NIOSH Nanotechnology Program

Vladimir Murashov, PhD
National Institute for Occupational Safety and Health

NIOSH

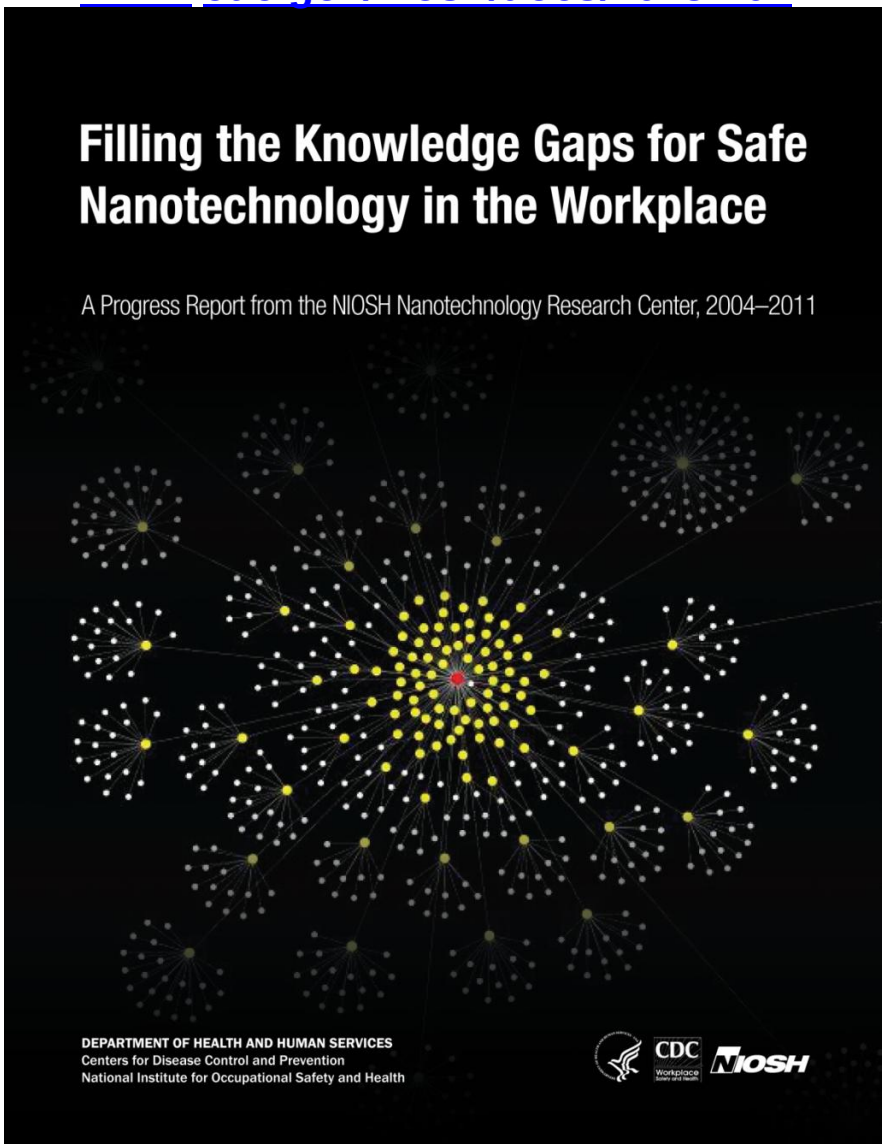
- Lead federal agency for research and guidance on occupational safety and health
- Mandated in the Occupational Safety and Health Act of 1970 to:
  - Produce criteria identifying toxic substances
  - Explore new problems … created by new technology
  - Provide criteria so that no employee will suffer diminished health, functional capacity or life expectancy as a result of work experience
- NIOSH Nanotechnology Research Center (NTRC) established in 2004

Four Overarching Goals

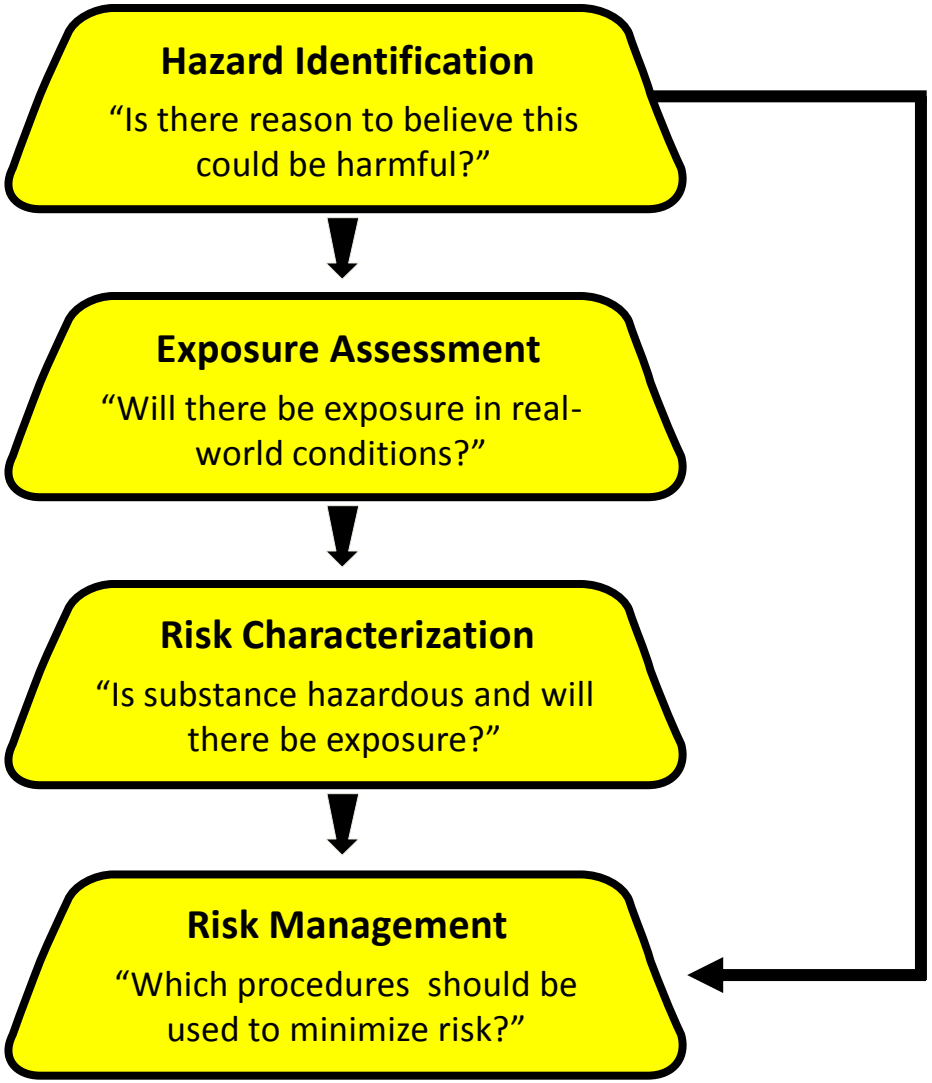
- Determine if nanomaterials pose a risk for workers
- Conduct research to prevent work-related injuries and illnesses
- Promote healthy workplaces
- Enhance global workplace safety

NIOSH Nanotechnology Progress Report

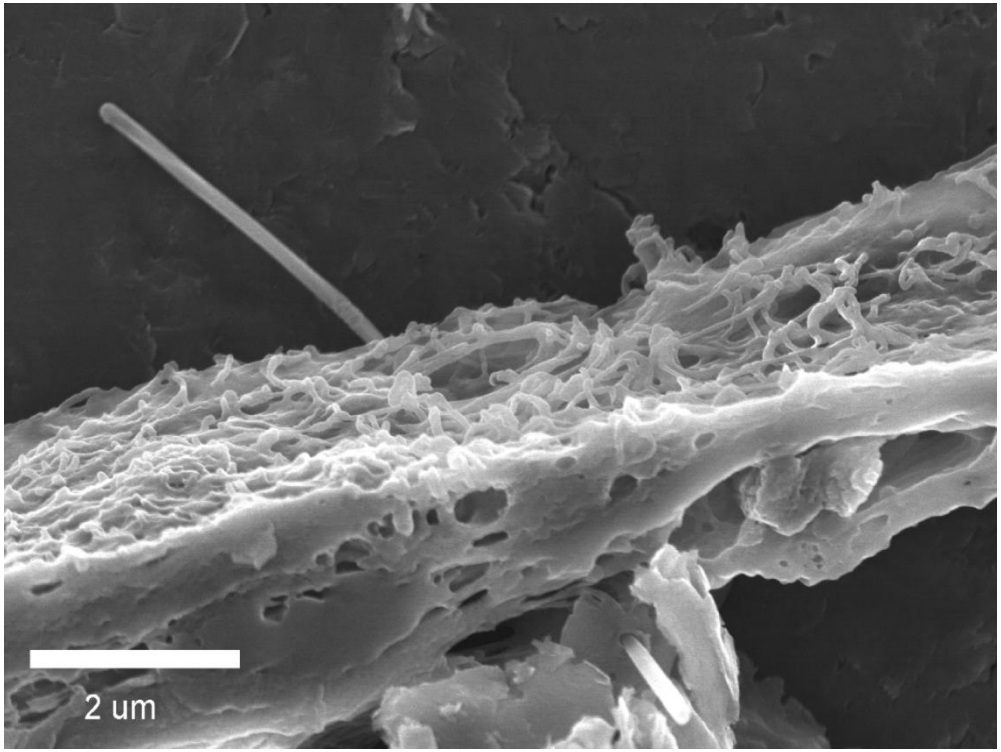
www. cdc.gov/niosh/docs/2013-101



Key Elements in Worker Protection



Hazard identification

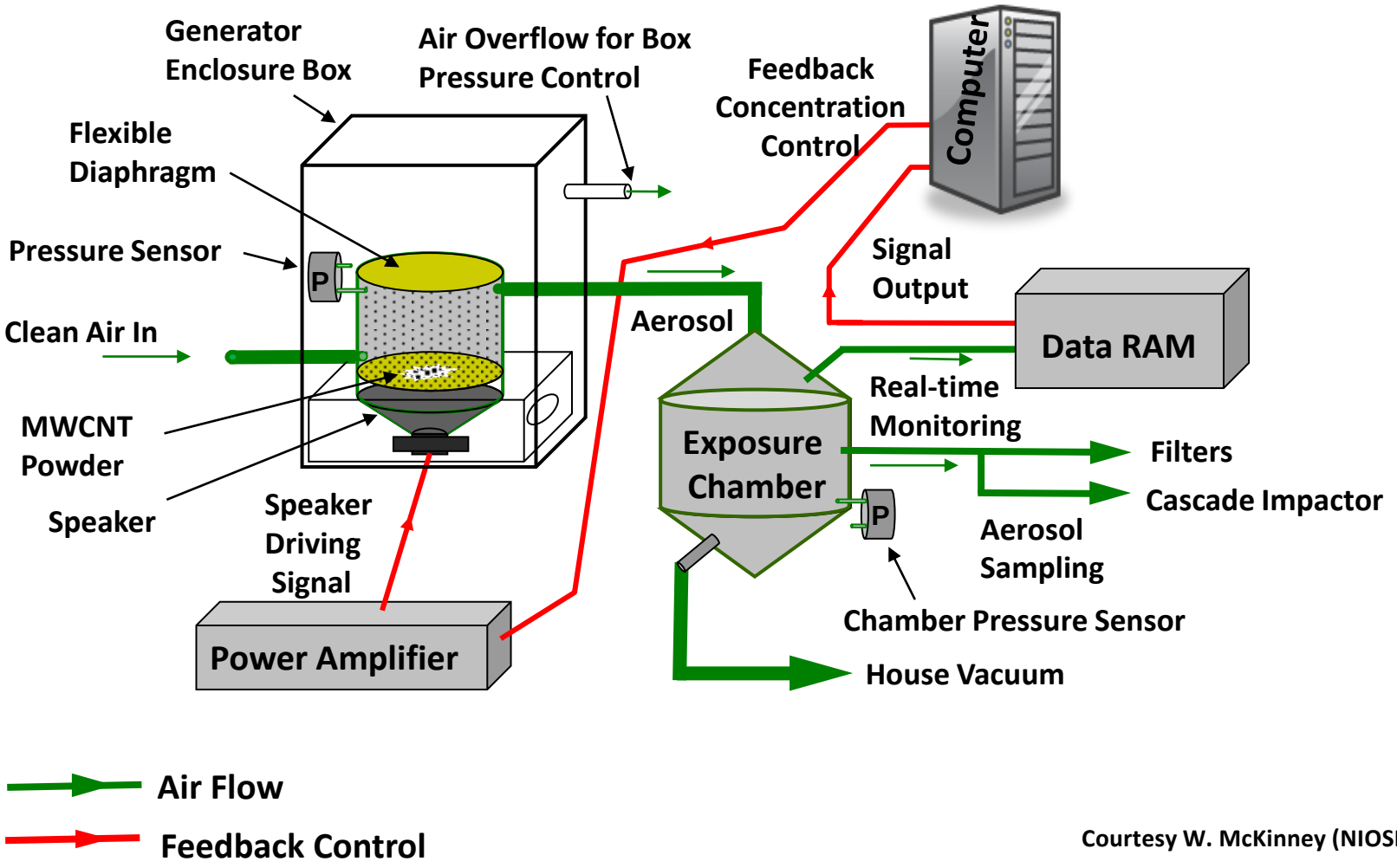


Courtesy R. Mercer (NIOSH)

Major outputs

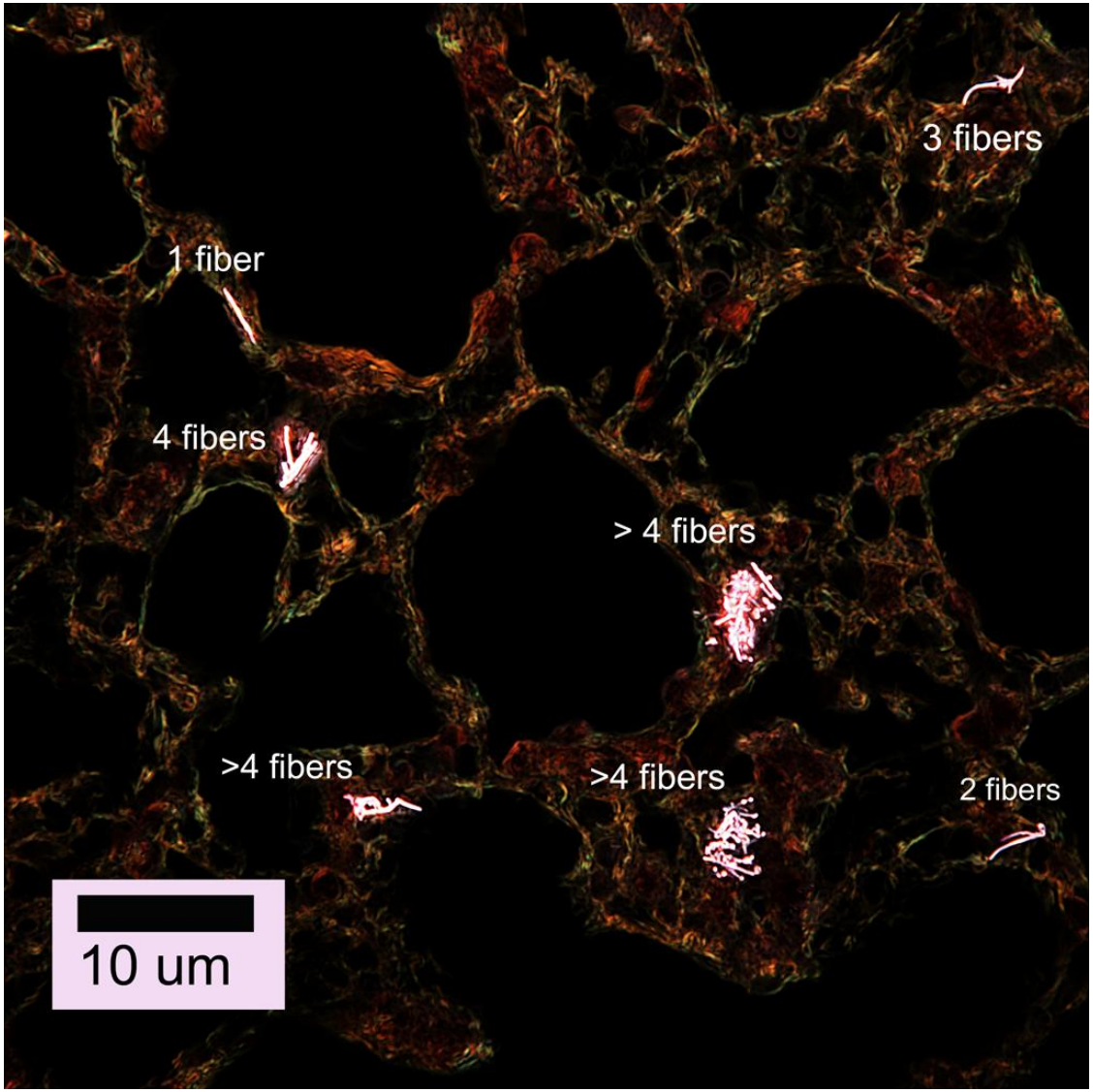
- Identified pulmonary and cardiovascular hazards of selected nanofibers in animals
  - SWCNT causes rapid and persistent fibrosis and cardiovascular dysfunction in mice
  - COOH-functionalized MWCNT less fibrotic than non-functionalized MWCNT
  - MWCNT can reach the intrapleural space in mice (site of mesothelioma for asbestos)
  - MWCNT and TiO_2 nanowires can induce inflammatory mediators in certain regions of the brain in mice
- Determined that nanoscale TiO_2 or carbon black is more inflammogenic than microscale TiO_2 or carbon black on a mass-dose basis
- Developed a system to generate nanoparticle aerosols for inhalation toxicologic studies

Diagram of accoustical generator and exposure system



Courtesy W. McKinney (NIOSH)

Magnified image of lung tissue



Courtesy B. Mercer (NIOSH)

Exposure assessment

Courtesy B. Mercer (NIOSH)

Exposure Assessment

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

Major outputs

- Conducted over 40 field assessments in nanomaterial manufacturer and user facilities
  - Exposures do occur in the workplace
  - Mass is still the primary metric for exposure, but additional metrics need to be explored (fiber count?)
  - Direct-reading approaches have a place
  - Confirmatory methods are needed
  - Controls can be effective
- Published a framework for conducting workplace emission testing (Nanoparticle Emission Assessment Technique)
- Developed innovative sampling methods for engineered nanomaterials

Sampling strategy

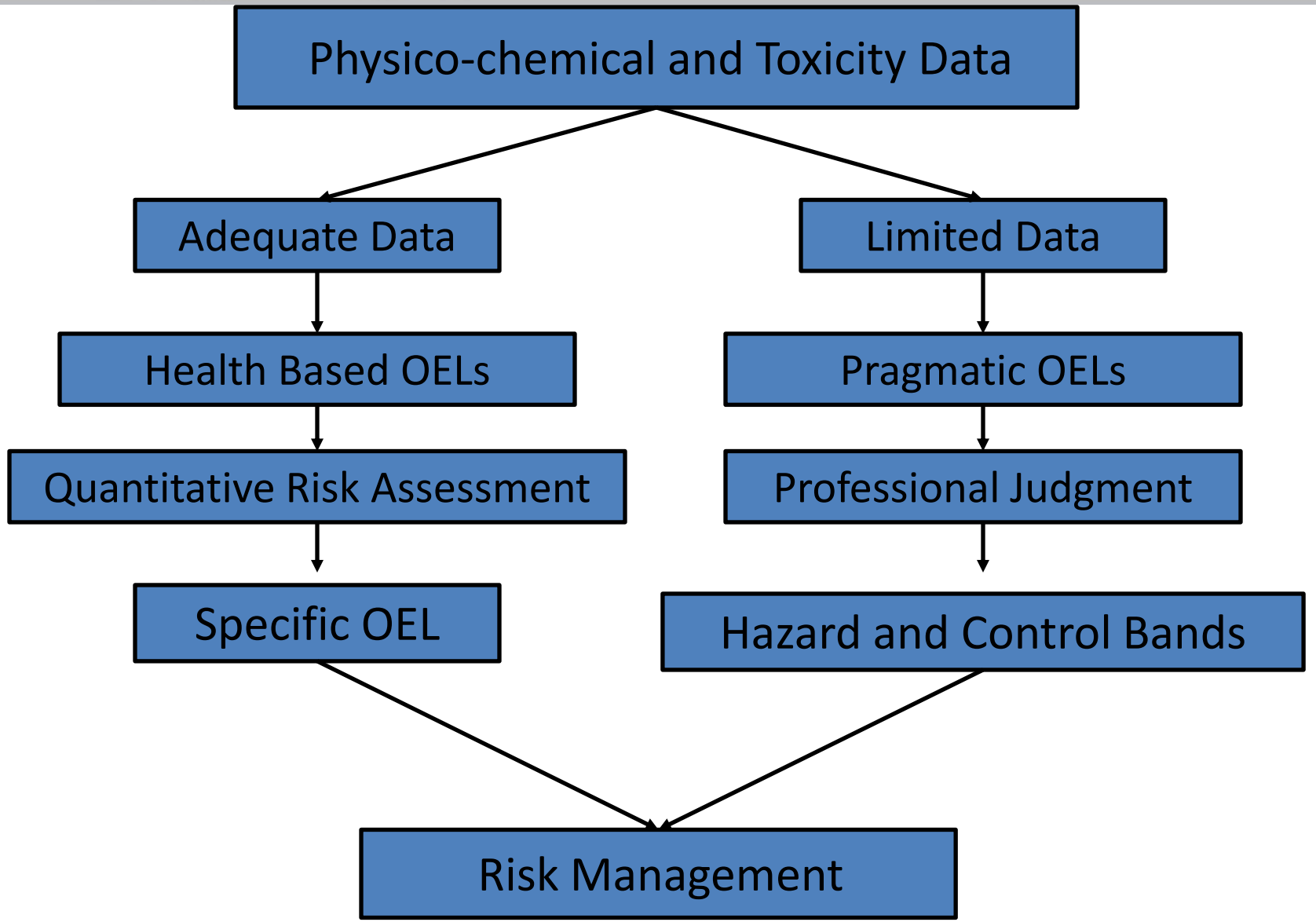
- Integrated samples
  - Core component of exposure assessment
  - Filter-cassette based
    - Elements
    - Electron Microscopy
  - Area and personal breathing zone
  - Full-shift and task-based

Courtesy D. Evans (NIOSH)

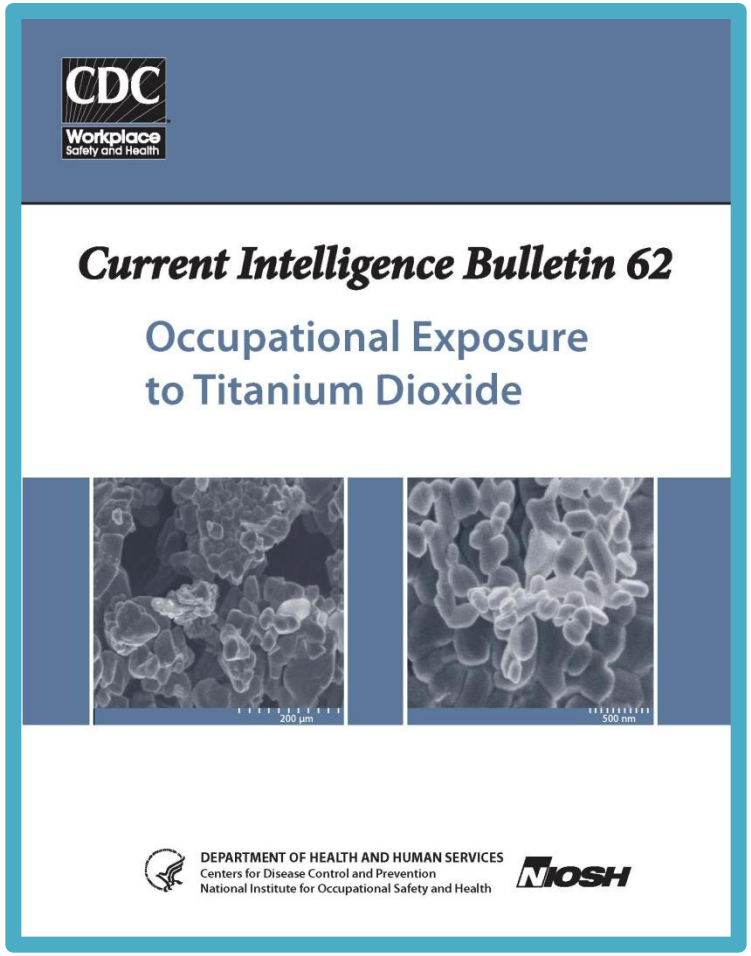
Risk characterization

Courtesy L. Turkevich (NIOSH)

Risk management

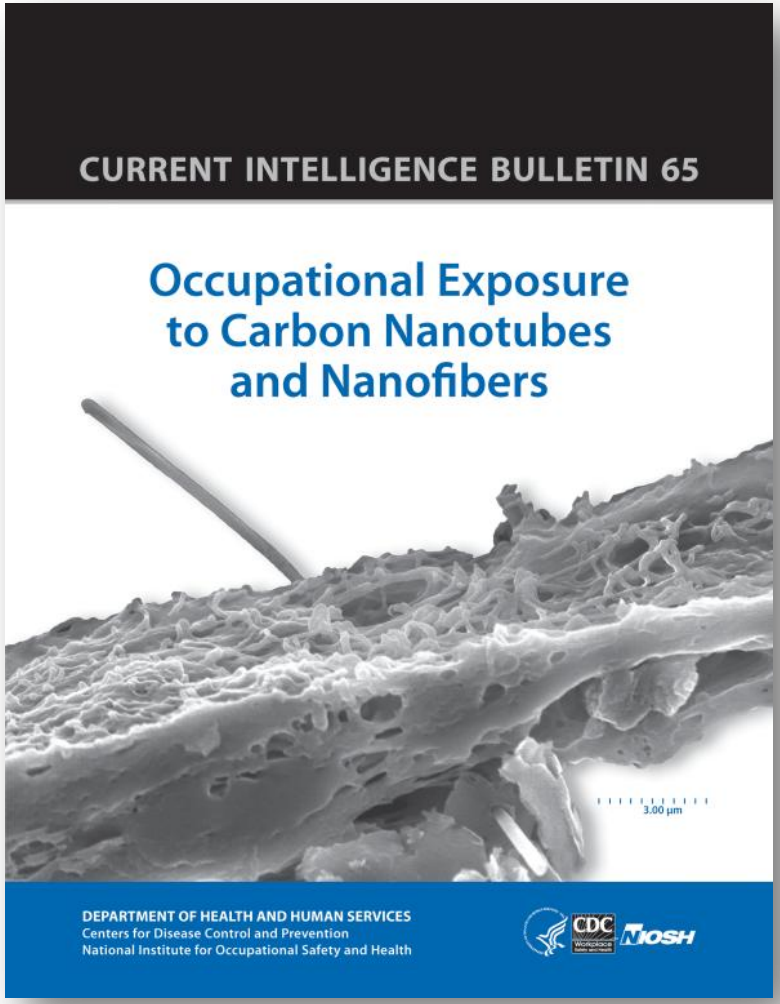


Intelligence bulletin 62



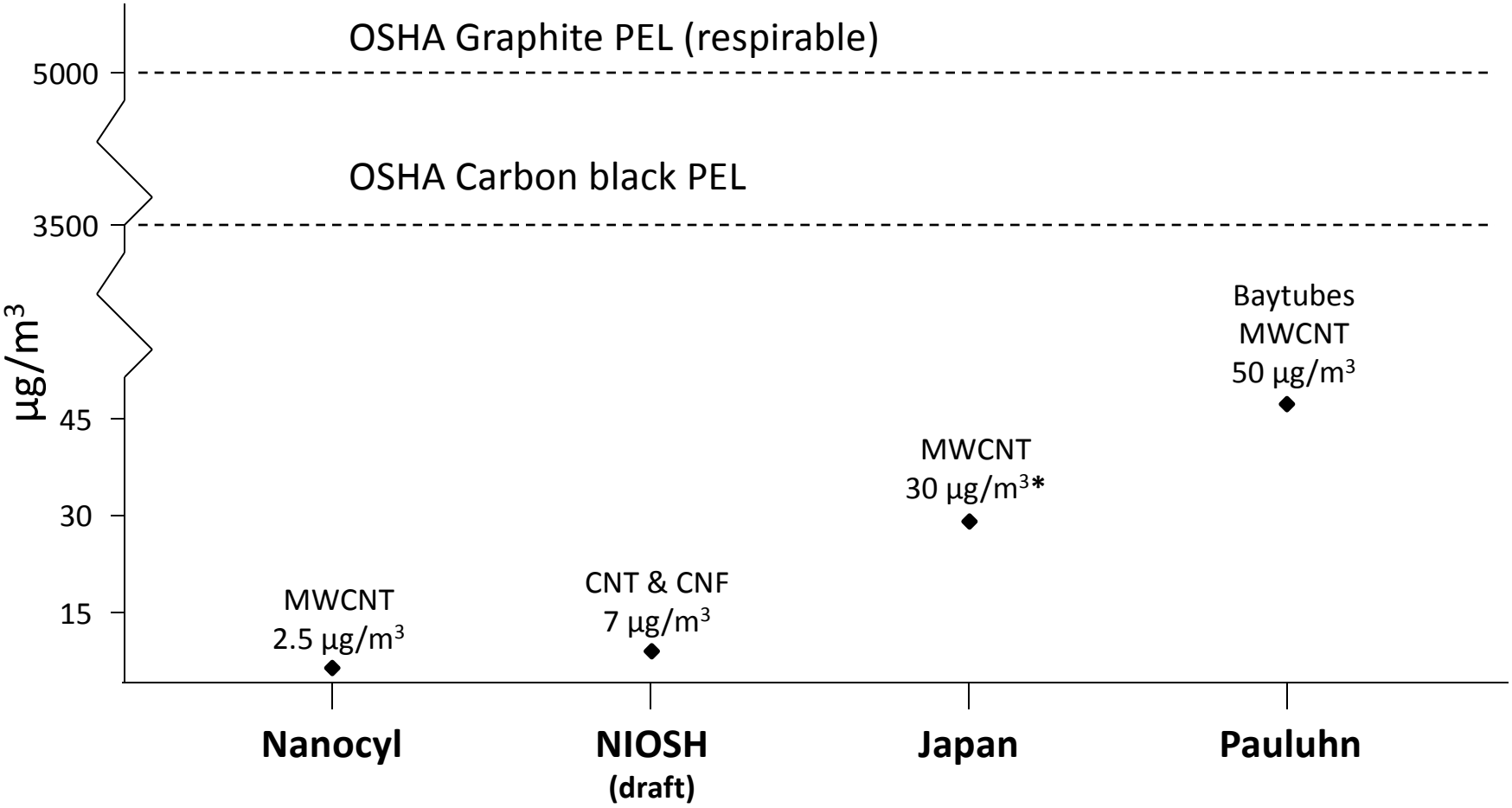
- Published in April, 2011
- Separate recommended exposure limits (RELs) by particle size:
  - Ultrafine TiO_2: 0.3 mg/m^3
  - Fine TiO_2: 2.4 mg/m^3
- Ultrafine TiO_2 classified as potential occupational carcinogen based on rat lung tumor data and secondary genotoxic mode of action.
- www.cdc.gov/niosh/docs/2011-160/

Current Intelligence Bulletin 65



- **Public review draft (Nov 2010)**
- Worker health concerns based on rodent data of early onset & persistent pulmonary fibrosis, as well as genotoxic effects and migration of CNT to the pleura.
- REL proposed at the LOQ for the NIOSH analytical method to measure elemental carbon: 7 µg/m^3 (as 8-hr time-weighed average concentration, respirable fraction)
- http://www.cdc.gov/niosh/docket/review/docket161A/

OELs for Carbon Nanotubes



BSI—0.01 f/ml [benchmark exposure limit-BEL] high aspect ratio nanomaterials –established at 1/10 asbestos OEL

*Period-limited (15-yr)

Risk management

Nanomaterial risk management should be part of overall health and safety program

Overall Company Health and Safety Program

- Management Leadership
  - Policies
  - Standards
- Employee Participation
- Planning
- Implementation
  - Risk Management
  - Training
  - Communication
  - Safe Practices
- Evaluation
- Corrective Actions
- Compliance Plan

Nanomaterial Risk Management Program

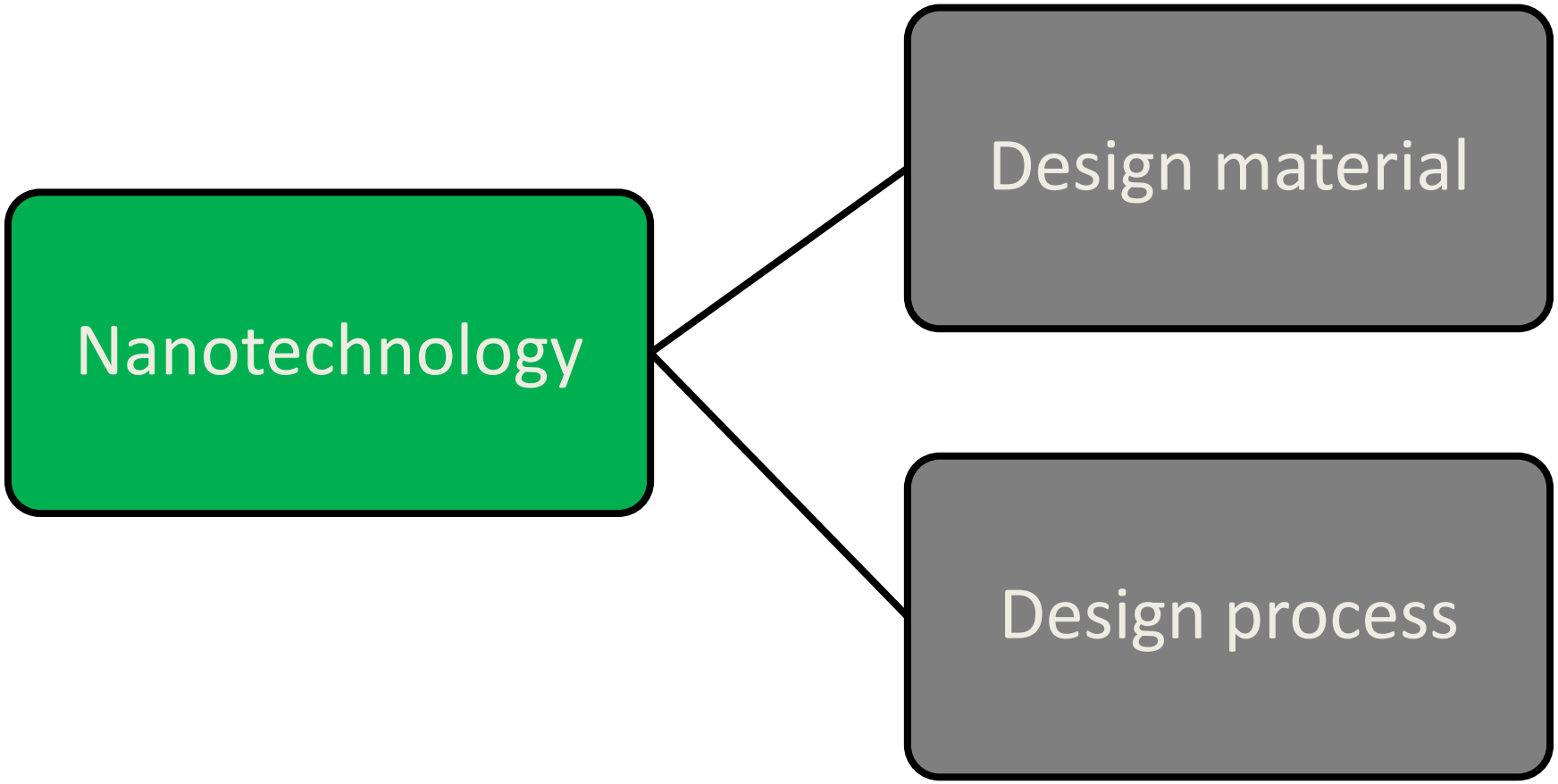
- Hazard Determination
- Process Review
- Exposure Evaluation
- Risk Characterization
- Controls

Hierarchy of Controls

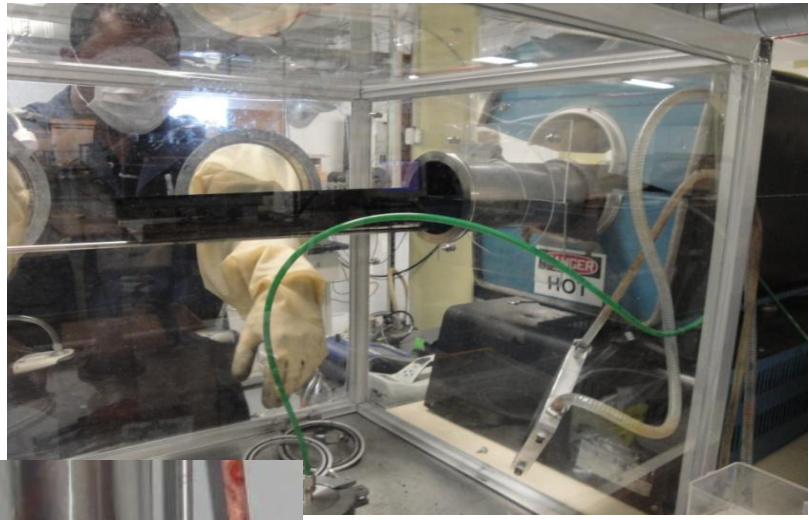
Elimination
↓
Substitution
↓
Isolation
↓
Engineering Controls
↓
Administrative Controls
- Biological Monitoring
- Medical Screening and Surveillance

↓
Personal Protective Equipment

Prevention through Design (PtD)

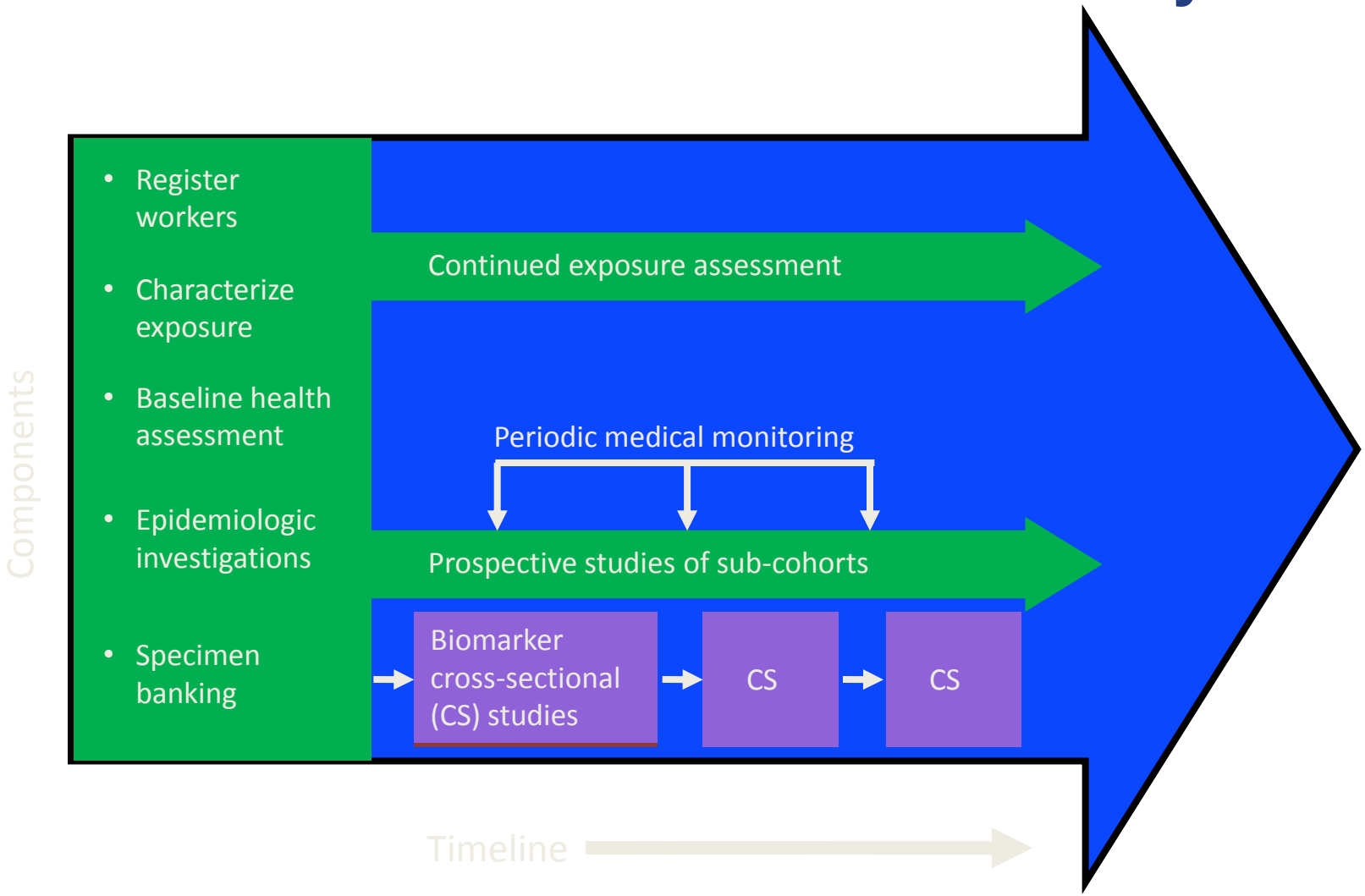


Conventional controls should work

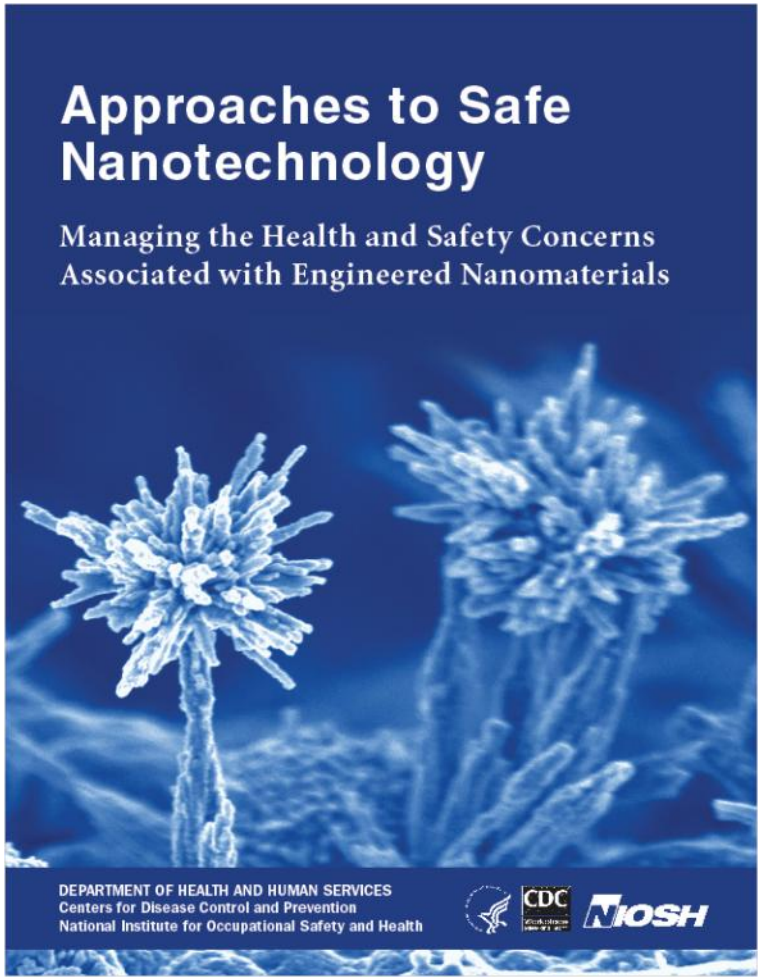


Courtesy D. Evans, M. Methner, K. Martinez (NIOSH)

Nanomaterials Worker Health Study

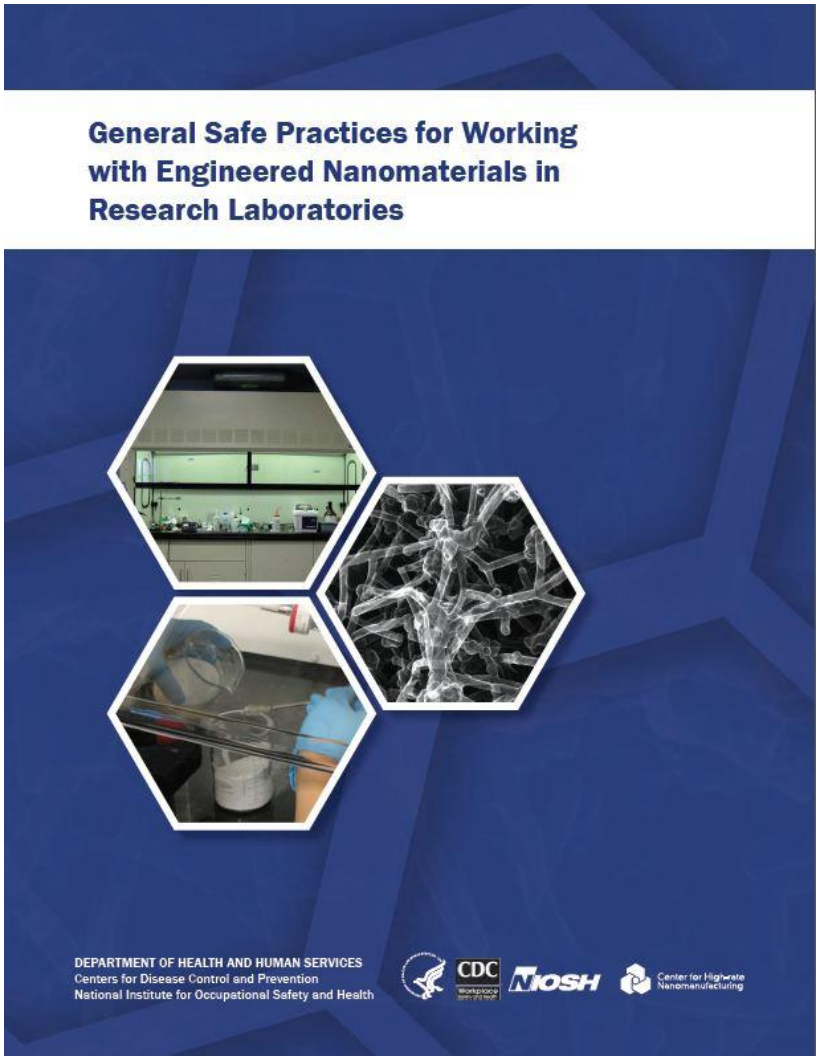


Nanotechnology Workplace Guidance



- First released in 2006, latest update 2009
- Basic guidance for building a responsible nanomaterials workplace management program
- Cited & used globally
- Follow-on documents with specific guidance – e.g., laboratories.
- www.cdc.gov/niosh/topics/nanotech

Laboratory Guidance



- Published in 2012
- Hazard identification
- Exposure assessment
- Exposure control
- Other considerations:
  - Control verification
  - Fire and explosion control
  - Health surveillance

www.cdc.gov/niosh/docs/2012-147/

Global coordination

Major outputs

- Established formal partnerships and collaborations with private, governmental and academic centers in the U.S. and globally
- Led the development of the first ISO standard on safety and health for nanotechnology (ISO/TR 12885:2008)
- Chaired the Organization for Economic Cooperation and Development (OECD) Working Party on Manufactured Nanomaterials Steering Group 8 on exposure measurement and exposure mitigation for manufactured nanomaterials
- Chaired the U.S. Technical Advisory Group to ISO TC229 (Nanotechnology) Working Group 3 Health Safety and the Environment
- Led the development of World Health Organization's guidelines on "Protecting Workers from Potential Risks of Manufactured Nanomaterials."

Global OSH standards development

- Public organizations:
  - United Nations (UN): World Health Organization (WHO), UN Institute for Training and Research (UNITAR)
  - Organization for Economic Cooperation and Development (OECD)
- Private organizations:
  - International Organization for Standardization (ISO)
  - ASTM International
  - *Good*Nano*Guide*

World Health Organization

WHO Guidelines on "Protecting Workers from Potential Risks of Manufactured Nanomaterials"

- Aim: to facilitate improvements in occupational safety and health of nanotechnologies in a broad range of manufacturing and social environments by incorporating elements of risk assessment and risk management framework and contextual issues in the guidelines structure.

- Call for Contributors, Reviewers and Donors at www.who.int/occupational_health/topics/nanotechnologies/en/

OECD Working Party on Manufactured NM SG8 Publications

Compilation and Comparison of Guidelines Related to Exposure to Nanomaterials in Laboratories

Emission Assessment for Identification of Sources and Release of Airborne Manufactured Nanomaterials in the Workplace: Compilation of Existing Guidance

Report of an OECD Workshop on Exposure Assessment and Exposure

Mitigation: Manufactured Nanomaterials

Comparison of Guidance on Selection of Skin Protective Equipment and Respirators for Use in the Workplace: Manufactured Nanomaterials

Identification, Compilation and Analysis of Guidance Information for Exposure

Measurement and Exposure Mitigation: Manufactured Nanomaterials
Preliminary Analysis of Exposure Measurement and Exposure Mitigation in Occupational Settings: Manufactured Nanomaterials

www.oecd.org/document/53/0,3746,en_2649_37015404_37760309_1_1_1_1,00.html

OECD Working Party on Manufactured NM

- **Under development in SG8**
  - Evaluating data and provide recommendation on measurement technologies and sampling protocols for determining concentrations of manufactured nanomaterials in air (Australia)
  - Case study for exposure assessment on manufactured nanomaterial: silver (USA/South Korea) and gold (South Africa)
  - Compilation of methods and models for assessing exposure to manufactured nanomaterial (USA)
  - Compilation of available information on disposal and treatment technologies of manufactured nanomaterials (USA)
  - Compilation of methods for measuring biodurability of nanomaterials in biological and environmental media (South Africa)

Published standards ISO/TC229

N	*Health & Safety Projects (WG3)*	*Lead*
1	Health and safety practices in occupational settings relevant to nanotechnologies. ISO/TR 12885:2008	USA
2	Endotoxin test on nanomaterial samples for in vitro systems -- Limulus amebocyte lysate (LAL) test. ISO 29701:2010	Japan
3	Generation of metal nanoparticles for inhalation toxicity testing using the evaporation/condensation method. ISO 10801:2010	Korea
4	Characterization of nanoparticles in inhalation exposure chambers for inhalation toxicity testing. ISO 10808:2010	Korea
5	Nanomaterial risk evaluation. ISO/TR 13121:2011	USA
6	Guidance on physicochemical characterization of engineered nanoscale materials for toxicologic assessment. ISO/TR 13014:2012	USA

Published standards (cont.) ISO/TC229

N	*Health & Safety Projects (WG3)*	*Lead*
7	Surface characterization of gold nanoparticles for nanomaterial specific toxicity screening: FT-IR method. ISO/TS 14101:2012	Korea
8	Occupational risk management applied to engineered nanomaterials. Part 1: Principles and approaches. ISO/TS 12901-1:2012	UK
9	Preparation of material safety data sheet (MSDS). ISO/TR 13329:2012	Korea

Standards under development ISO/TC229

N	*Health & Safety Projects (WG3)*	*Lead*
10	Occupational risk management based on control banding approach	France
11	Guidance on toxicological screening methods for eng. nanomaterials	USA
12	Guidance on sample preparation methods for eng. nanomaterials	USA
13	Determination of muramic acid as a biomarker for silver nanoparticles activity	Iran
14	Guidance on the voluntary labelling of consumer products containing manufactured nano-objects	France

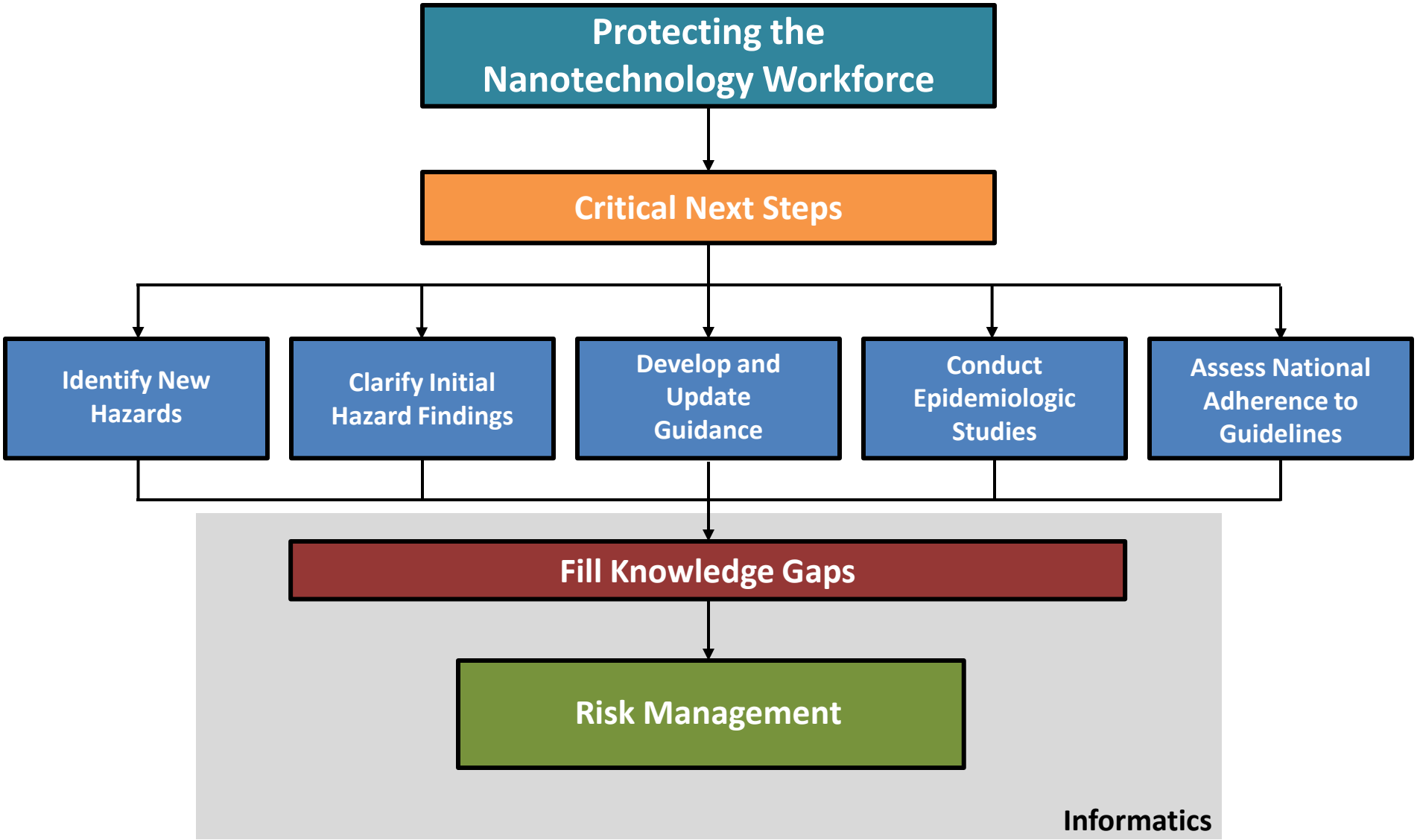
Proposed standards under consideration ISO/TC229

N	*Health & Safety Projects (WG3)*	*Lead*
15	General framework for the development of occupational exposure limits for nano-objects and their aggregates and agglomerates	USA
16	*In vitro* methodologies to assess nanomaterial biodurability	South Africa
17	Effect of Nanoparticles on Cell Oxidative Stress	USA
18	Effect of Nanoparticles on Cell Viability (MTS Assay)	USA
19	EPR method to characterize generation of reactive oxygen species	Korea
20	Nanoparticles: counting and sizing using single particle ICP-MS	Netherlands
21	Requirements of nanomaterial working solutions for in vitro testing	Japan

ISO/TC229 Organizational Relationship

Contact:
HBenko@ansi.org

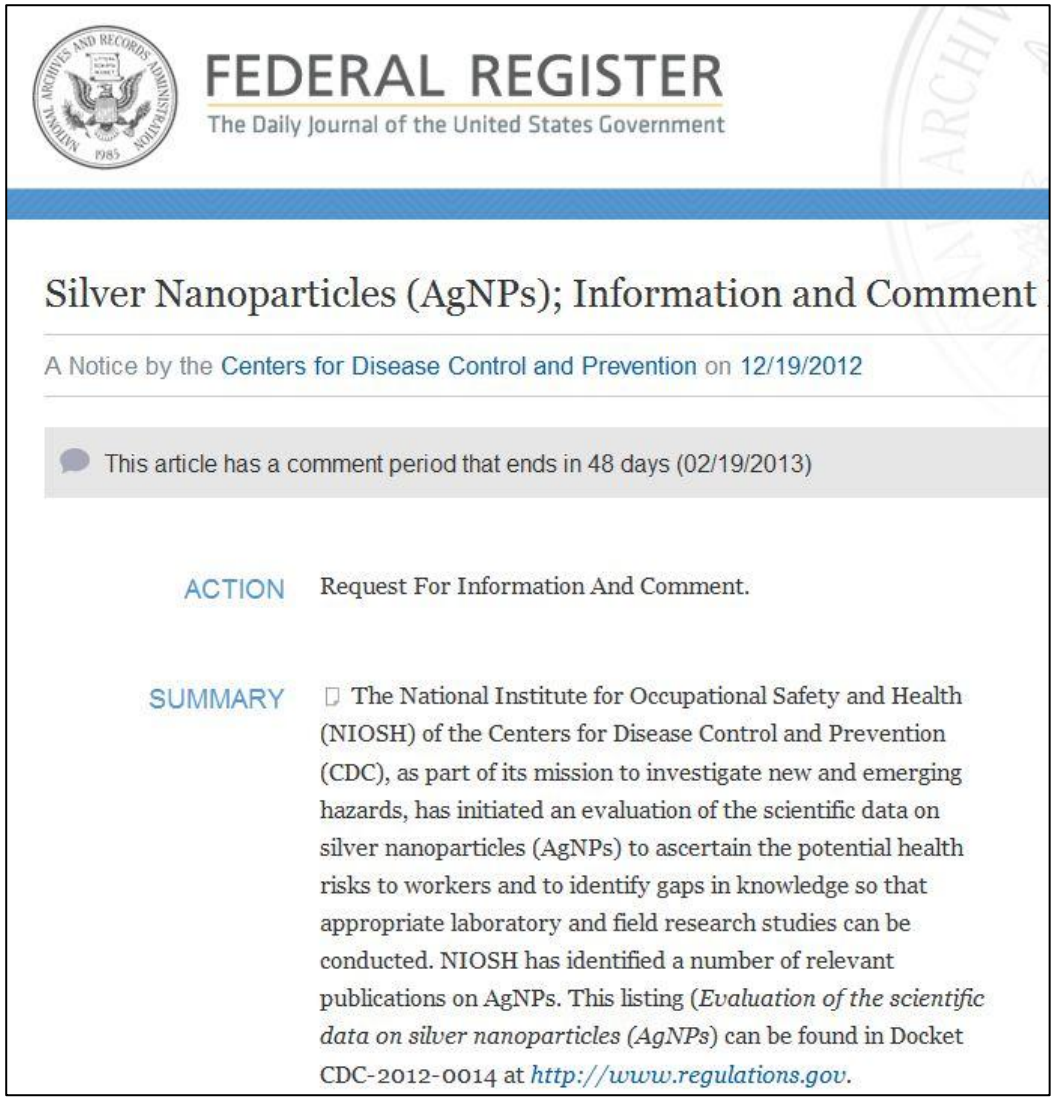
NIOSH Focus for 2013–2016



- Identify new hazards
  - Nanoscale silver, cellulose, graphene
  - Explosive potential
  - Advanced nanomaterials
  - Cardiovascular and immune effects
- Clarify initial hazard findings
  - Carcinogenicity of carbon nanotubes
  - Predictive *in vitro* screening/identify biomarkers
  - Mechanisms of action

- Develop and update guidance
  - Conduct QRA/develop single material OELs
  - Use hazard banding and categorical OELs
  - Incorporate Prevention through Design (PtD)
  - Develop global partners
- Conduct epidemiological studies
  - Study carbon nanotube (CNT) and carbon nanofiber (CNF) workers
  - Investigate feasibility of registries/medical screening
- Assess national adherence to guidelines
  - Determine if precautionary guidance is being used
  - Collaborate with international organizations on global assessment
  - Address hot spots

Federal Register Notice for nanosilver



FEDERAL REGISTER
The Daily Journal of the United States Government

Silver Nanoparticles (AgNPs); Information and Comment

A Notice by the Centers for Disease Control and Prevention on 12/19/2012

This article has a comment period that ends in 48 days (02/19/2013)

ACTION Request For Information And Comment.

SUMMARY The National Institute for Occupational Safety and Health (NIOSH) of the Centers for Disease Control and Prevention (CDC), as part of its mission to investigate new and emerging hazards, has initiated an evaluation of the scientific data on silver nanoparticles (AgNPs) to ascertain the potential health risks to workers and to identify gaps in knowledge so that appropriate laboratory and field research studies can be conducted. NIOSH has identified a number of relevant publications on AgNPs. This listing (*Evaluation of the scientific data on silver nanoparticles (AgNPs)* can be found in Docket CDC-2012-0014 at *http://www.regulations.gov*.

- Request for information
- for nanosilver to ascertain health risks to workers and to identify research gaps:
  - toxicity data
  - health effects in workers
  - workplaces and products
  - workplace scenarios with potential for exposure
  - measurement methods and exposure data
  - control measures

Journal of Occupational and Environmental Hygiene, 9: D12–D22
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DOI: 10.1080/15459624.2012.638217

Commentary
Progression of Occupational Risk Management with Advances in Nanomaterials

Vladimir Murashov, Paul Schulte, and John Howard

National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Washington, D.C.

INTRODUCTION

Nanotechnology has been touted as a transformative technology that would encompass a broad range of products and application areas and improve many aspects of human life. As nanotechnology matures, the complexity of its main product, nanomaterials, increases. Four generations of nanomaterials have been defined by a World Technology Evaluation Center (WTEC) Report,[1] namely, passive nanomaterials, active nanomaterials, integrated nanosystems, and molecular nanosystems. According to the Woodrow Wilson Nanotechnology Consumer Product Inventory,[2] there are over 1000 self-identified nano-enabled consumer products on the market. Most of these products are based on first-generation "passive nanomaterials." Limited understanding of passive nanomaterial hazards has challenged traditional occupational health risk assessment and management approaches. New approaches including suggestions for the development and adoption of proactive approaches to nanotechnology risk assessment and control have been proposed.[3] Unlike reactive approaches, where risk control measures are applied to well characterized hazards, proactive or anticipatory approaches aim at minimiz-

and nanosystems may present more complex health risks than passive nanomaterials,[10] risk assessment studies specifically directed at these materials in the workplace need to be funded and conducted.

It was recognized that nanotechnology and advanced nanomaterials raise issues that are more complex and far-reaching than many other innovations.[11] Therefore, approaches to the overall risk governance of emerging technologies, which can be defined as a comprehensive oversight framework encompassing regulatory and non-regulatory approaches to risk assessment and risk management, may need to be validated and modified as appropriate.

In this Commentary, some of the complex issues pertaining to the occupational safety and health risk implications of active nanomaterials and nanosystems are explored.

NANOMATERIAL COMPLEXITY

Generations of Nanomaterials

Advancement of nanotechnology can be characterized by a number of factors, such as the nature of the manufacturing processes used to produce nanomaterials, breadth of nanotech-

Hazards of advanced nanomaterials

- Unknown but appear similar to passive nanomaterials
- Possibility of novel biological response and unique transport properties
- Many designed to interact directly with biological systems

Risk management of advanced nanomaterials

- Opportunity to understand risks that may occur from development and use of nanomaterials before they enter mainstream manufacturing
  - Design out potential hazards
  - Lower exposure to workers
- Integration of soft and hard law approaches

Conclusions

- Some engineered nanomaterials can cause adverse health effects
- Some nanomaterials are more hazardous than bulk materials
- Some workers are being exposed to engineered nanomaterials and are at risk of adverse effects
- Nanomaterial exposures can be controlled to relatively safe levels

NIOSH Nanotechnology Topic Page

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

Thank you!