fe, Ni, quantum dots, and graphene
 - Extension of life cycle to composites, laminates, and applications

NFRT Site Selection

Exposure Assessment

Sector		Food							
Sector		Electronics							
Sector		Medicine							
Sector		Energy							
Sector		Materials							
Work Places	Nanomaterial Type								
	CNT/CNF	Metal Oxides	Dendrimers	Other					
Lab Research									
Start up/Pilot									
Manufacturing									
Production									
Disposal									



Industry-Wide Studies (NIOSH/DSHEFS)

Exposure Assessment

- Phase I (Completed)
 - Feasibility of industrywide studies on engineered carbonaceous nanomaterials (ECN)
- Phase II (Current)
 - Exposure Assessment of carbon nanotubes (CNT) & carbon nanofibers (CNF)
- Phase III (Future)
 - Epidemiologic and Biomarker Studies

IWSB Phase I

Exposure Assessment

Objectives:

- Estimate US workforce and quantify production
- Estimate use of engineering & administrative exposure controls
- Use information to determine feasibility of industry-wide ECN studies

Accomplishments:

- Compiled information on 61 eligible (beyond R&D-scale) companies (with about 600 workers) & interviewed 30 who agreed to be surveyed
- Most feasible ECN population for study is CNT & CNF manufacture, use and distribution workforce (~500 workers)

IWSB Phase II

Exposure Assessment

Objectives:

- Characterize full-shift and task-specific exposures in a representative sample of U.S. CNT and CNF manufacturers
 - Consider several types of workforces
 - Primary manufacturers
 - Secondary manufacturers (users)
 - Redistributors
 - Emphasizing filter-based measurements (NMAM 5040 for elemental carbon and NMAM 7402 for electron microscopy)
- Collect exposure information that may be used in an future epidemiologic study

IWSB Phase II

Exposure Assessment

Accomplishments: Conducted site visits at 11 facilities from 2010-present

- Primary Manufacturers
 - 3 facilities produced mainly MWCNTs
 - 1 focused solely on SWCNTs

Secondary Manufacturers

- Semi Conductor research (n=2)
 - CNTs in solution for spray coating (100 g)
 - CNT based inks used in screen printing
- Dispersion of CNTs and CNFs into Resins and Polymers (n=5)
 - High heat mixing, extrusion
 - Composite Materials

IWSB Phase III

Exposure Assessment

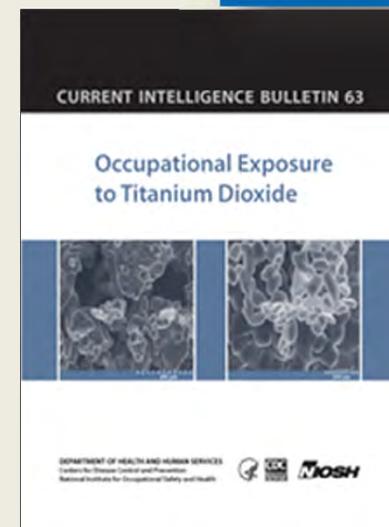
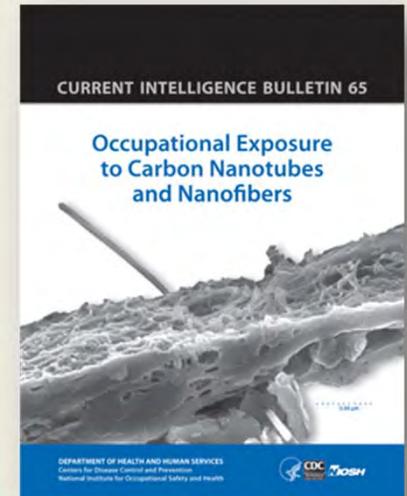
- Developing cross-sectional study protocol
 - Biomarkers of early health effects related to best exposure metric
 - Enrollment of companies/employees
 - Baseline physical
 - Non-invasive biological sample collection
 - Collection of information on other influential factors
- Considering a prospective records-based cohort study
 - Main outcomes of interest: pulmonary fibrosis, cardiovascular disease, cancer
 - Small current workforce may require international pooled

Risk Characterization

Is substance hazardous and will there be exposure?

Conduct Risk Assessment for High Volume Nanomaterials

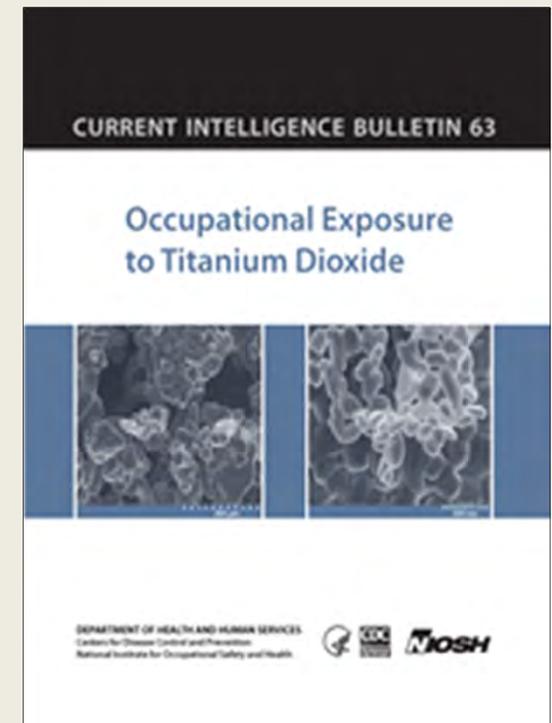
- Gather and analyze hazard data for authoritative recommendations
- Developed nanoparticle lung models
- Risk assessments on two key nanomaterials:
 - *TiO₂ and Carbon Nanotubes/fibers*
- Coordinated development of Current Intelligence Bulletins
- Developed Recommended Exposure Limits: first issuance by a government agency



NIOSH Current Intelligence Bulletin

Titanium Dioxide

- Hazard assessment
- NIOSH proposed REL:
 - 2.4 mg/m³ for fine TiO₂
 - 0.3 mg/m³ for Ultrafine (Nano) TiO₂
- Exposure assessment recommendations
- Control technologies
- Research needs

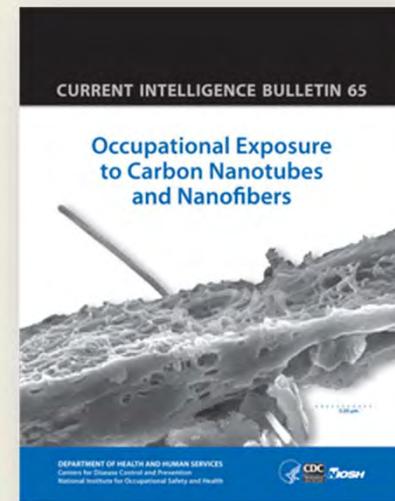


www.cdc.gov/niosh/docs/2011-160/pdfs/2011-160.pdf

NIOSH Current Intelligence Bulletin

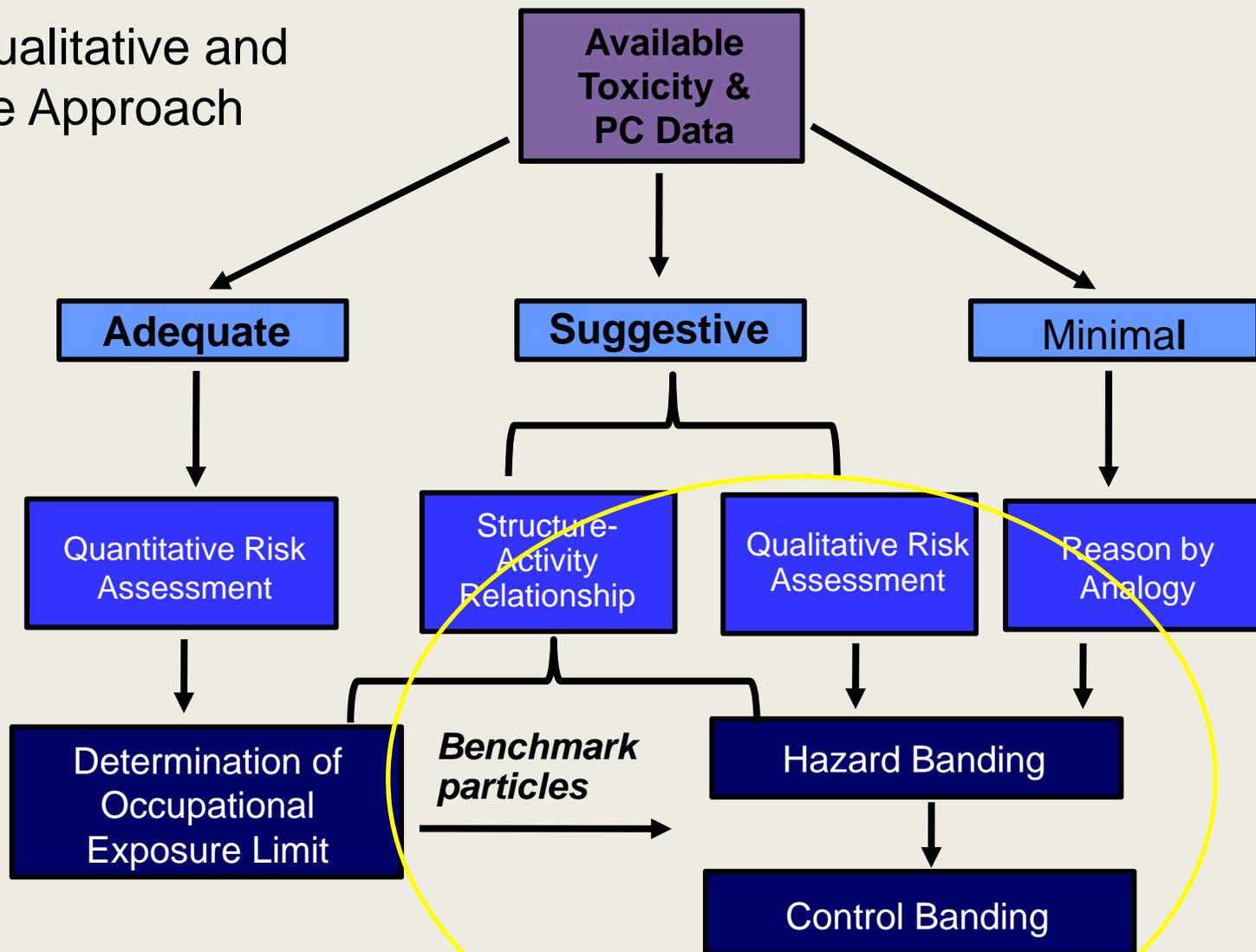
Carbon Nanotubes and Nanofibers

- Summarize the hazards
- Dose-response risk assessment
NIOSH proposed REL:
 - 1 $\mu\text{g}/\text{m}^3$ for CNT and CNF
- Exposure assessment guidance
- Evaluation of controls
- Research needs



<http://www.cdc.gov/niosh/docket/review/docket161A/>

Possible Qualitative and Quantitative Approach



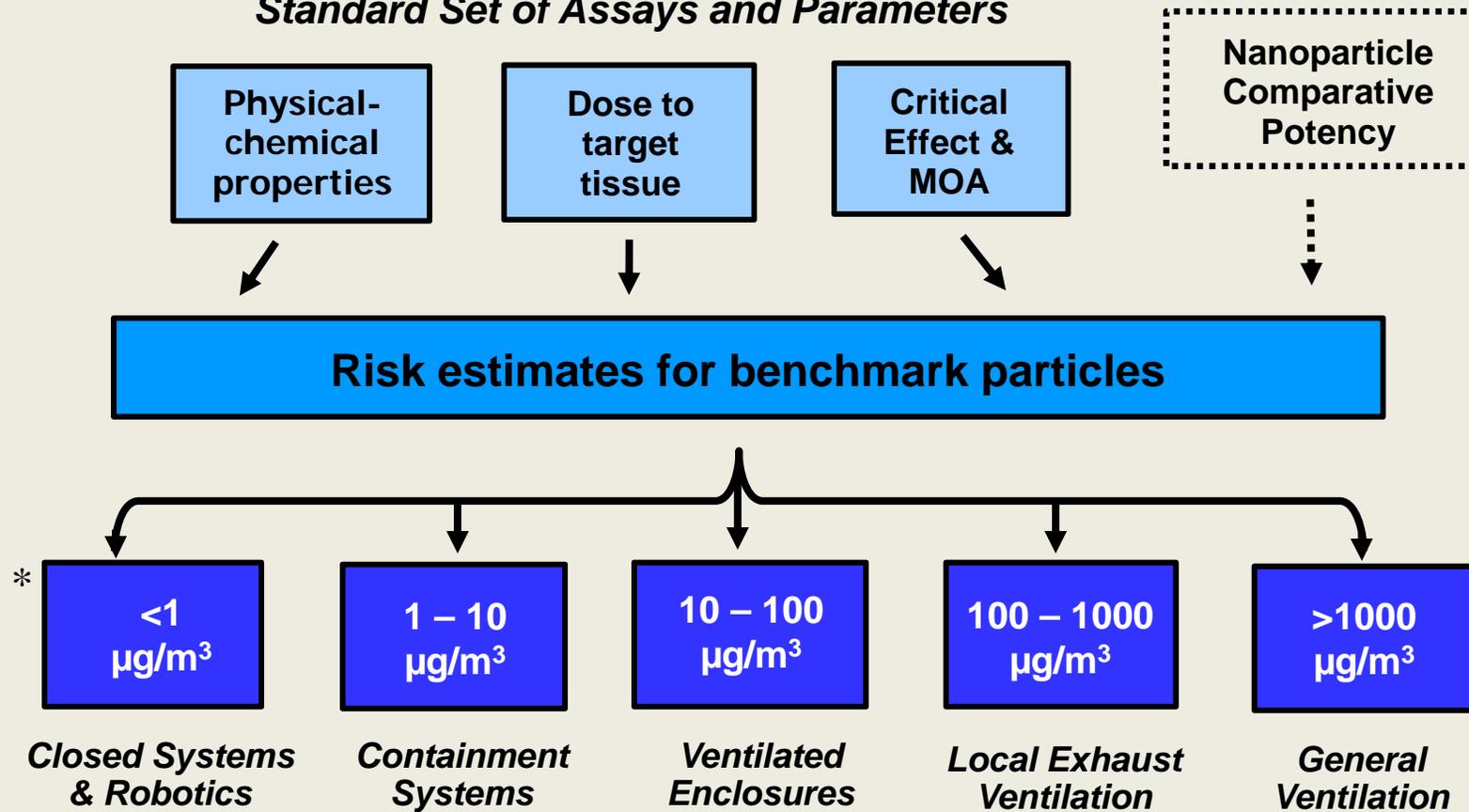
[Adapted from Schulte et al. 2010, J Nanopart Res]

PC: physical-chemical



Implementing Risk Assessment into Hazard and Exposure Control Banding

Standard Set of Assays and Parameters



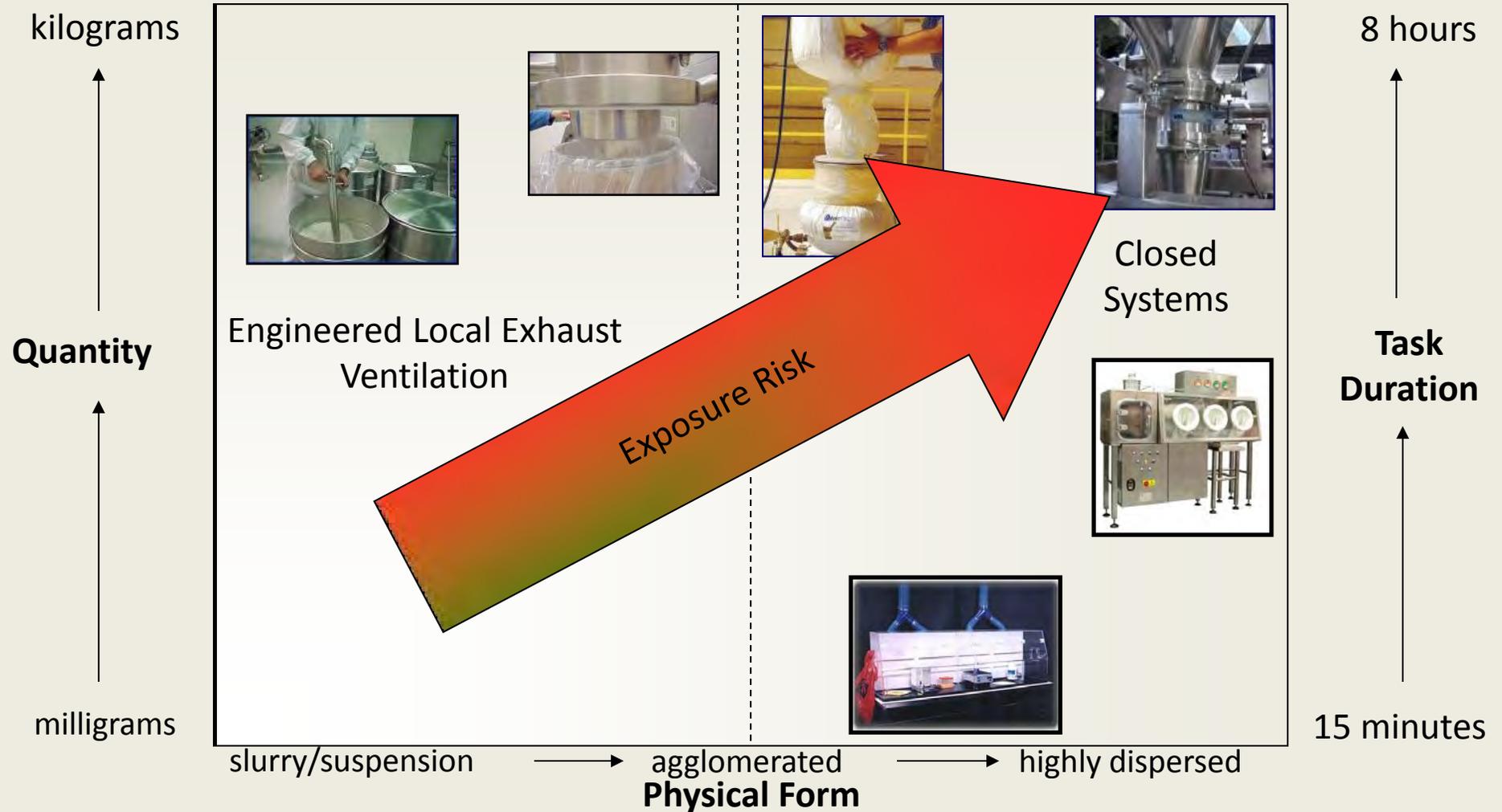
* Exposure control bins & systems based on: Naumann et al. 1996; Ader et al. 2005; Zaik & Nelson 2008; 8-hr TWA concentrations

Utility of Risk-Based Categorical Approach

- Provide tool to develop initial exposure control bands (and re-assess as new data available).
- Develop minimum data standards for harmonization across studies.
- Develop data base with standard parameters for pooled data analyses.
- Provide framework for testing and refining hypotheses.
- Provide systematic evaluation for designing safer materials.

Match Qualitative Risk Assessment with Actual Experience

1 ← Benchmark Classes → 4

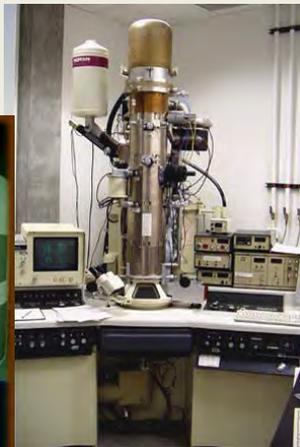


Special thanks to Donna Heidel, NIOSH



Risk Management

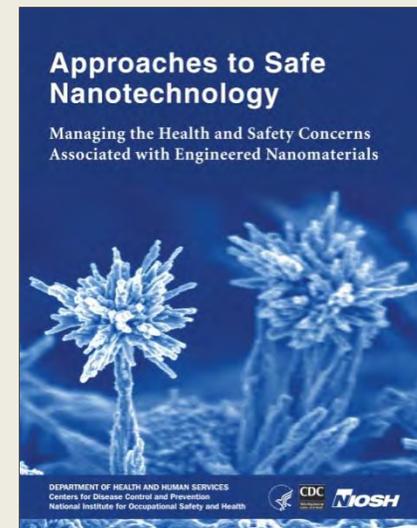
Develop procedures to minimize exposures



NIOSH Basic Risk Management Guidance

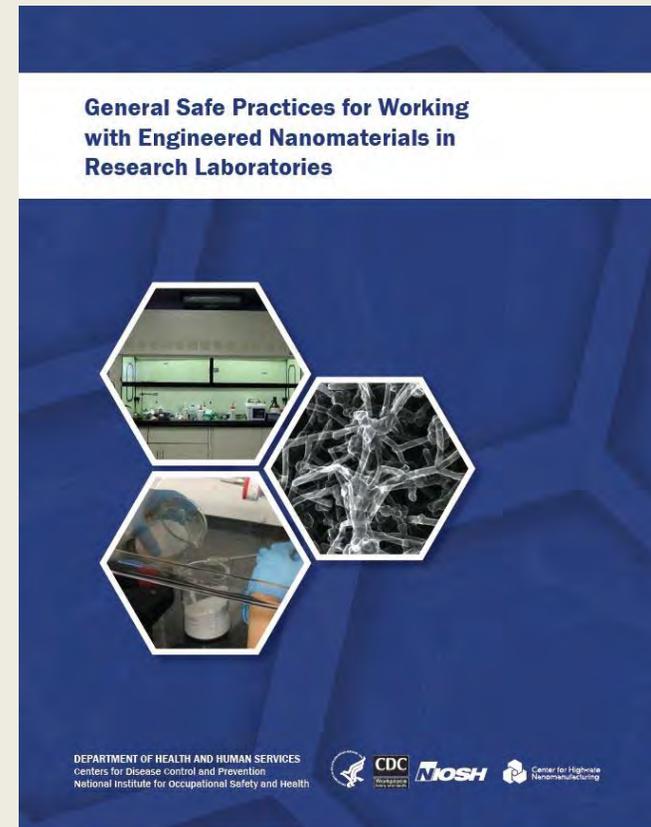
- One of first and most widely recognized guidance products
- First issued in October 2005, updated twice
- Compilation of NIOSH results
- Cited globally
- Basis for national programs

www.cdc.gov/niosh/topics/nanotech



Basic Guidance for Handling Nanomaterials in Research Laboratories

- Published May 2012
- Provides laboratory specific information on the following:
 - Risk management
 - Hazard Identification
 - Exposure Assessment
 - Exposure controls
 - Elimination/Substitution
 - Isolation/Engineering Controls
 - Administrative controls
 - Personal protective equipment
 - Local Exhaust Ventilation



Basics of nanomaterial laboratory safety

How does the potential for exposure risk change with each of the following product forms?

Solid

Liquid

Dry powder

Basics of nanomaterial laboratory safety

- How is it best to handle nanomaterials in the laboratory?
 - Keep them in a solid or liquid state if possible
 - Keep them in unbreakable closed containers when stored or transferred between workstations
 - Use appropriate engineering controls (i.e. fume hood, glovebox, or local exhaust ventilation)
 - Do not generate nanoparticle aerosols on open benchtops. Use appropriate exhaust and/or containment systems.
 - Work tasks involving the use of nanomaterials should always use the minimum quantity required for the process.



Basics of nanomaterial laboratory safety

- Follow all posted laboratory requirements regarding required personal protective equipment
- Obtain training prior to working with nanomaterials and follow instructions
- Do not eat or drink in the laboratory
- Follow good housekeeping procedures. Clean all potentially contaminated working surfaces when visibly contaminated and/or at least once a day.
 - Use wet wiping or a HEPA vacuum on dry materials
- Wash hands before eating, smoking, or leaving the worksite
- Keep laboratory doors closed and limit access



NIOSH has drafted a document titled *“Current Strategies for Engineering Controls in Nanomaterial Production and Downstream Handling Processes”*

- **Objective:** To provide guidance regarding approaches and strategies to protect workers by using available engineering controls for engineered nanomaterials in the workplace.
- **Topics**
 - Summary of exposure control strategies
 - Overview of engineering controls for nanotechnology processes
 - Evaluation of control effectiveness
- Based on best available current knowledge of how workers may be exposed and provide guidance on exposure control and evaluation
- Intended to be used as a reference by plant managers and owners who are responsible for making decisions regarding capital allocations, as well as health and safety professionals, engineers, and industrial hygienists who are specifically charged with protecting worker health

Common Processes and Control Approaches

- **Identifies common production and downstream tasks associated with worker exposure, including:**
 - Leakage from reactors and powder processing equipment
 - Manually harvesting product from reactors
 - Transporting/transferring of intermediate products to the next process
 - Dumping powders into processing equipment
 - Weighing out powder/packaging material for shipment
 - Changing filters on dust collection systems and vacuum cleaners
 - Machining of products containing nanomaterials (e.g., cutting, grinding, drilling)
- **Provides potential for control approaches for each of these tasks and presents relevant research on control effectiveness**
- **Discusses approaches for evaluating control effectiveness**
 - The assessment of control effectiveness is essential for verifying that the exposure goals of the facility have been successfully met
- **Provides list of sources of information on risk management and engineering control design guidance**

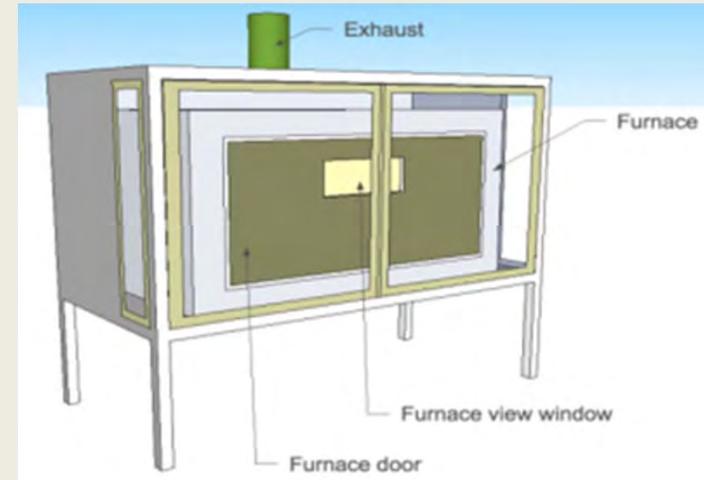
Material Handling—Ventilated Enclosures



- **Dry powder handling** is a high exposure activity
- New Nano enclosure adopted from pharmaceutical industry may provide good exposure control option
 - Typically employ lower air velocities (70-80 fpm) to reduce turbulence/loss of product
 - Often include airflow indicators, HEPA/ULPA filtration, bag in/bag out filter removal systems

Reactor Operations—Fugitive Emissions

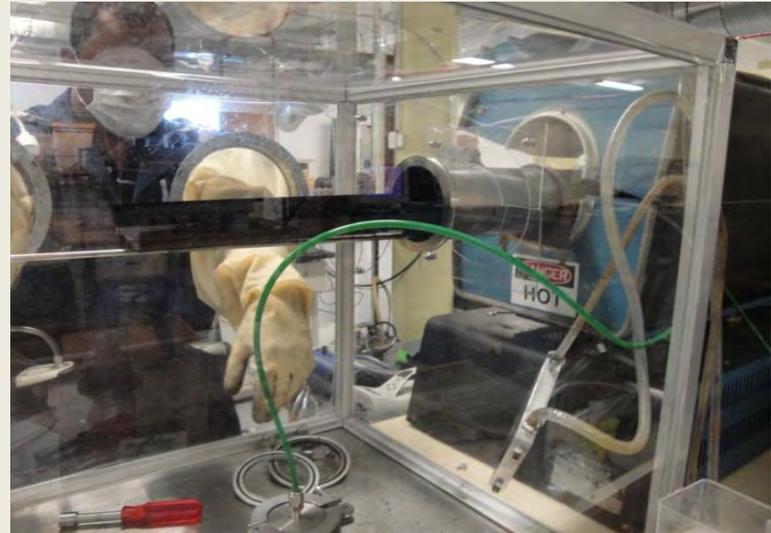
- Fugitive emissions from reactors have been identified as a source of exposure to nanoparticles in the workplace
- Company used a ventilated enclosure to contain reactor particle emissions/leaks
 - These enclosures are commercially available from a variety of manufacturers but are custom designed for each application
- Design of these enclosures needs to consider:
 - Reactor access
 - Process control visibility and operations
 - Reactor heat generation and control



Reactor Harvesting and Cleaning

- **Reactor harvesting** is commonly done by brushing or scraping product off of catalyst
- The use of gloveboxes or other enclosures have shown good containment of materials during this procedure
- **Reactor cleaning** is a standard process which has been shown to lead to worker exposure
- Company purchased a commercially available fume extractor and fabricated a custom LEV flange
- Particle concentrations were reduced by an average of 88-96%

(Methner, M. JOEH. 2008; 5: 6, D63-D69)



Product Offloading and Packaging

- **Continuous liner** — works by providing a continuous flexible barrier between the product and operator
- Worker pulls down bag and seals the bottom using a tie-off or heat seal
- Container is filled to desired weight
- Two seals are applied to the top of the liner between drum top and filling head



- **Inflatable Seal**— seal is pneumatically inflated when powder product is being offloaded and deflates when transfer is completed

Prevention through Design

- **Pre-manufacturing Hazard Review**
 - Preliminary Hazard Review is a good first start and entry to safety systems engineering approaches.
 - Identification of potential hazards and proper design
 - Hazard control may be less costly at this point (retrofitting isolation valves to process equipment).
- **Need to move towards inherent safety approaches**
 - Design out hazard at the source
 - Use closed material transfer systems
 - Modify process (e.g. place CNTs into solution)
 - Simplify equipment/processes
 - Redundant, independent controls to avoid common causes of failure.



Fumbling for his recline button, Ted unwittingly instigates a disaster

PtD for Nanotechnology

- Apply Prevention through Design principles to nanotechnology
 - Facilities, processes, tasks, tools
 - Nanomaterial design: design for safety
- Focused workshop
 - Aug 2012, CNSE, Albany
 - Action paper reports in progress
- Working with three nanomaterial companies
 - Expansion plans
 - Start up



Hierarchy of Controls

- Engineers are vital to minimizing occupational risks through the application of the hierarchy of controls
- The engineering design process provides the framework for the application of prevention through design



Business Value

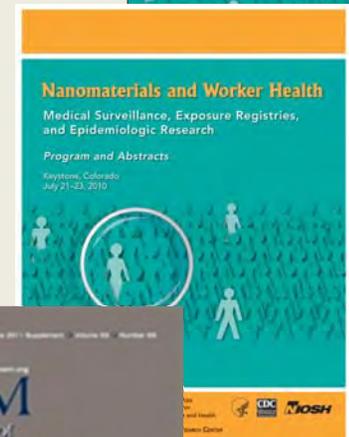
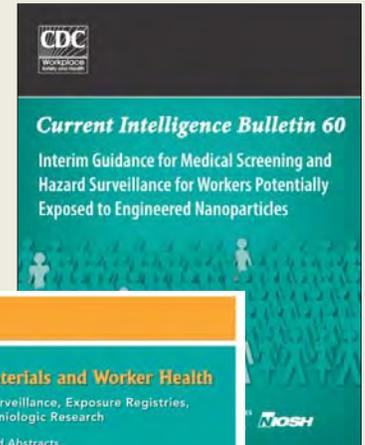
- The AIHA Value Strategy* demonstrated the most significant business contributions result from...
 - Anticipating worker exposures and designing process improvements to reduce or eliminate these exposures
 - Aligning health and safety interventions with business goals
 - Integrating health and safety risk management requirements into the design process
 - Facilities, equipment, tools, processes, products and work flows
- ...resulting in significant contributions to business profitability

**www.ihvalue.org*

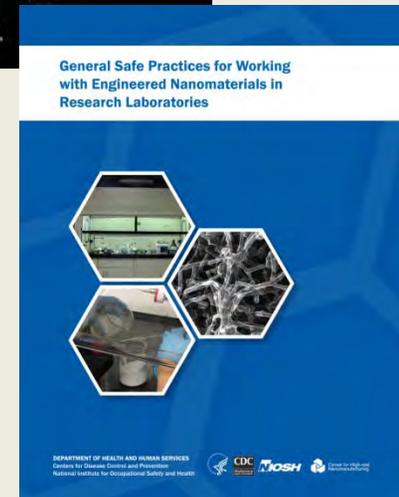
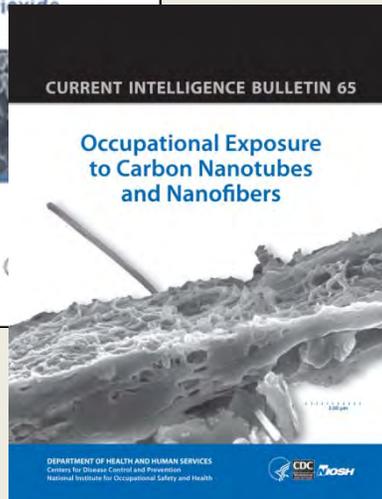
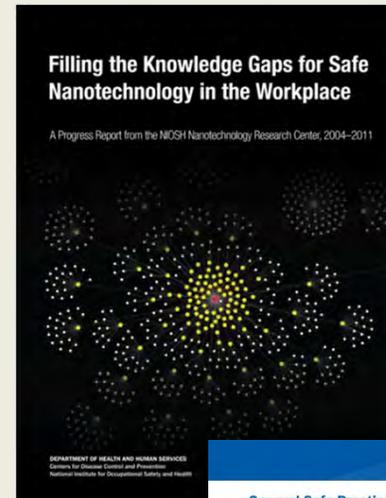
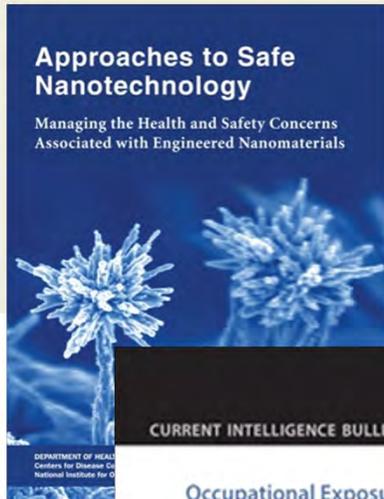
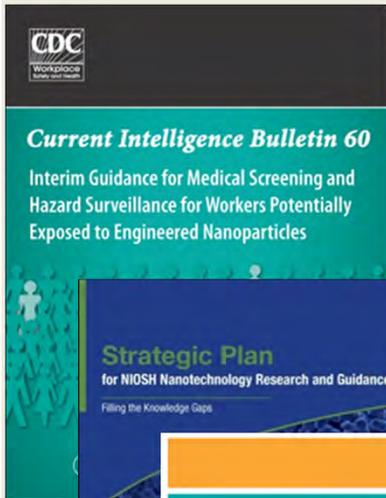


Epidemiology and Surveillance

- Coordinated development of Interim Guidance for Medical Screening and Hazard Surveillance
- Organized a workshop on the topic
- Special Issue of JOEM: June 2011



Key Communication Products



National and International Collaborations

US Government

- Represent NIOSH to the NNI: NSET and NEHI (J. Howard Co-chairs)
- Relationships with NTP, CPSC, OSHA, EPA, DoD
- Signature Initiative: Sustainable Nanomanufacturing

State Programs

- California
- Massachusetts

Memoranda of Understanding and Strong Partnerships

- College of Nanoscale Science and Engineering (CNSE)
- Center for High-Rate Nanomanufacturing (CHN)
- Center for Multifunctional Polymer Nanomaterials and Devices
- Rice U/ICON

International Consensus Bodies

- ISO TC 229
- OECD WPMNM



Future Work

- Verify controls
- Demonstrate risk mitigation practices
- Better market research to identify exposed workers
- Life cycle studies of 1st generation materials
- Evaluate next generation materials
- Evaluate emerging materials: e.g. Cellulose nanocrystals, graphene,
- Integrate key program areas: PtD, Control Banding

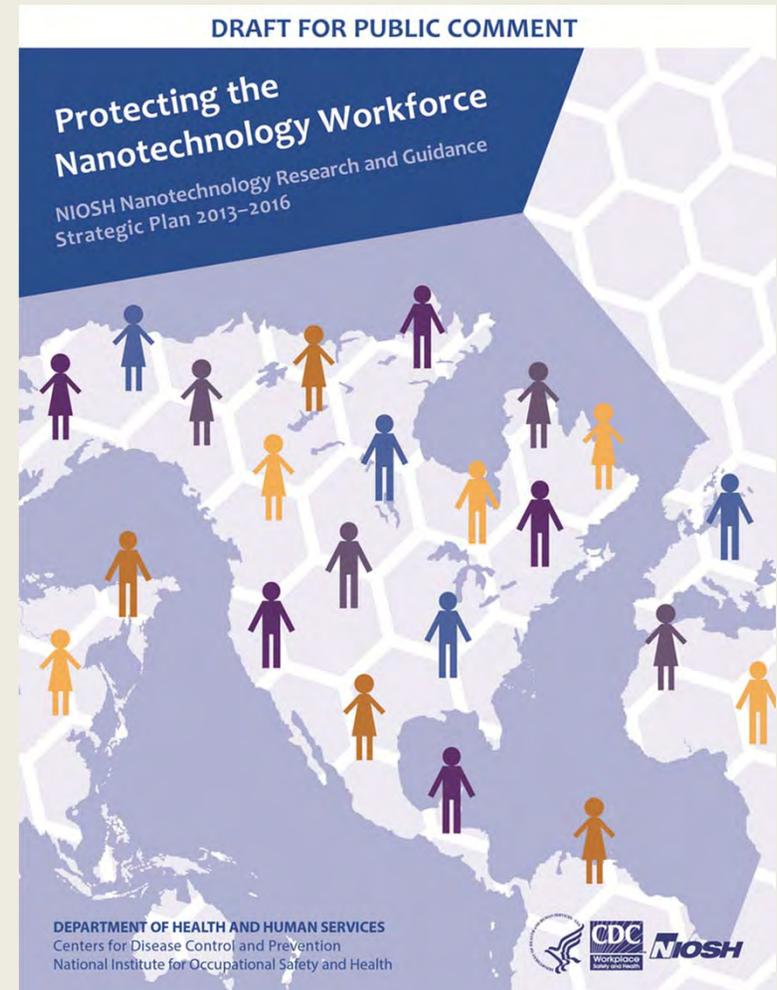
Proposed Goals for 2013- 2016

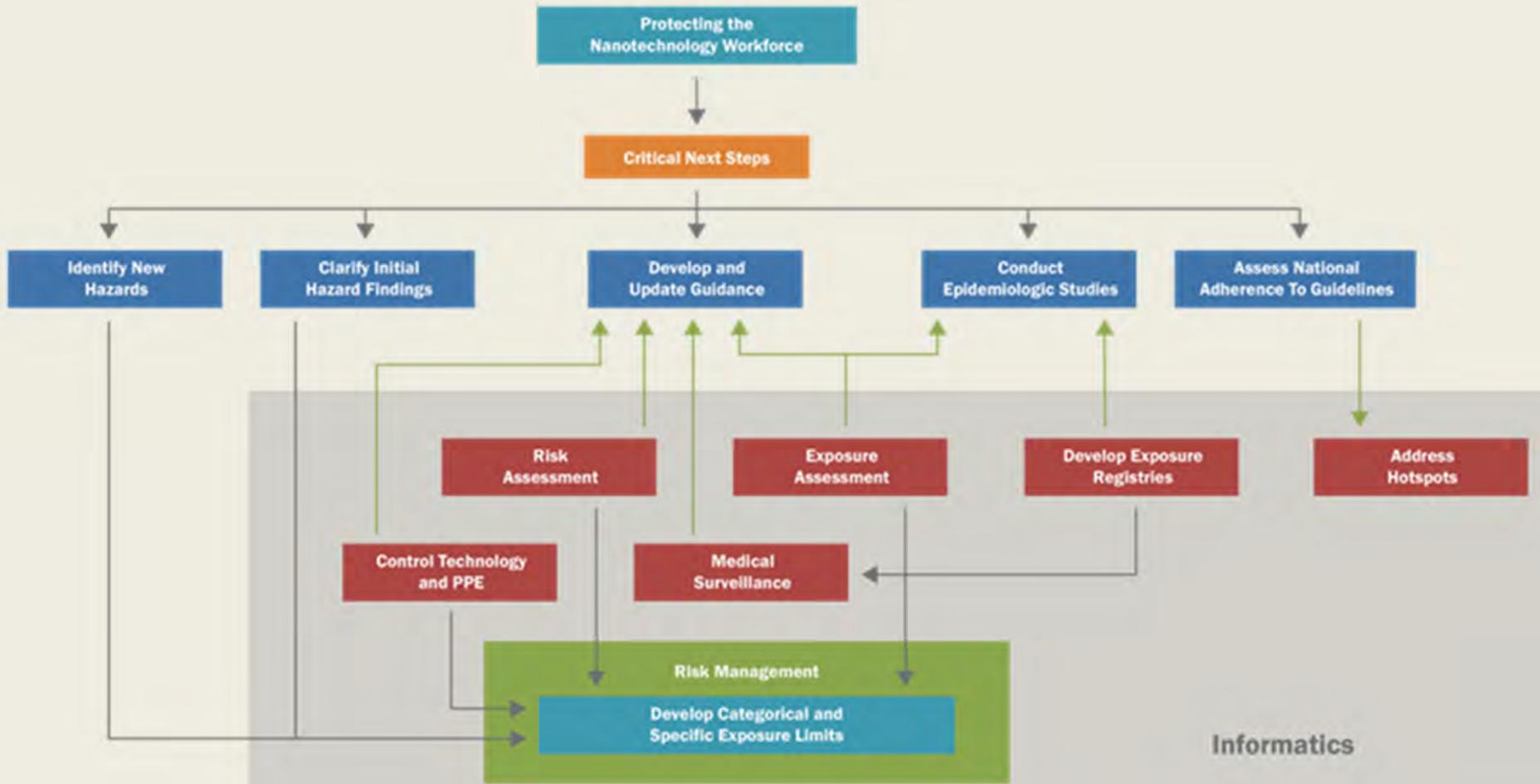
1. Increase understanding of new hazards and related health risks to nanomaterial workers
2. Expand the initial hazard findings
3. Support the creation of guidance materials to inform nanomaterial workers, employers, health professionals, regulatory agencies, and decision makers about hazards, risks, and risk management approaches.
4. Support epidemiologic studies for nanomaterial workers including medical and exposure studies
5. Assess and promote national adherence with risk management guidance.



10 Critical Research Areas

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





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

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Guidance & Publications

10 Critical Topic Areas

Frequently Asked Questions

Partnerships & Collaborations

News & Events

Other Resources

Hazards & Exposures

Diseases & Injuries

Safety & Prevention

Chemicals

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NANOTECHNOLOGY

Overview

Nanotechnology is the manipulation of matter on a near-atomic scale to produce new structures, materials and devices. This technology promises scientific advancement for many sectors such as medicine, consumer products, energy, materials and manufacturing. Nanotechnology is somewhat loosely defined, although in general terms it covers engineered structures, devices, and systems that have a length scale between 1 and 100 nanometers. At this size, materials begin to exhibit unique properties that affect physical, chemical, and biological behavior. Researching, developing, and utilizing these properties is at the heart of new technology.

As with any new technology, the earliest and most extensive exposure to hazards is most likely to occur in the workplace. Workers within nanotechnology-related industries have the



Spotlights

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800-CDC-INFO (800-455-4647)



NIOSH

Thank you!

kmartinez@cdc.gov

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