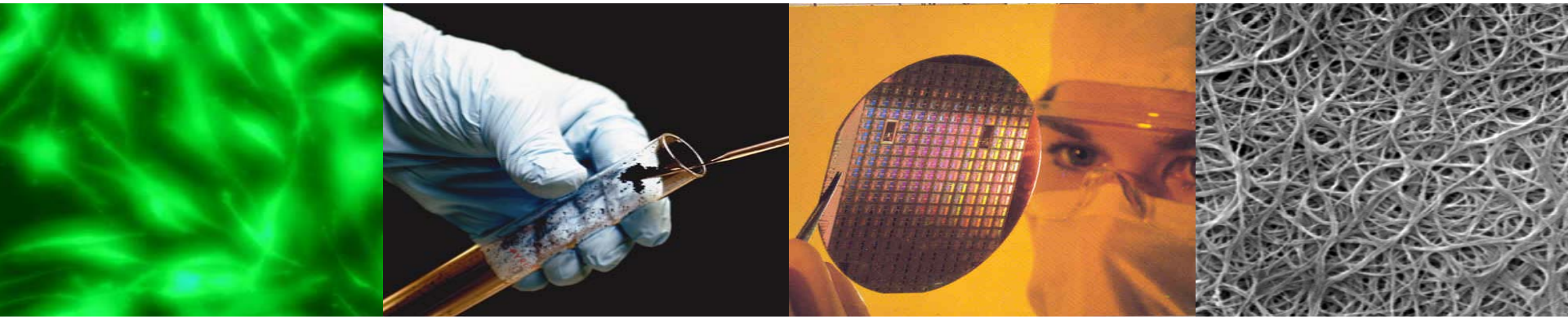
PUBLIC HEALTH GRAND ROUNDS

Office of the Director

April 15, 2010

Preventing Adverse Health Effects from Nanotechnology

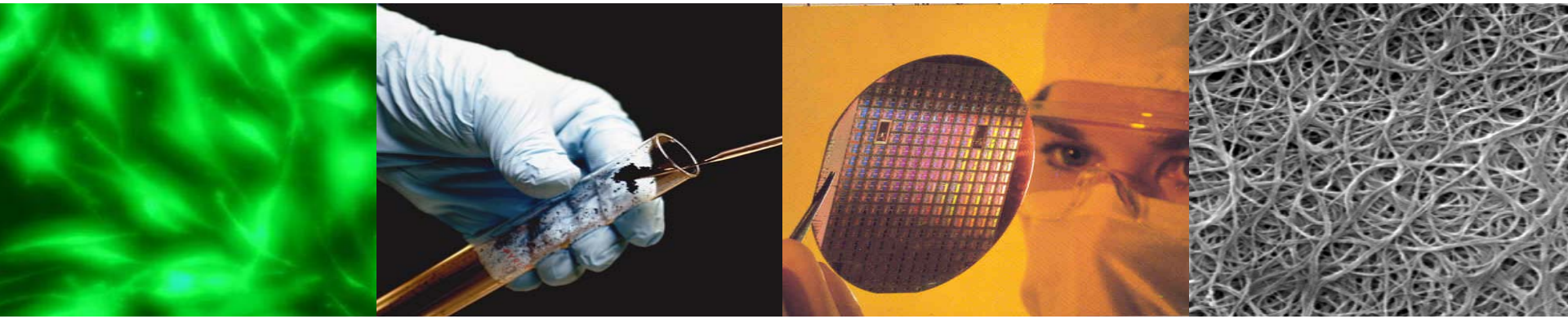


National Institute for Occupational Safety and Health

Outline

- **Paul A. Schulte, PhD**
  - *Nanotechnology: The 3rd Industrial Revolution?*
- **Mark D. Hoover, PhD, CHP, CIH**
  - *Public Health Applications of Nanotechnology*
- **Sally Tinkle, PhD**
  - *NIH: Harnessing the Powers of Nanotechnology for Human Health*
- **Vincent Castranova, PhD**
  - *Hazard Assessment of Nanomaterials: Why Is It so Challenging?*
- **William D. Hunt, PhD**
  - *Nanotechnology at Georgia Tech: Forging the Small*
- **Kristen Kulinowski, PhD**
  - *Global Efforts to Prevent Occupational Hazards from Nanotechnology*

NANOTECHNOLOGY: THE 3RD INDUSTRIAL REVOLUTION



Paul A. Schulte, PhD
Manager, Nanotechnology Research Center
National Institute for Occupational Safety and Health

NANOTECHNOLOGY: THE 3RD INDUSTRIAL REVOLUTION

- What is nanotechnology
- Applications of nanotechnology
- Concern about health and safety effects of nanoparticles

Nanotechnology

- Development of materials at the atomic, molecular, or macromolecular levels with at least one dimension in the range of 1-100 nanometers
- Creating and using structures, devices, and systems that have novel properties and functions because of their small and/or intermediate size
- Ability to control or manipulate matter on the atomic scale

How Little is “Nano?”

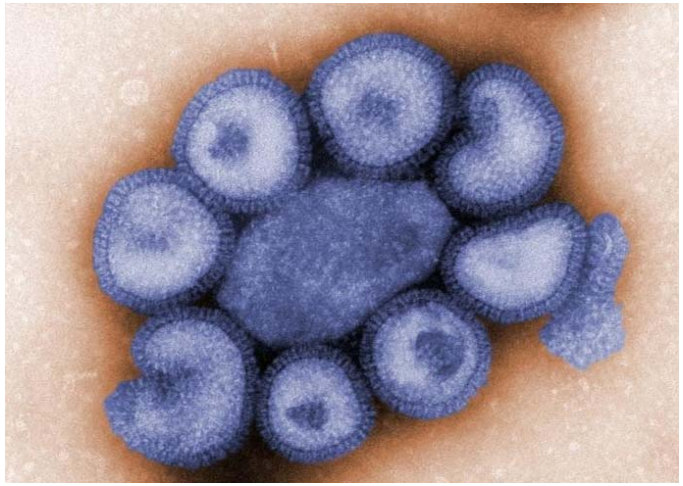
If the diameter of the Earth represented

1 meter…

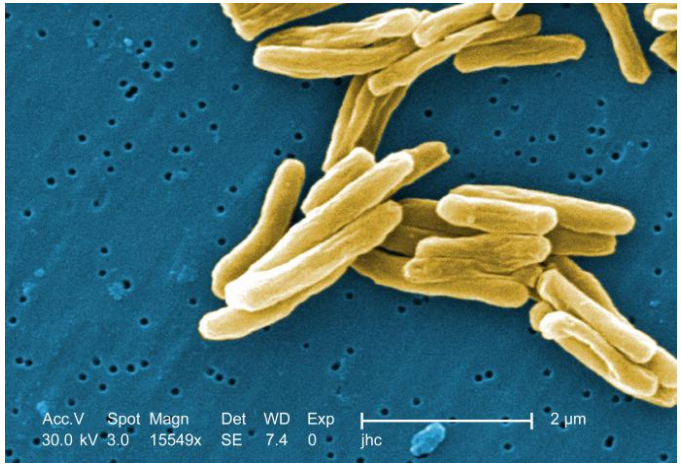
1 nanometer

would be the size of a dime

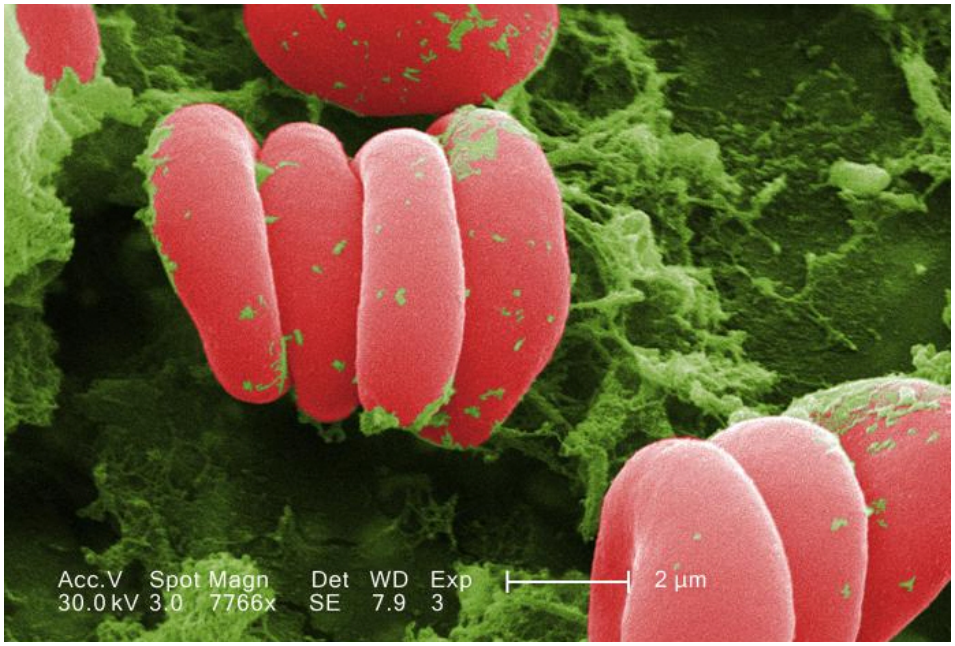
Size of Nanoparticles Relative to Microorganisms and Cells



Influenza virus
75-100 nM



Tuberculosis bacteria
2,000 nM



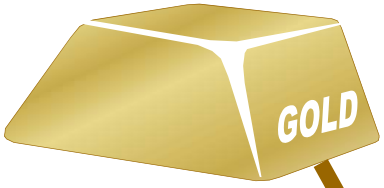
Red blood cells
8,000 nM

Photographs by Dr. F. A. Murphy and Janice Haney Carr, Public Health Image Library

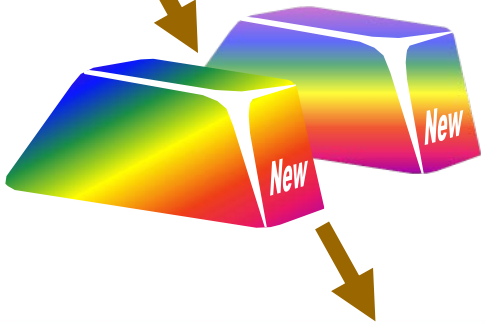
Not Only Smaller, But Different

Same Properties

60 nm bar



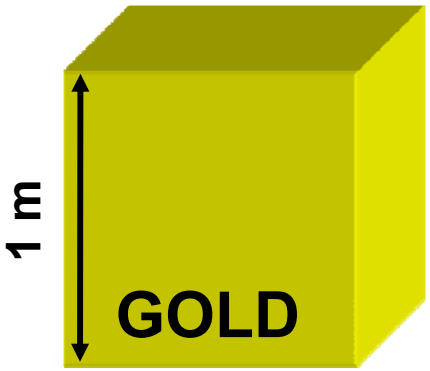
30 nm bar



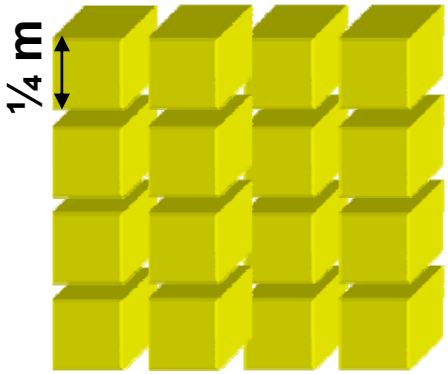
New Properties

- Lower melting point
- Useful as catalyst
- Different color
- Different conductivity

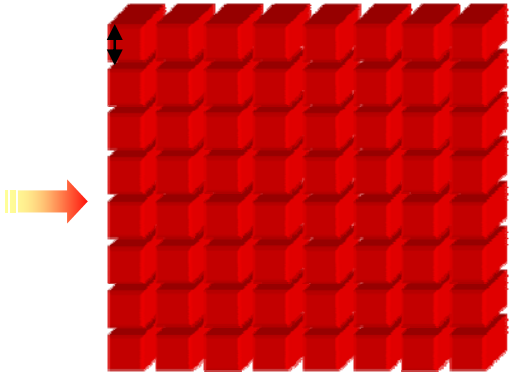
New Properties of Matter Based on Size and Surface Area



Each side=1 M
Mass≈43,000 lb
Surface Area (SA)=6 m^2
≈ 8 ft x 8 ft room



Each side=1/4 M
Mass≈43,000 lb
SA=24 m^2

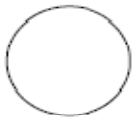


Each side=1 nM
Mass≈43,000 lb
SA=6 billion m^2 ≈ 2500 $miles^2$
State of Delaware= 2490 $miles^2$

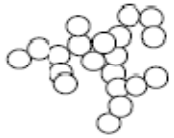
What Could a "Nanoparticle" Be?

Particle Categories

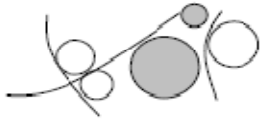
Classes of engineered nanoparticles



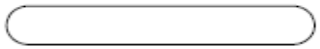
A. Spherical homogeneous



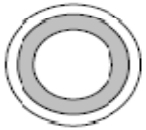
D. Agglomerate homogeneous



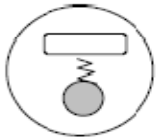
G. Heterogeneous agglomerate



B. Fibrous homogeneous

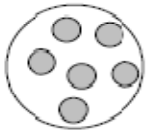


E. Heterogeneous concentric

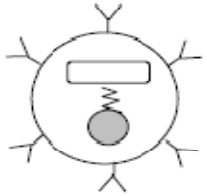


H. Active particle

C. Non-spherical homogeneous



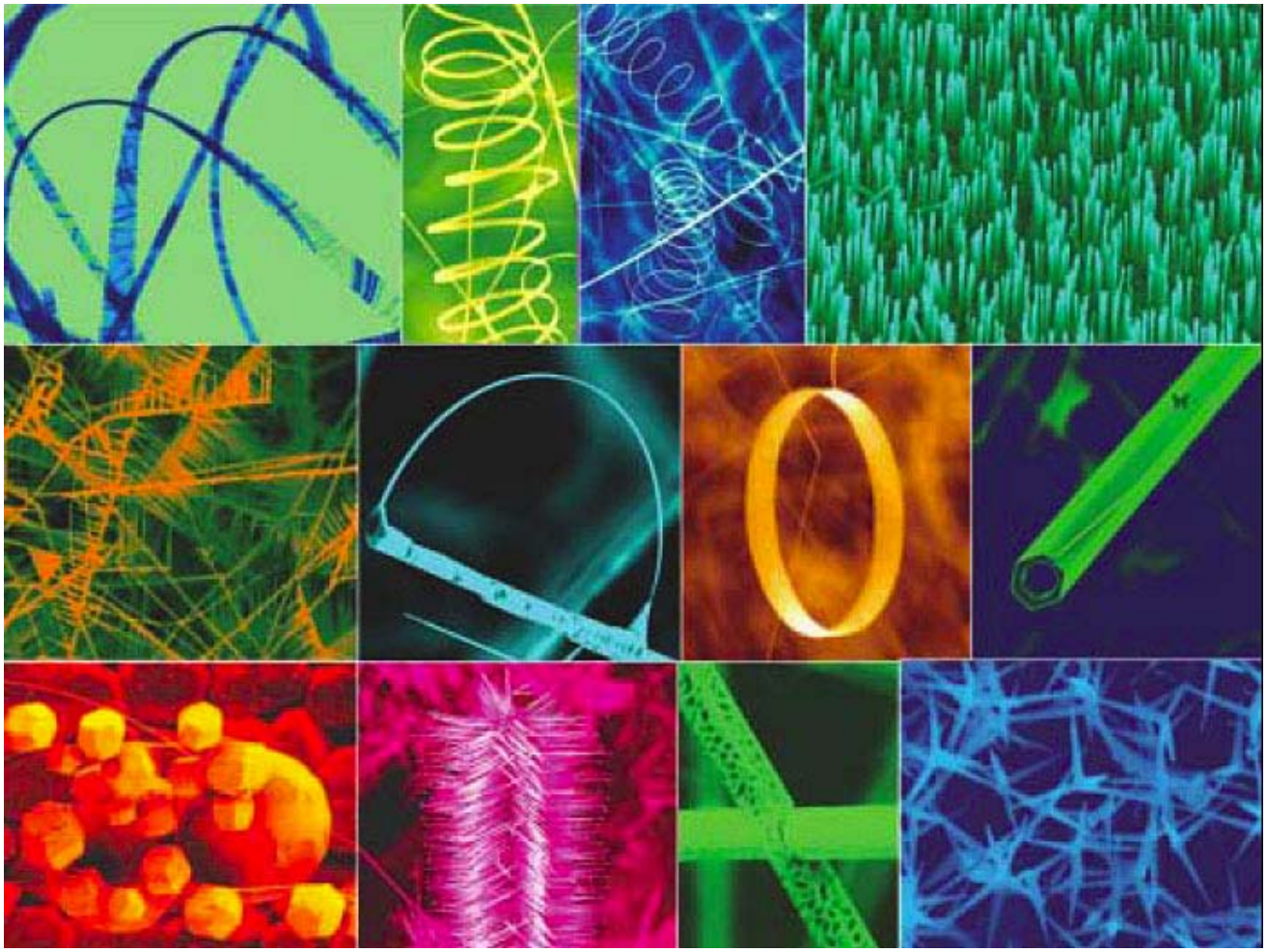
F. Heterogeneous distributed



I. Multifunctional particle

Same Composition—Different Shape

Zinc Oxide Nanoparticles



Materials Today June 2004. Zhong Lin Wang, Georgia Institute of Technology

NANOTECHNOLOGY: THE THIRD INDUSTRIAL REVOLUTION

- What is nanotechnology
- Applications of nanotechnology
- Concern about health and safety effects of nanoparticles

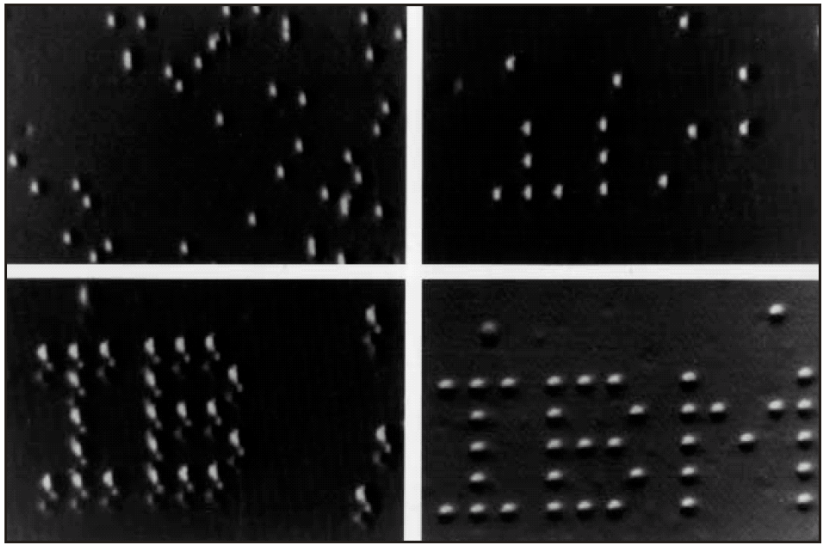
Why is Nanotechnology of Great Interest?

- **Imparts useful properties to materials**
  - Stronger
  - Lighter
  - More durable
  - Different melting temperatures
- **Enhanced electrical conductivity**
  - More transistors on integrated chip
- **Enhanced chemical reactivity**

All of these point to the possibility of creating new and very powerful applications

Potential Revolution in Manufacturing

- **See and manipulate one atom at a time – building molecular tools**
  - Using 35 Xenon atoms to spell out a logo
- **Copy nature – mimic self replication**



Source: IBM Research

Applications of Nanotechnology

Agriculture	More efficient, targeted delivery of plant nutrients, pesticides
Automotive	Lighter, stronger, self-healing materials
Biomedical	Targeted therapeutics, enhanced detection, new structural materials
Energy	More efficient fuel cells, solar collectors
Environmental	New pollution control and remediation tools, sensors
Food	New safety sensors, food preservatives, nutrient additives
Materials	Self-cleaning glass, stain resistant, stronger materials, body armor
Water	New purification approaches

Early Nano-enabled Consumer Products Are on the Market Now

Mercedes
CLS-class

Mercedes-Benz

Eddie Bauer
Ruston Fit Nano-
Care khakis

Eddie Bauer

3M Adper Single
Bond Plus
dental adhesive

3M

Samsung Nano
SilverSeal Refrigerator

SAMSUNG

Wyeth Rapamune
immuno-suppressant

Wyeth

Wilson Double
Core tennis balls

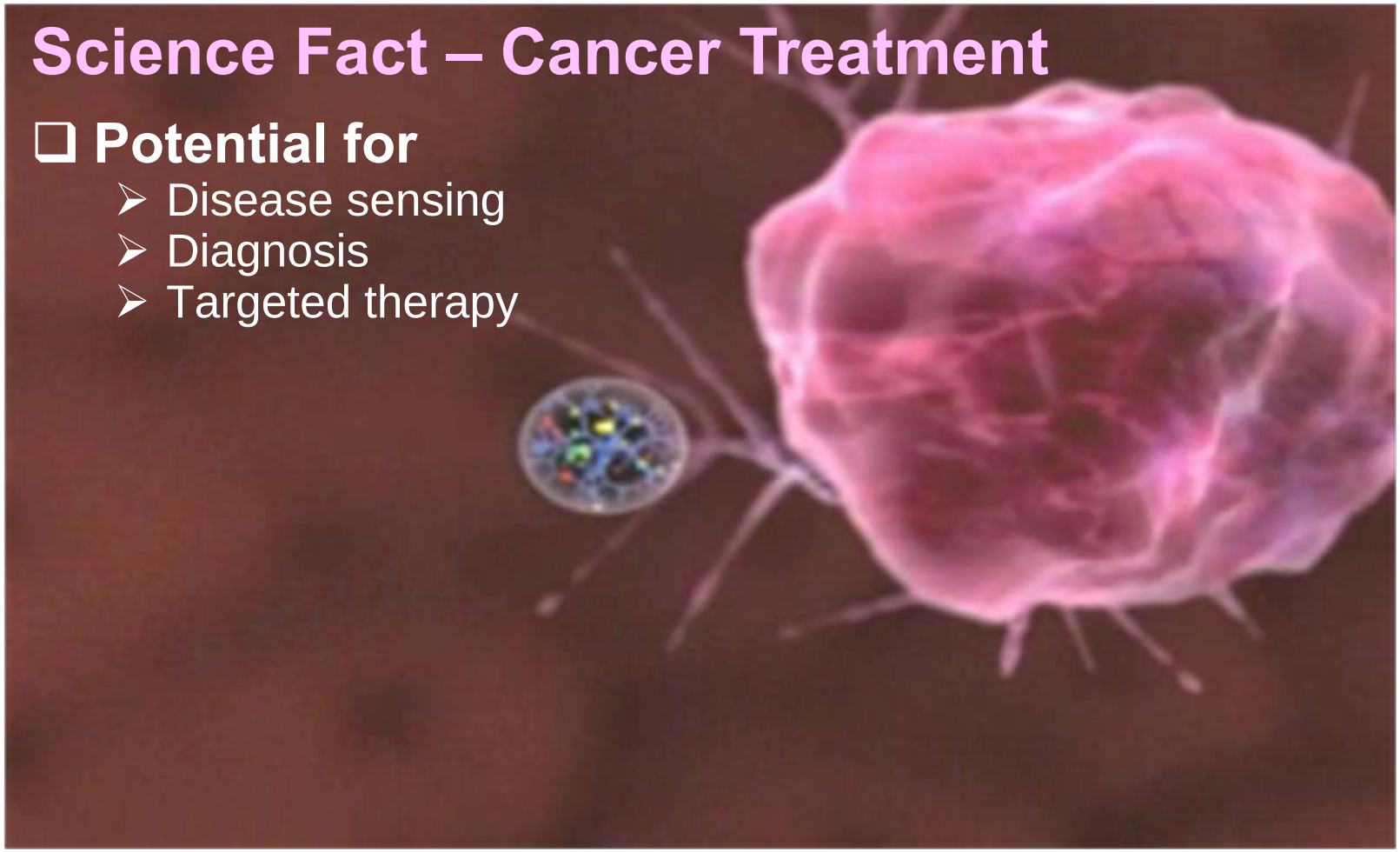
Provided by Larry Gibbs, Stanford University, 2006

Nanoparticulate fuel additives = 10% better fuel economy

Nanocomposite body moldings = 20% lighter

Nanoscale catalysts = 20% reduction in emissions

Nanotechnology and Health: Turning Fiction to Reality



Source: Burnham Institute

NANOTECHNOLOGY: THE THIRD INDUSTRIAL REVOLUTION

- What is nanotechnology
- Applications of nanotechnology
- Concern about health and safety effects of nanoparticles

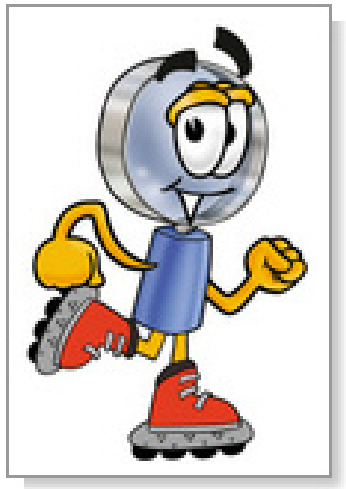
Basis for Concern about Health and Safety Effects of Nanoparticles

- **Findings from air pollution epidemiology**
  - Particles < 2.5 µm associated with respiratory and cardiovascular effects
- **Studies of industrial fumes (e.g., welding fumes) and combustion (e.g., diesel) products**
  - Wide range of effects: pulmonary and eye irritation, fever, lung cancer
- **Initial animal inhalation studies of engineered nanomaterials**
  - Pulmonary fibrosis, granulomas, and inflammation
  - Lung cancer, mesothelioma-like effects
  - Cardiovascular effects: oxidative stress, plaque

Basis for Concern about Health and Safety Effects of Nanoparticles (con't)

- **Nanomaterials have been shown to**
  - Translocate from nose to brain
  - Translocate from lungs to most organ systems
  - Have potential for skin penetration



Major Knowledge Gaps Related to Nanotechnology Health and Safety

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)

NIOSH Safety and Health Topic:

Nanotechnology

NIOSH is the leading federal agency conducting research and providing guidance on the occupational safety and health implications and applications of nanotechnology.

Stakeholders

Occupational Safety and Health Practitioners
Information for those involved in the development of nanomaterial risk management programs.

Researchers
Information for academics and other individuals who are pursuing nanotechnology related research.

Industry Employers and Workers
Information for those who make or use nanomaterials in the workplace.

Policymakers and Media
Information for decision makers and communication professionals.

Hazard Identification Gaps

- **What are the hazards of the major types of nanoparticles?**
  - NIOSH: Identified pulmonary fibrosis and atherosclerosis
- **What are the mechanisms of action?**
  - NIOSH: Demonstrated that the formation of highly reactive oxygen compounds cause tissue damage

TOXICOLOGICAL SCIENCES 90(1), 188–197 (2006)
doi:10.1093/toxsci/kfj075
Advance Access publication December 9, 2005

Nitric Oxide and Reactive Oxygen Species Production Causes Progressive Damage in Rats after Cessation of Silica Inhalation

Dale W. Porter,*,[1] Lyndell L. Millecchia,* Patsy Willard,* Victor A. Robinson,* Dawn Ramsey,† Jeffery McLaurin,† Amir Khan,† Kurt Brumbaugh,* Christoper M. Beighley,* Alexander Teass,† and Vincent Castranova*

*National Institute for Occupational Safety and Health, *Health Effects Laboratory Division, Morgantown, WV 26505 and †Division of Applied Research and Technology, Cincinnati, Ohio 45226*

Received September 1, 2005; accepted December 4, 2005

Exposure Assessment Gaps

- **What exposures are occurring now?**
  - To workers, consumers, and the environment
- **How should exposure be measured and what metrics (mass, surface area, particle count) should be used?**
- **NIOSH has conducted field assessments at 26 worksites and demonstrated exposure to nanoparticles**

Nanoparticle Emission Assessment Technique (NEAT) for the Identification and Measurement of Potential Inhalation Exposure to Engineered Nanomaterials — Part A

M. Methner [a]; L. Hodson [a]; C. Geraci [a]

[a] National Institute for Occupational Safety and Health (NIOSH), Nanotechnology Research Center, Cincinnati, Ohio

First published on: 16 December 2009

Nanoparticle Emission Assessment Technique (NEAT) for the Identification and Measurement of Potential Inhalation Exposure to Engineered Nanomaterials—Part B: Results from 12 Field Studies

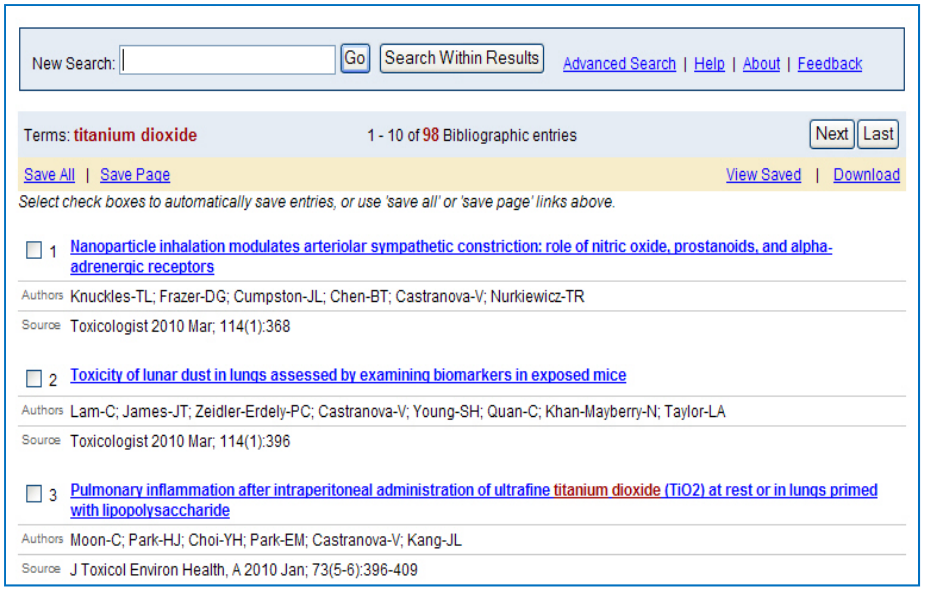
M. Methner [1]; L. Hodson [1]; A. Dames [1]; C. Geraci [1]

[1] National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Cincinnati, Ohio

First published on: 06 January 2010

Risk Characterization Gaps

- **Can animal data accurately predict human risk?**
  - Value of short-term tests
  - NIOSH: Conducted risk assessments on **titanium dioxide** and carbon nanotubes
- **What are the risks for various population exposed to nanomaterials?**
  - Identify cohorts at risk
  - Value of exposure registries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Terms: titanium dioxide 1 - 10 of 98 Bibliographic entries Next Last

Save All | Save Page View Saved | Download

Select check boxes to automatically save entries, or use 'save all' or 'save page' links above.

1 Nanoparticle inhalation modulates arteriolar sympathetic constriction: role of nitric oxide, prostanoids, and alpha-adrenergic receptors

Authors Knuckles-TL; Frazer-DG; Cumpston-JL; Chen-BT; Castranova-V; Nurkiewicz-TR

Source Toxicologist 2010 Mar; 114(1):368

2 Toxicity of lunar dust in lungs assessed by examining biomarkers in exposed mice

Authors Lam-C; James-JT; Zeidler-Erdely-PC; Castranova-V; Young-SH; Quan-C; Khan-Mayberry-N; Taylor-LA

Source Toxicologist 2010 Mar; 114(1):396

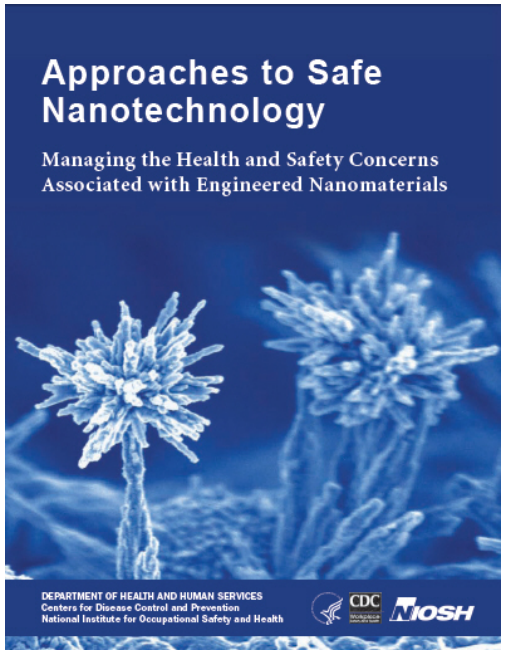
3 Pulmonary inflammation after intraperitoneal administration of ultrafine titanium dioxide (TiO2) at rest or in lungs primed with lipopolysaccharide

Authors Moon-C; Park-HJ; Choi-YH; Park-EM; Castranova-V; Kang-JL

Source J Toxicol Environ Health, A 2010 Jan; 73(5-6):396-409

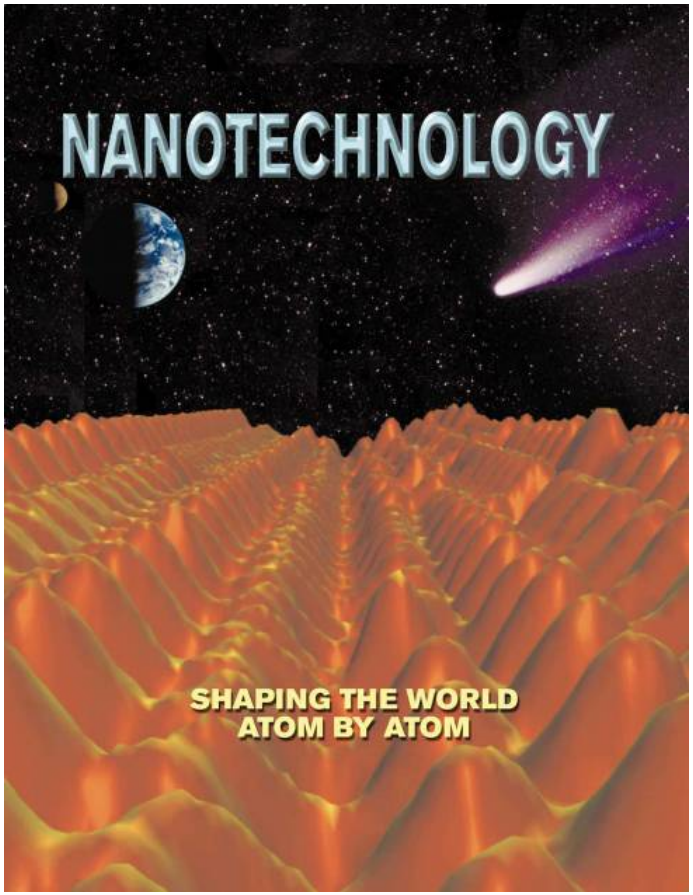
Risk Management Gaps

- **What are the limits of controls?**
  - NIOSH: Defined exposure limits to titanium dioxide
- **What exposure limits can be recommended for individual and categories of nanoparticles?**
- **What medical surveillance is appropriate for people exposed to nanomaterials?**
  - NIOSH: Developed various guidance documents

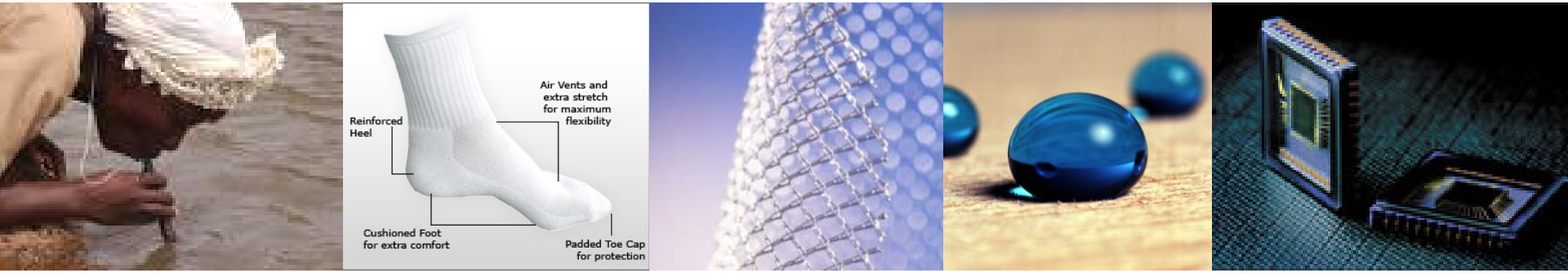


Potential: Great Societal Benefit
Challenge: Responsible Development

Women cotton thread workers, circa 1890



PUBLIC HEALTH APPLICATIONS OF NANOTECHNOLOGY



Mark D. Hoover, PhD, CHP, CIH
Senior Research Scientist
National Institute for Occupational Safety and Health

PUBLIC HEALTH APPLICATIONS OF NANOTECHNOLOGY

- **Applications span a broad spectrum**
  - Prevention of disease or injury
  - Medical diagnosis and treatment
  - Reducing environmental and energy impact
- **A compendium of nanotechnology products and applications can be found at http://www.nanotechproject.org/inventories**

Prevention of Disease or Injury

Personal water purification

"Lifestraw"

"Lifesaver" water bottle

Industrial water purification

Nano-enabled systems

Contamination control

Anti-microbial surface treatments

Prevention of STDs

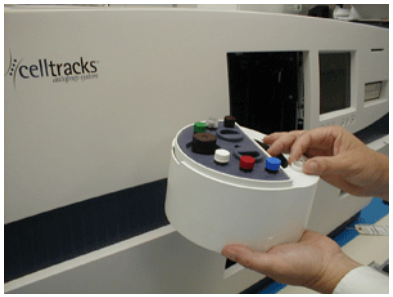
Liquid condoms

Medical Diagnosis and Treatment

Home diagnostic testing

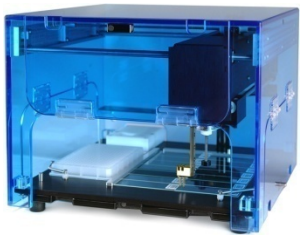
Gold nanoparticle protein binding

Laboratory diagnostic testing



Magnetic nanoparticle cell sorters

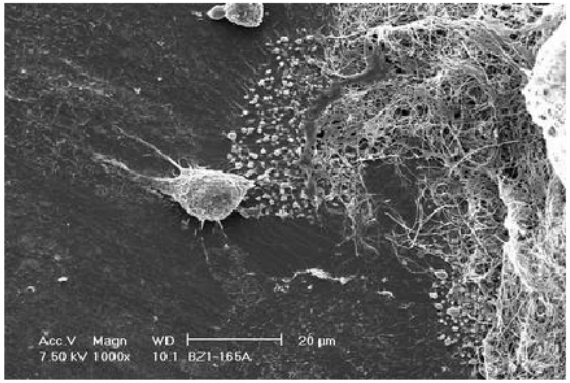
Micro-array diagnostics



Nano chip technologies

Bone repair media

Researchers at the University of California, Riverside have published findings that show, for the first time, that bone cells can grow and proliferate on a scaffold of carbon nanotubes. Scientists found that the nanotubes, 100,000 times finer than a human hair, are an excellent scaffold for bone cells to grow on.



Nano "scaffolds"

Reducing Environmental and Energy Impact

Functional coatings

Inert or activated surfaces

Self-cleaning glass

Nano-enhanced UV and rain actions

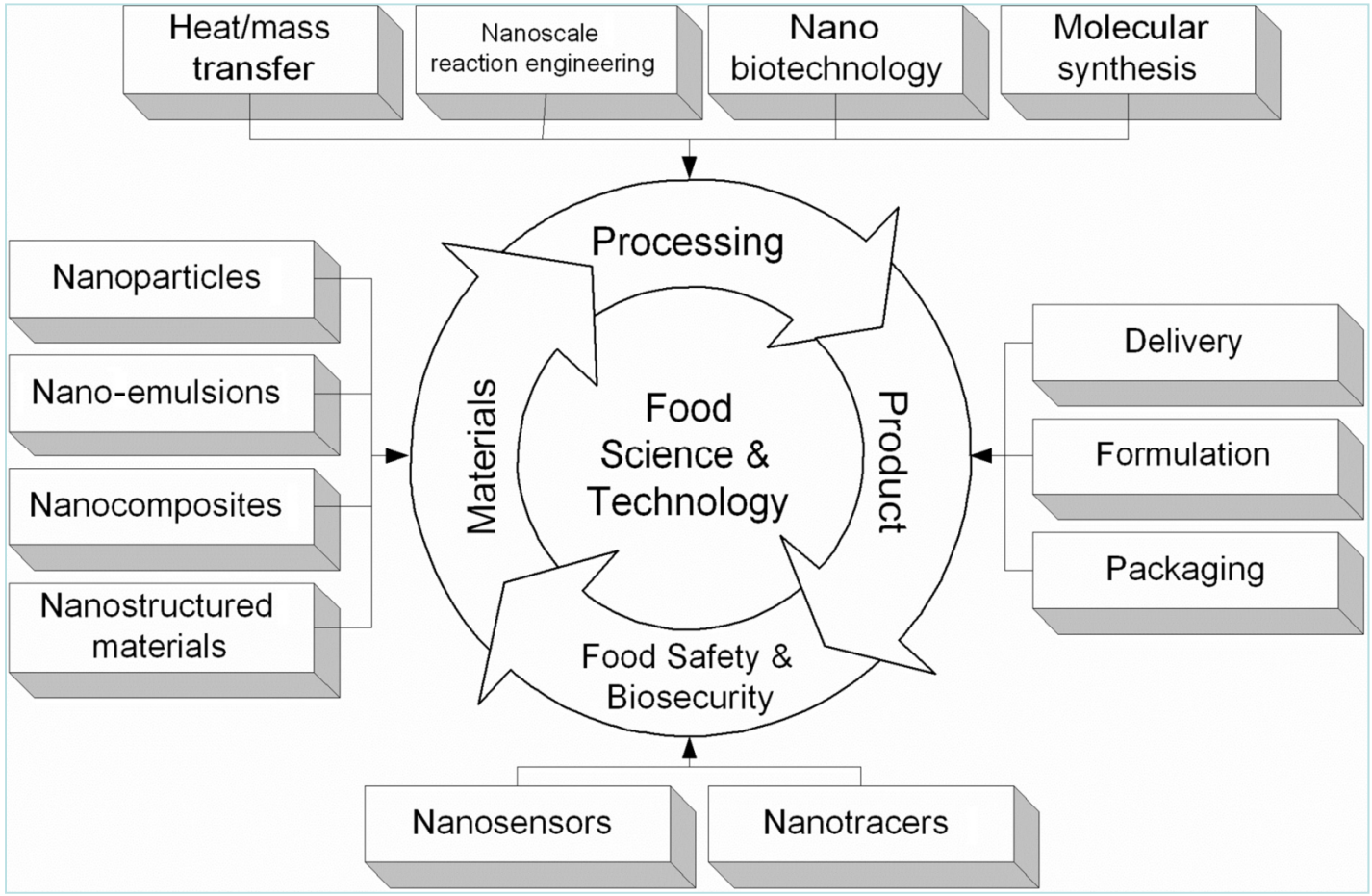
Energy conservation

Nano-formulated insulation

Electronics

Light-emitting diodes

An Instructive Applications Example: Nanotechnology in the Food Industry

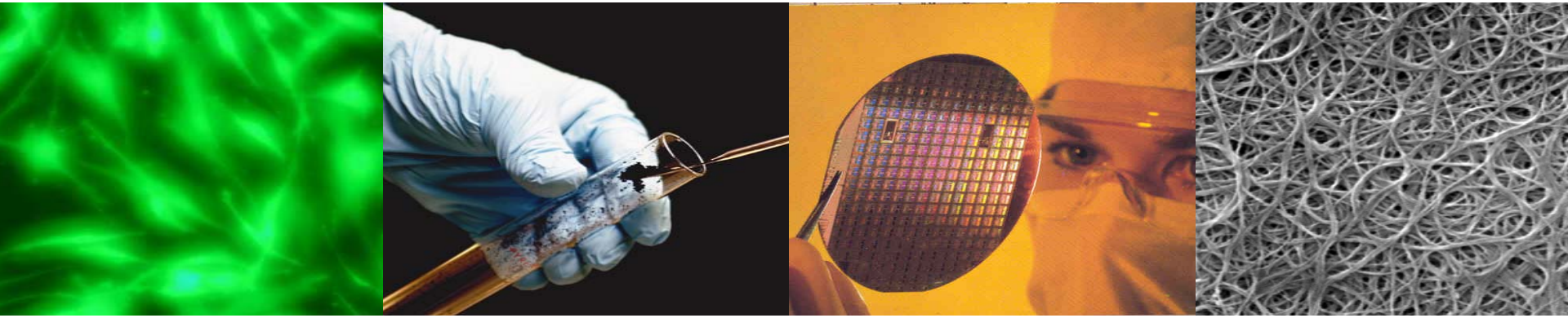


Weiss et al., J Food Science, 71(9): R107-R116, 2006.

Enhancing the Future for Public Health Applications of Nanotechnology

- **Applications span a broad spectrum**
  - Prevention of disease or injury
  - Medical diagnosis and treatment
  - Reducing environmental and energy impact
- **Opportunities**
  - Understand the scope of potential applications
  - Foster the matching of priority public health concerns with development and application of efficient and cost-effective nano-enhanced solutions

NIH: HARNESSING THE POWER OF NANOTECHNOLOGY FOR HUMAN HEALTH

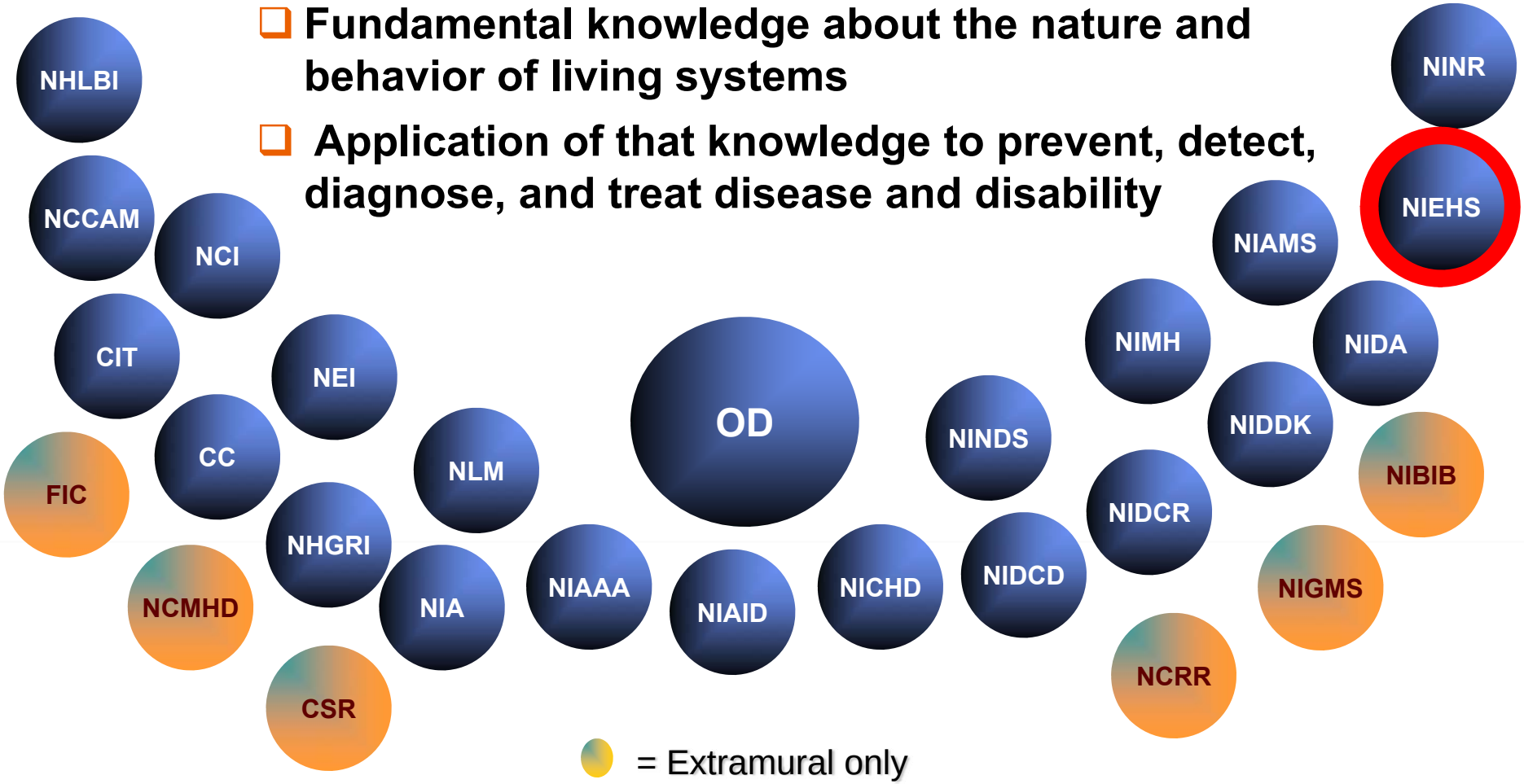


Sally S. Tinkle, Ph.D.
Senior Science Advisor
National Institute of Environmental Health Sciences
National Institutes of Health

National Institutes of Health

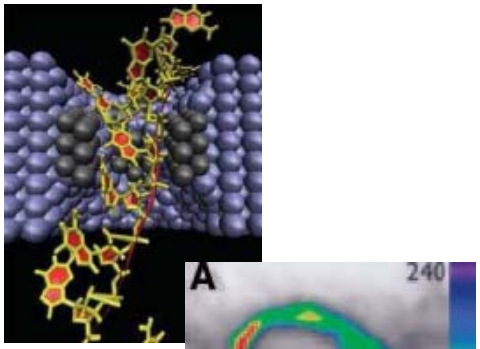
Science in Pursuit of

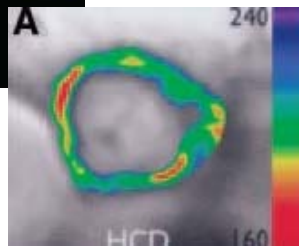
- Fundamental knowledge about the nature and behavior of living systems
- Application of that knowledge to prevent, detect, diagnose, and treat disease and disability

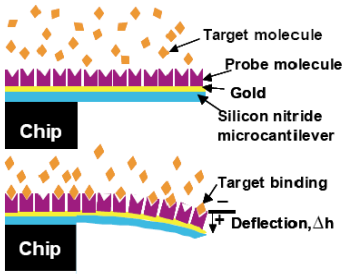


Nanotechnology Enables New Biomedical Solutions

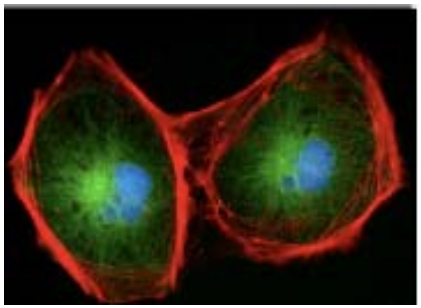
Diagnosis Early Detection

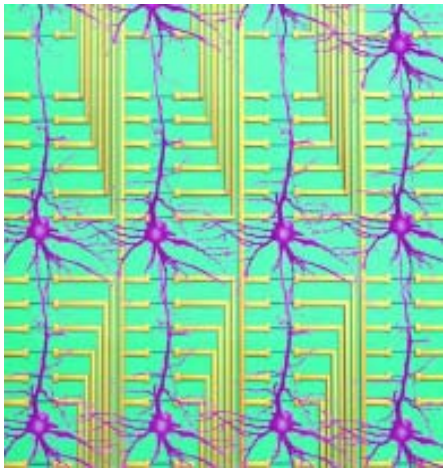




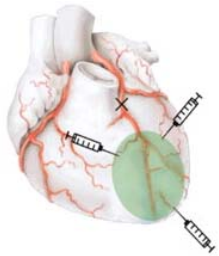


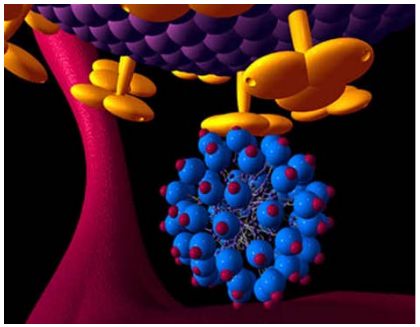
Cellular and Organ System Function

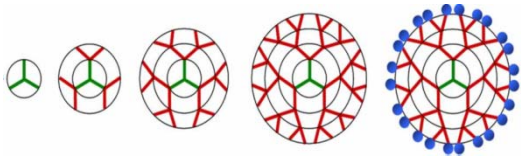




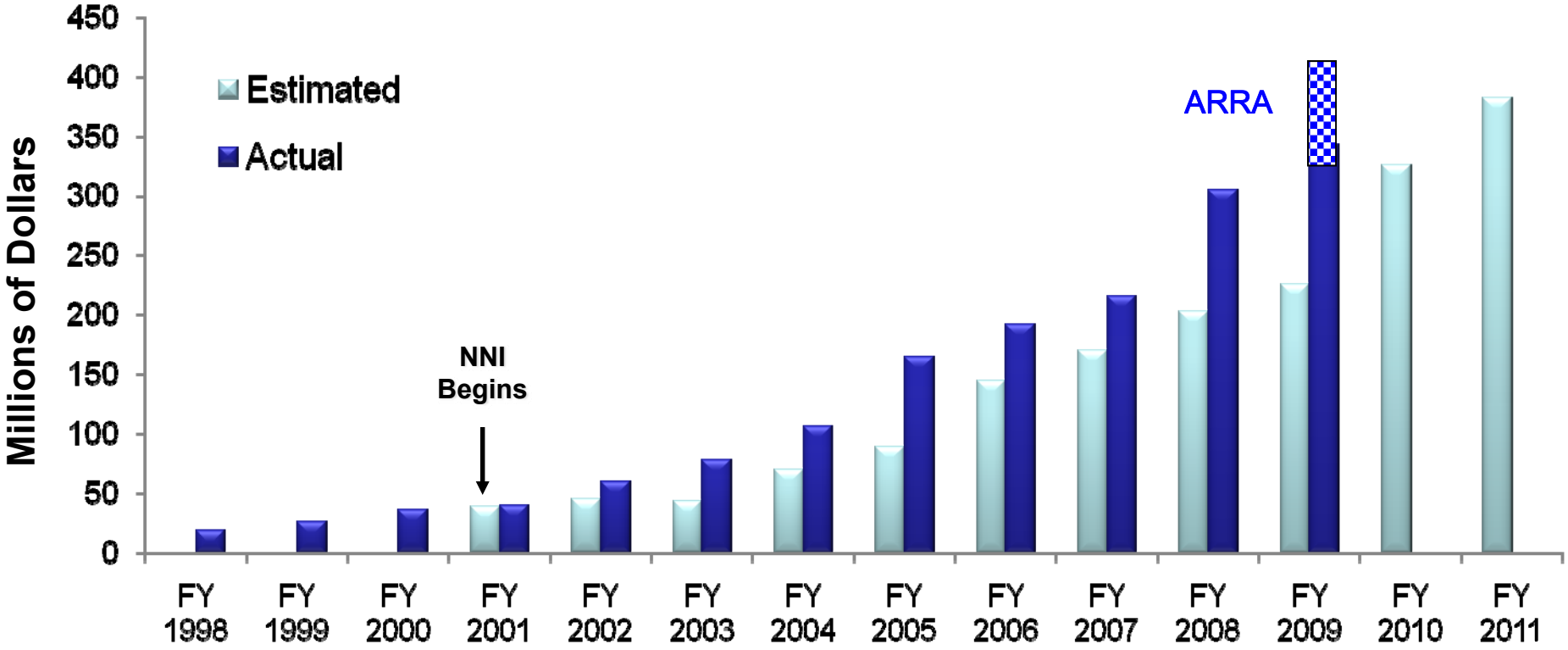
Therapeutics Intervention







NIH Nanotechnology Funding



SBIR/STTR Actual

FY	2001	2002	2003	2004	2005	2006	2007	2008	2009
$M	4.4	7.9	7.3	11.9	16.3	17.2	19.5	31.1	

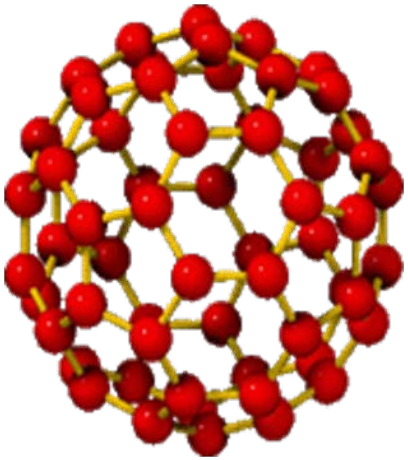
Slide courtesy of Jeffery Schloss, NHGRI, NIH
NNI, National Nanotechnology Initiative

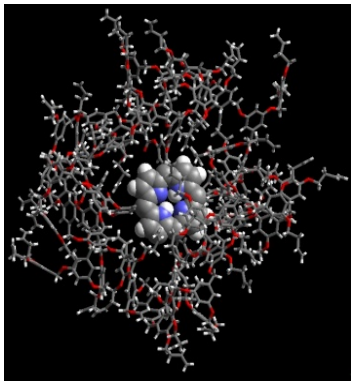
NIEHS Nanotechnology Health and Safety Initiative

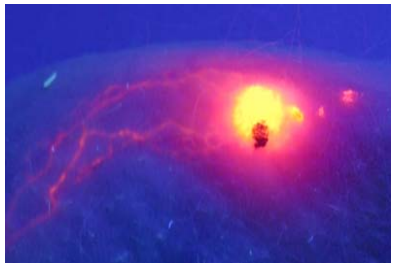
- **Goal**
  - Determine of the relationship between the physical and chemical properties of engineered nanomaterials and biological response
  - Identify nanomaterial design principles that maximize benefit and minimize risk to humans and the environment
- **Research Components**
  - Material characterization
  - Physiological response
  - Pathobiological response
  - Informatics / predictive models
  - Training

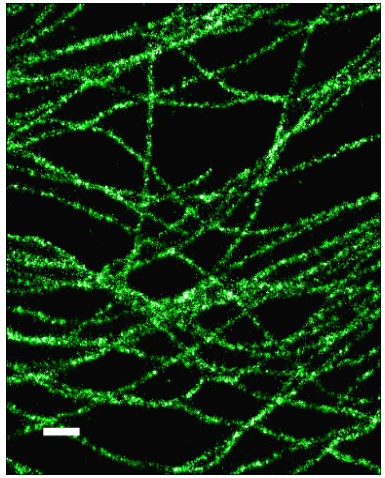
NIEHS Extramural Research Programs

- **Challenge:** Develop reliable and reproducible methods to assess exposure and biological response/toxicological endpoints
- **Challenge:** Understand more precisely how chemical composition and structural arrangements of dictate biological interaction









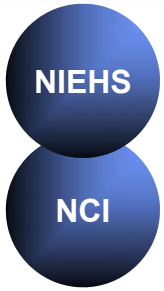
Inter-Institute Collaborations

NIBIB-NIEHS-NCI NanoInformatics Collaboration

- **Need:** Create publically available ontology and interoperability framework between existing nanomaterials databases
- **Mechanism:** Four year contract

NIEHS-NCI NanoStructural Biology Collaboration

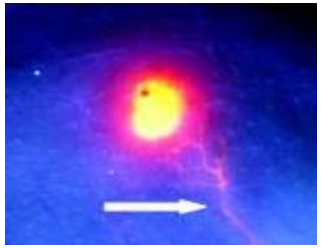
- **Need:** Create database of structural attributes of nanomaterials and their relationship to biology
- **Mechanism:** Task order, annual renewal

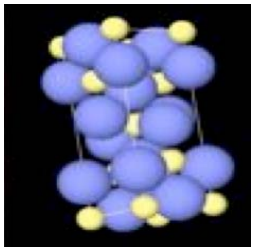


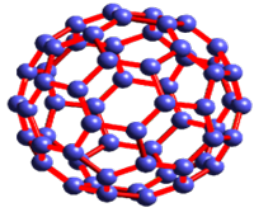
NIBIB, National Institute of Biomedical Imaging and Bioengineering
NIEHS, National Institute of Environmental Health Sciences
NCI, National Cancer Institute

National Toxicology Program

- **Cadmium based "quantum dots"**
  - Role of skin integrity on pharmacokinetic studies after dermal exposure
- **Titanium dioxides**: Dermal pharmacokinetics
  - Impact of coatings and crystal state
- **Carbon based fullerenes**: Pulmonary and oral toxicity
  - Impact of size of C60 aggregates
- **Multiwalled carbon nanotubes**
  - Influence of length and diameter on pulmonary toxicity
- **Ceric oxide**
  - Role of particle size on pulmonary toxicity
- **Nanosilver**
  - Role of particle size and shape on PK and toxicity



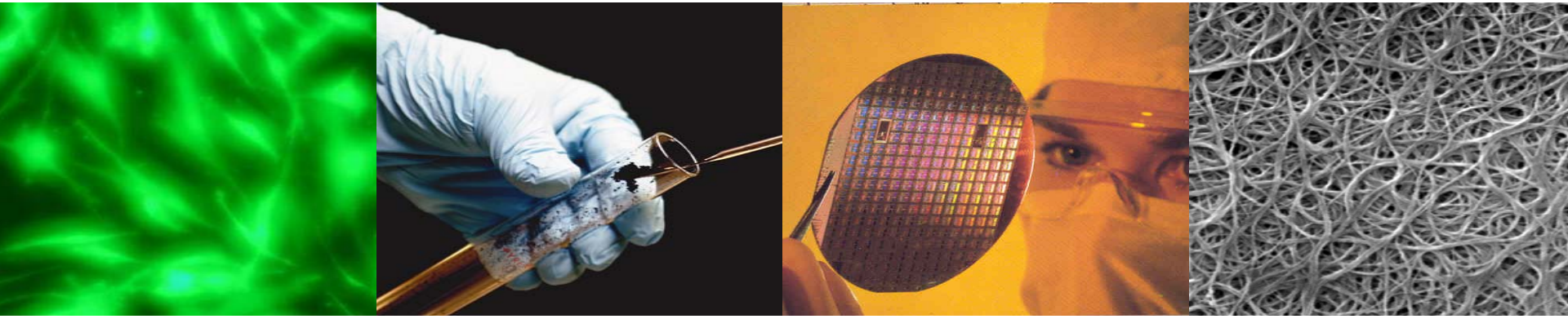




Next Steps for NIH

- Expand the applications of nanotechnology to solve critical biomedical research questions
- Extend NIH presence in the global nanotechnology research community
- Enlarge the health and safety portfolio to identify the basic design principles to engineer nanomaterials for maximum benefit to society with minimal risk of unintended consequences

HAZARD ASSESSMENT OF NANOMATERIALS: WHY IS IT SO CHALLENGING?



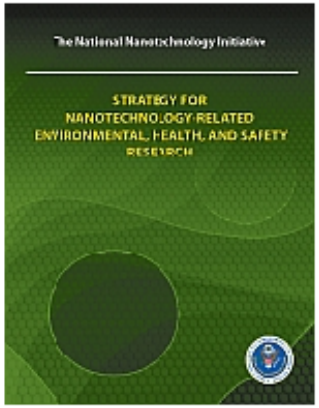
Vincent Castranova, PhD
Branch Chief
Pathology and Physiology Research Branch
Health Effects Laboratory Division
National Institute for Occupational Safety and Health

Hazard Assessment (Evaluation of Bioactivity) Is Essential for Nanoparticles

- **Nanoparticles exhibit unique physiochemical properties distinct from fine (micrometer size) particles of the same composition**
- **Unique properties**
  - Yield unique applications
  - Make unique bioactivity likely
- **Yet, nanoparticles are currently regulated by OSHA and EPA under standards for the fine analogue**
  - Example: Carbon nanotubes are currently regulated as fine graphite

National Nanotechnology Initiative
http://www.nano.gov

NNI Strategy for Nanotechnology-Related Environmental, Health, and Safety Research Released



The Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the Committee on Technology, National Science and Technology Council (NSTC) released the document Strategy for Nanotechnology-Related Environmental, Health, and Safety Research (PDF), describing the NNI's strategy for addressing priority research on environmental, health, and safety (EHS) aspects of nanomaterials.

NNI Research Priorities for Nanomaterials and Their Effects on Human Health

- **Develop and validate animal models to**
  - Quantify dose-response
  - Determine the relationship between physical and chemical properties of nanoparticles and their bioactivity
- **Develop high throughput, predictive, *in vitro* tests to evaluate nanoparticle bioactivity**
- **Ultimately, extrapolate data to responses of humans to nanoparticle exposure**

1. Hazard Assessment Issues: Animal Models

- **Determine responses to nanoparticles via different routes of exposure (pulmonary, dermal, oral, intravenous)**
- **Evaluate responses at site of exposure and distal sites**
- **Evaluate the relationship between responses to short-term vs long-term exposures**
- **Evaluate responses to well-characterized sets of nanoparticles**
- **Characterize nanoparticles both "as produced" and "as delivered" to the test system**
  - Example: Issue of agglomeration in physiological saline and that agglomeration decreases the bioactivity of nanoparticles

2. Hazard Assessment Issues: *In Vitro* Tests

- **Use appropriate *in vitro* tests**
  - Must know mechanisms of action for each nanoparticle
    - Damage resulting from generation of reactive products
    - Altered cell division resulting in abnormal (mutated) cells
- **Use doses relevant to those used in animal models (µg/surface area of exposed cells)**
- **Technical challenges**
  - Interference of nanoparticles with assay indicator chemicals
  - Adsorption of nutrients from the assay medium

3. Hazard Assessment Issues: Extrapolation to Humans

- **Use doses relevant to human exposures**
  - Need human exposure data
  - Translate exposure dose to surface area of target tissue in humans (an example for lung exposure: µg/alveolar surface area)
- **Use structure sizes relevant to human exposures**
  - Identify nanoparticle structure size distribution in workplace air
  - Nanoparticles agglomerate in physiological saline
  - Need to develop biocompatible dispersants, which do not mask surface reactivity (diluted alveolar lining fluid), to obtain appropriate structure size distributions

NIOSH Hazard Assessment Research Priorities

- **Studying carbon black, single-walled carbon nanotubes (SWCNT), multi-walled carbon nanotubes (MWCNT), TiO_2spheres and wires, silicon nanowires, silver, nickel, quantum dots, ZnO, WC-Co, 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**

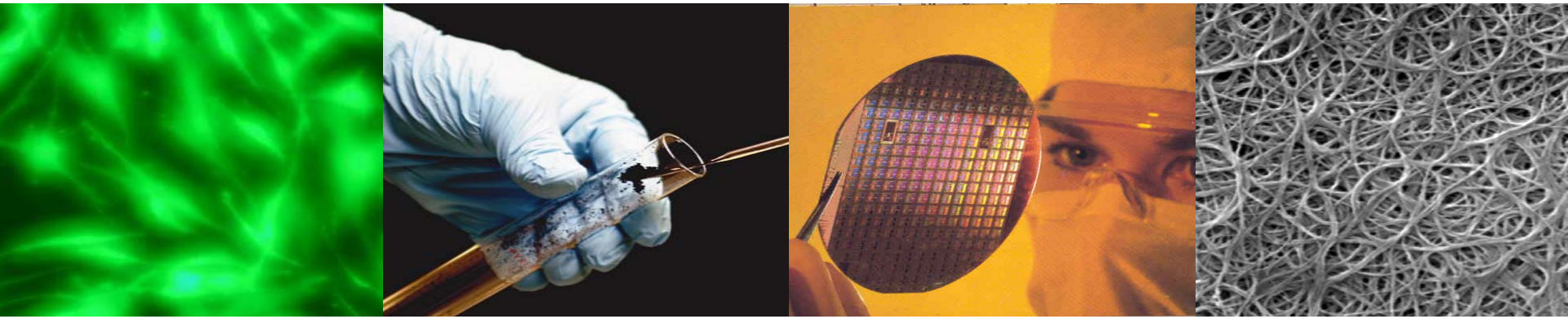
TiO2, titanium dioxide
ZnO, zinc oxide
WC-Co, tungsten carbide/cobalt

NIOSH Hazard Assessment Research Key Accomplishments

- **Pulmonary exposure to**
  - Carbon nanotubes cause rapid and persistent fibrosis in mice
  - Certain nanoparticles (SWCNT or TiO_2) can cause cardiovascular dysfunction
  - MWCNT or TiO_2 nanowires can induce inflammatory mediators in certain regions of the brain
- **Carbon nanotubes**
  - Multi-walled nanotubes can reach the intrapleural space (site of mesotheliomia)
  - Single-walled nanotubes can interfere with cell division

SWCNT, single-walled carbon nanotubes
MWCNT, multi-walled carbon nanotubes
TiO_2 , titanium dioxide

NANOTECHNOLOGY AT GEORGIA TECH: FORGING THE SMALL



William D. Hunt, PhD
Professor
School of Electrical and Computer Engineering
Georgia Institute of Technology

DISCLOSURE: Professor W. D. Hunt is the Chief Technical Officer and has 1/3 ownership in Zen Sensing, LLC

Overarching Nanotechnology Goals at Georgia Tech

- **Develop new types of devices and systems with nanotechnology components**
- **Collaborate with Emory Medical School and CDC**
  - Vital importance of complementary set of skills and practical and translation of science to practice
- **Move the technology developments to the marketplace**
- **Guide students and post-docs to a career in nanotechnology**
  - Importance of student education related to ethics and safety

Nanotechnology Research Centers at Georgia Tech

- **Georgia Tech is a NNIN member**
  - Housed in the Marcus Nanotechnology Research Center
- **The Nanotechnology Center for Personalized and Predictive Oncology**
  - Lead S. Nie; Funding NCI/NIH
- **The Nanomedicine Development Center**
  - Lead G. Bao; Funding NIH Roadmap Initiative in Nanomedicine
- **The Program of Excellence in Nanotechnology**
  - Lead G. Bao; Funding NHLBI/NIH

NNIN, National Nanotechnology Infrastructure Network
NCI, National Cancer Institute, NIH
NHLB, National Heart, Lung and Blood Institute, NIH

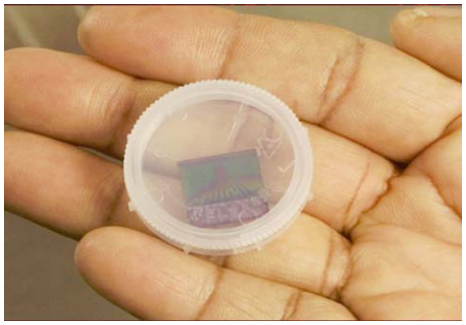
Nanomedicine Research Projects at Georgia Tech

- Bioconjugated nanoparticle probes for molecular and cellular imaging (S. Nie)
- Blood analysis by nanophontonic near infrared spectroscopy (A. Adibi)
- Fluorescent RNA probes (Molecular Beacons) for *in vivo* analysis (G. Bao)
- ZnO nanobelts for energy harvesting for implants (Z.L. Wang)
- Nanofluidics for sample handling for DNA analysis (P. Kohl)

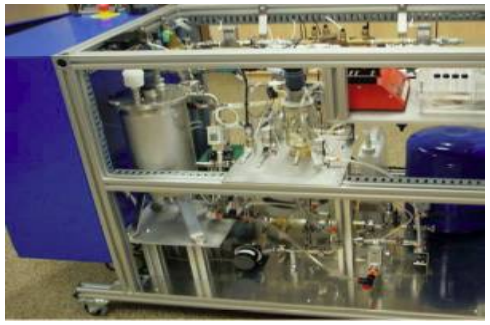
Biohazard Water Analyzer and Detector Using Carbon Nanofiber Arrays

- **Principle**
  - Carbon nanofiber-DNA conjugates and billions of nanofibers on a chip
- **Application – Biohazard water analyzer**
  - Measures the total and viable cell concentrations
  - Detects common and rare pathogens associated with waterborne illnesses - *E. coli* O157:H7, C*ryptosporidium* and *Giardia* species

Carbon nanofiber



Biosensor chip



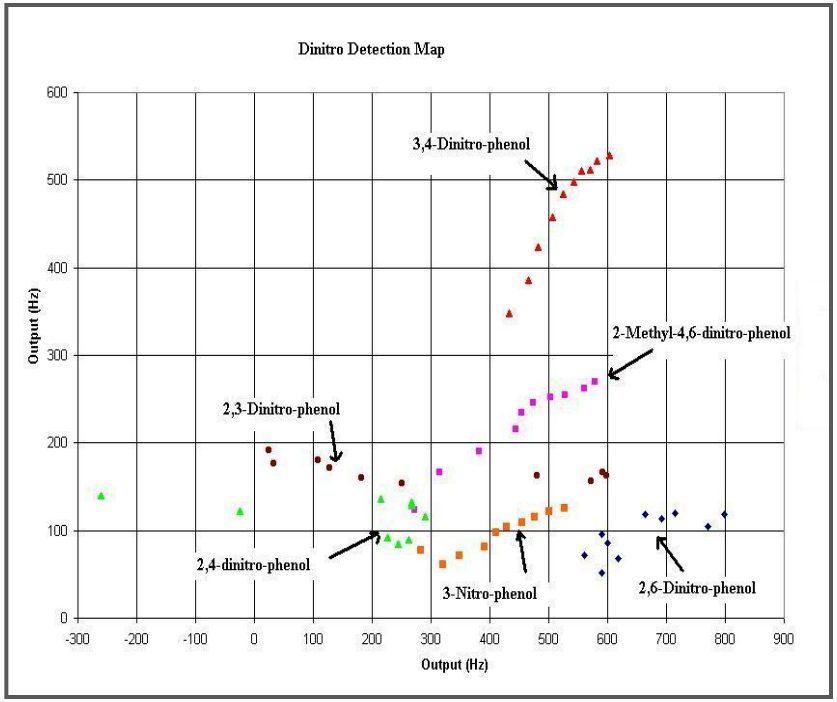
Biohazard analyzer system

Bruce Gale, University of Utah, Alan Cassell, NASA Ames Research Center
Neil Gordon, Early Warning Inc., Devin Brown, Georgia Tech

Biomolecular Recognition Using a Digital Radio

Principle

- Detecting conformational change, a critical aspect of almost all biomolecular interactions, in vapor phase using a nanoscale hydrogel
- Differentiation between close chemical analogs, indistinguishable by mass spectrometry: small molecules(~300 Daltons), lipids, proteins, DNA, cells



Application – Real-time analysis of exhaled breath

- Detection of methylated DNA, phosphorylated proteins

Professor William D. Hunt, School of Electrical and Computer Engineering
Georgia Institute of Technology

Ethically Contentious Research and Innovation:

"Ethics is Not a Four Letter Word"

Roberta Berry, JD, PhD
Assoc. Prof. of Public Policy
Principal Investigator

Wendy Newstetter, PhD
Dir. of Learning Sciences Research, Dept. of Biomedical Engineering Co-Principal Investigator

Robert Kirkman, PhD
Assoc. Prof. of Public Policy
Dir., Center for Ethics & TechnologyCo-Principal Investigator

Kathy Kinlaw, MDiv
Assoc. Dir., Emory Center for Ethics Principal Investigator

Edward Queen, PhD, JD
Dir., Ethics and Servant Leadership
Emory Center for Ethics
Co-Principal Investigator

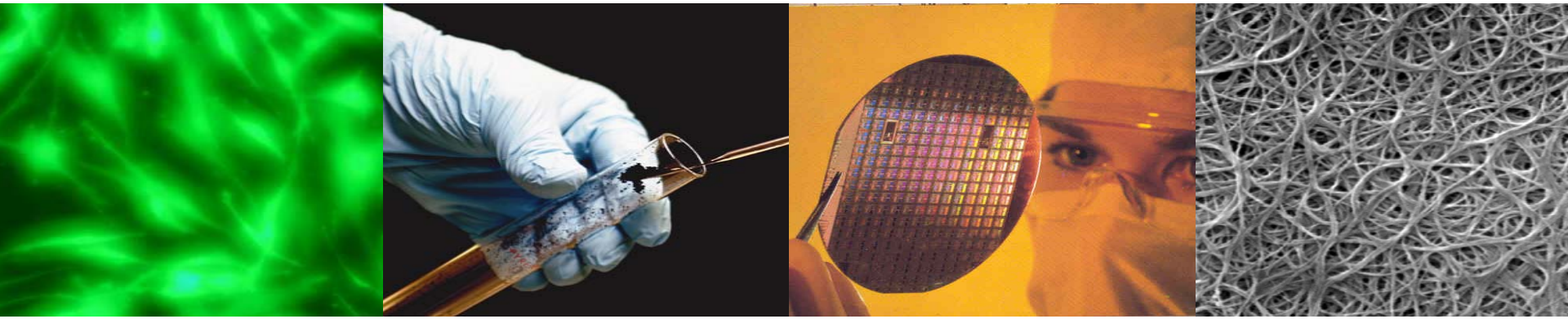
Gillian Hue, PhD
Fellow, Emory Center for Ethics, Program in Science and Society
Senior Personnel

Leslie Wolf, JD, MPH
Assoc. Prof. of Law
Principal Investigator

Martha Elks, MD, PhD
Assoc. Dean for Med. Ed.
Prof. and Chair of Med. Ed.
Principal Investigator

Background Photo
Courtesy of National Science Foundation

GLOBAL EFFORTS TO PREVENT OCCUPATIONAL HAZARDS FROM NANOTECHNOLOGY



Kristen M. Kulinowski, PhD
***Executive Director*, Center for Biological and Environmental Nanotechnology**
***Director*, International Council on Nanotechnology**
Faculty Fellow in Chemistry
Rice University

IMAGE CREDITS: Rice University, NIOSH

GLOBAL EFFORTS TO PREVENT HUMAN HEALTH HAZARDS FROM NANOTECHNOLOGY

- **Gaps**
  - Greater knowledge base on hazard than exposure
  - Occupationally-relevant research is almost non-existent
  - No quantitative exposure limits to inform occupational practice

RESULT
Research knowledge base
has little practical application to human health

GLOBAL EFFORTS TO PREVENT HUMAN HEALTH HAZARDS FROM NANOTECHNOLOGY

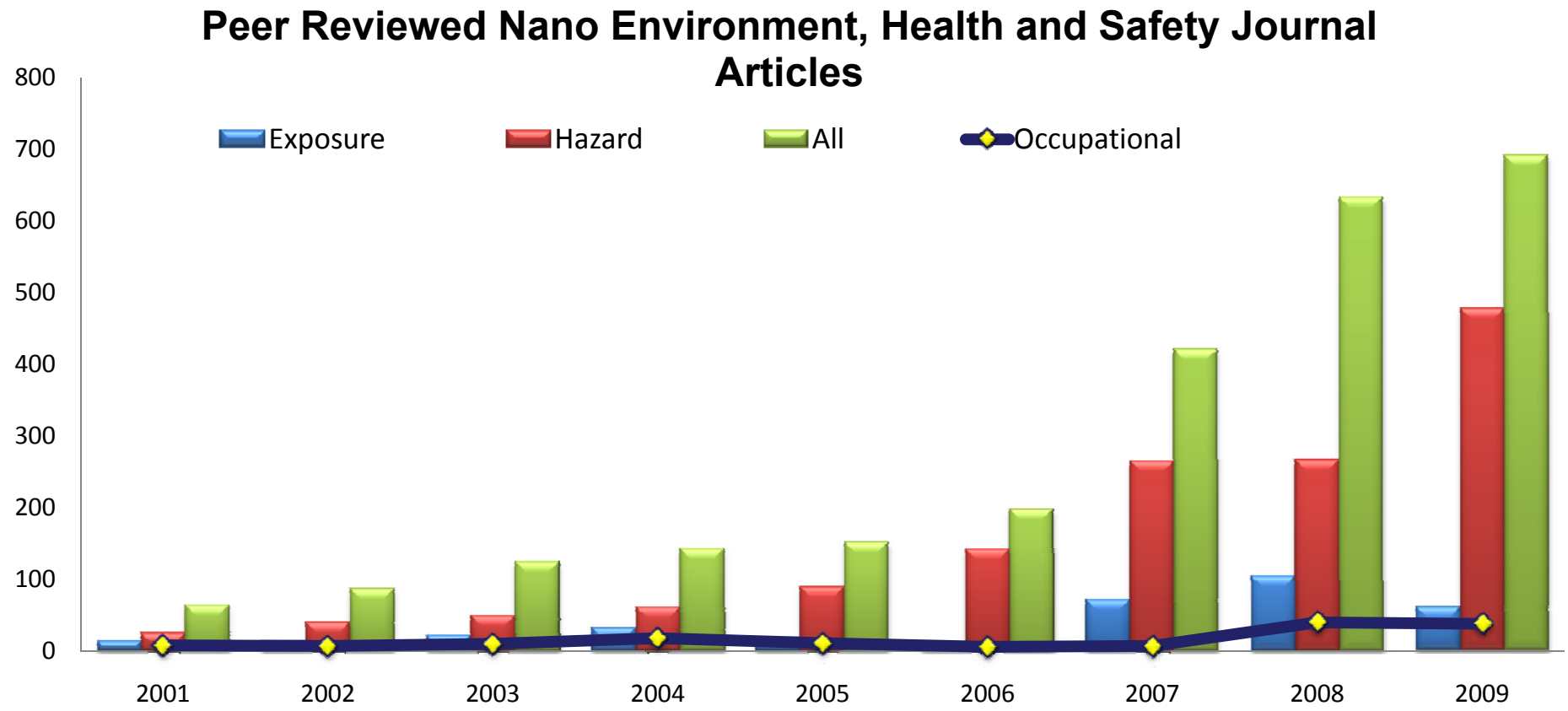
- **Progress to Bridge the Gaps**
  - Government: Guidance documents and first regulatory decisions
  - International bodies: Standards and outreach to emerging economies
  - Grassroots and consortia: Research protocols and practical tool

RESULT

Lots of activity, little high level coordination

- **Bringing It All Together**

Occupationally Relevant Research is Lagging



Less than 6% of all nano impacts research is of high occupational relevance

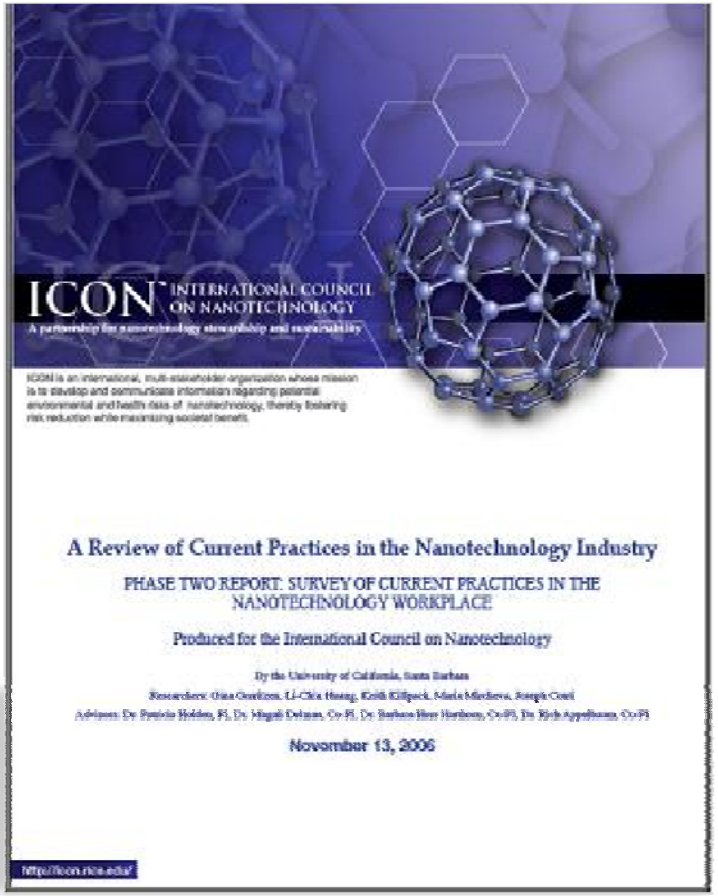
All , All published research relating to the potential environmental, health and safety effects of nanomaterials
Occupational Health , e.g., efficacy of gloves, respirators; workplace exposure assessment

SOURCE: ICON Virtual Journal of Nano Environment, Health and Safety http://icon.rice.edu/research.cfm

Stakeholders Seek Information about Good Practice

Comprehensive, international survey of handling practices in the nanotech workplace

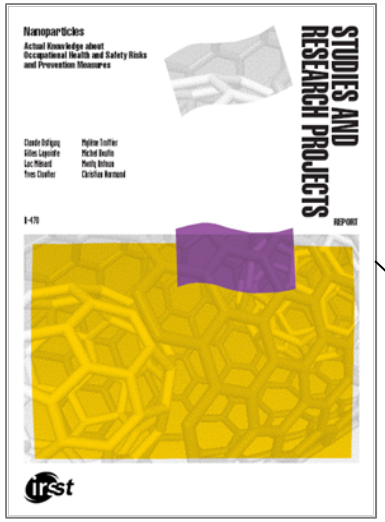
"Surveyed organizations reported that they believe there are special risks related to the nanomaterials they work with…and that they are ***actively seeking additional information on how to best handle nanomaterials****."*



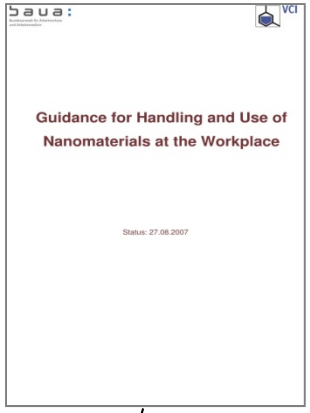
Survey respondents were nanomaterial manufacturers, users and researchers in industry, academia and independent and government labs from North America, Europe, Asia and Australia.

SOURCE: http://tinyurl.com/iconsurvey

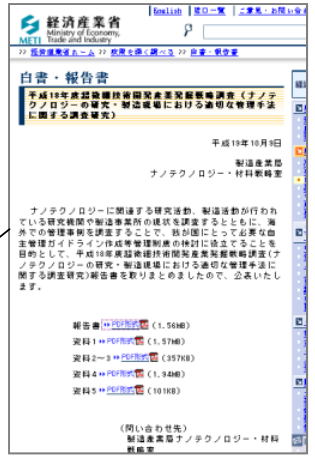
Government Guidance Documents



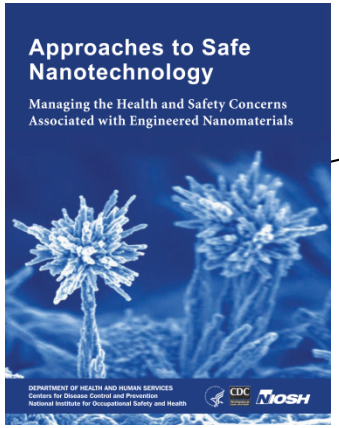
IRSST



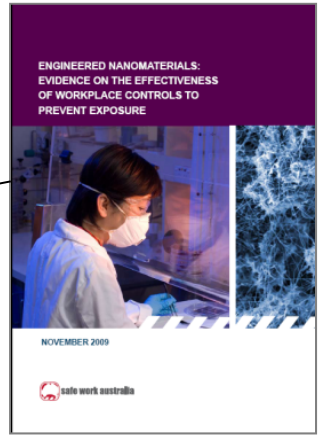
BAuA
UK HSE



METI
JNIOSH



NIOSH



Safe Work
Australia

IRSST, Institut de recherche Robert-Sauvé en santé et en sécurité du travail
BAuA, (German) Federal Institute for Occupational Safety and Health
HSE, Health and Safety Executive
METI, Ministry of Economy, Trade and Industry (Japan)
NIOSH, Japan National Institute for Occupational Safety and Health

Regulatory Developments of Note in the United States

- **Toxic Substances Control Act (TSCA)**
  - Manufacturers have registered dozens of nanoscale materials under TSCA
  - Special rules issued for carbon nanotubes
    - Recognize nanotubes as new substances
    - Require use of protective measures in the workplace
- **Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)**
  - Companies fined for failing to register nanoscale products making antimicrobial claims

Regulatory Developments of Note in Europe

- **REACH = Registration, Evaluation, Authorization and Restriction of Chemical Substances**
  - Low-volume registration thresholds
  - Manufacturers required to provide toxicity information
  - Extends to existing as well as new chemicals
- **European Parliament**
  - Calling for “nano” label to inform consumers about nano ingredients

Global Activities of Established International Bodies

Organization for Economic Cooperation and Development INTERGOVERNMENTAL GROUP

- Safety testing on representative set of nanomaterials; development of test guidelines for assessing nanomaterial toxicity
- Primarily government officials

ISO/TC 229 Nanotechnologies: VOLUNTARY STANDARDS

- Developing consensus standards for terminology, characterization, and health & safety
- technical Report on health & safety practices in occupational settings
- Multi-stakeholder: government, industry, legal, academic, non-governmental

World Health Organization: NON-GOVERNMENTAL

- Collaborating Centers developing information on hazards, risks, and controls
- Doing outreach to emerging countries on safe handling of nanomaterials
- Non-governmental but partners with government

Grassroots Groups and Consortia

GoodNanoGuide*:

http://www.goodnanoguide.org

- Online resource for developing and sharing safe handling protocols

International Alliance for NanoEHS Harmonization*

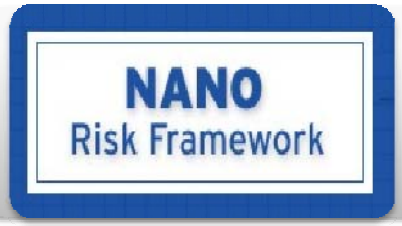
http://www.nanoehsalliance.org

- Grassroots effort by research scientists to develop validated toxicity protocols

NanoImpactNet* (EU)

http://www.nanoimpactnet.eu

- Coordinating test strategies, screening tools and risk assessment methodologies



NanoRisk Framework

http://www.nanoriskframework.com

- Risk management framework developed by DuPont and Environmental Defense Fund

*Significant NIOSH participation or sponsorship

International Council on Nanotechnology

INCLUSIVE: Multi-stakeholder cooperation

GLOBAL: International perspective

TECHNICAL: Grounded in science

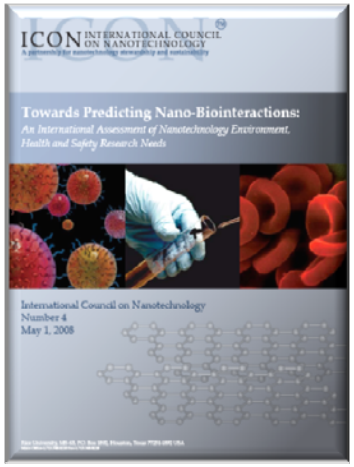
PROACTIVE: Stewards for sustainability

Developing and communicating information regarding potential environmental and health risks of nanotechnology to foster risk reduction and maximize societal benefit.

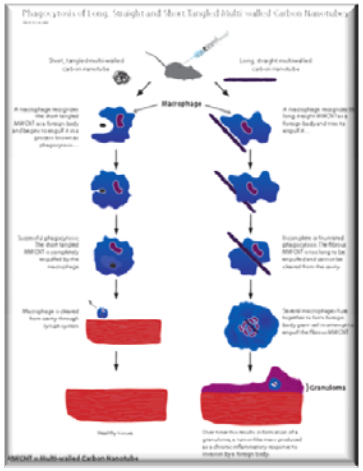
http://icon.rice.edu

ICON is a Valuable Source of Credible Information

Survey



Reports



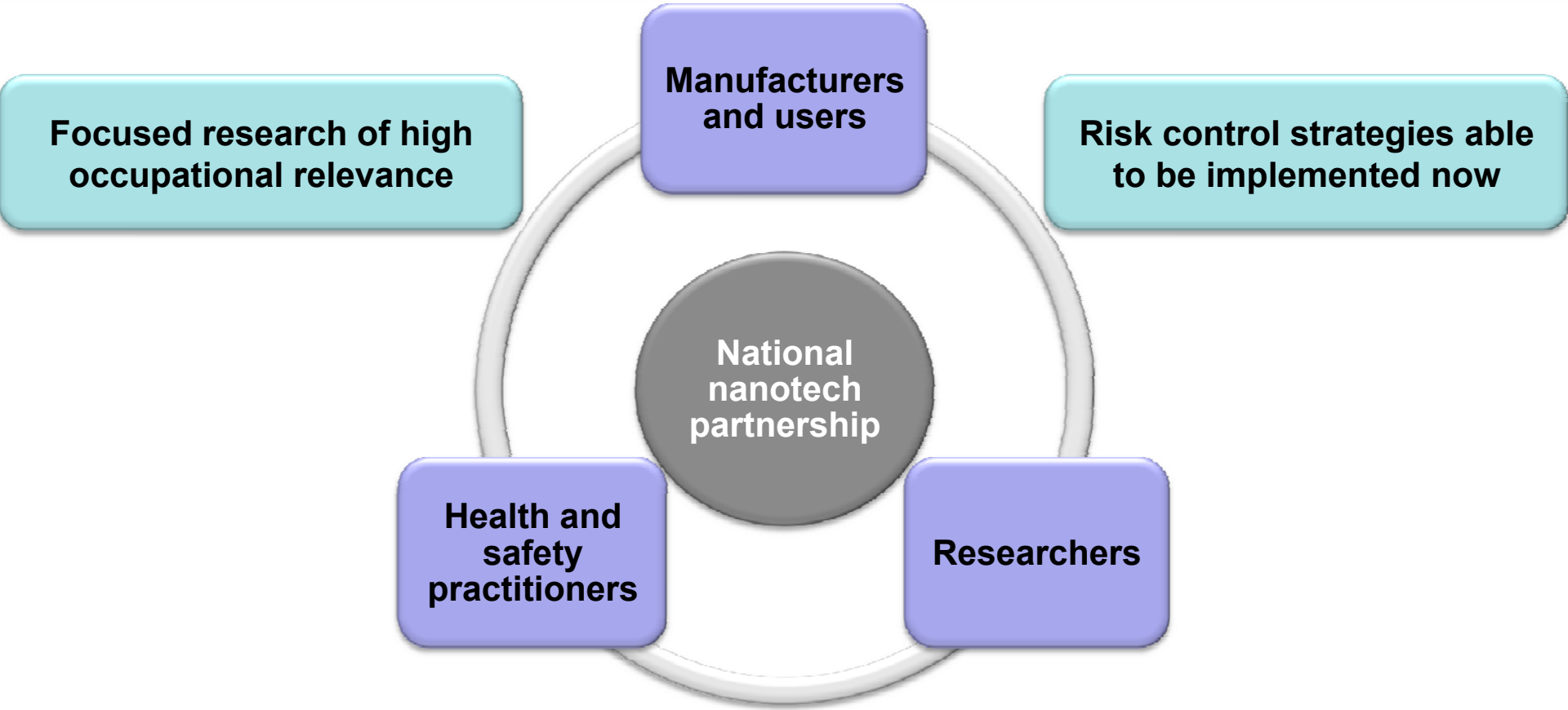
Backgrounders

nanoEHS VIRTUAL JOURNAL

Knowledge Base

http://icon.rice.edu

Bringing It All Together



Howard and Murashov, J Nano Particle Res (2009) 11:1673–1683

PUBLIC HEALTH GRAND ROUNDS

Office of the Director

April 15, 2010