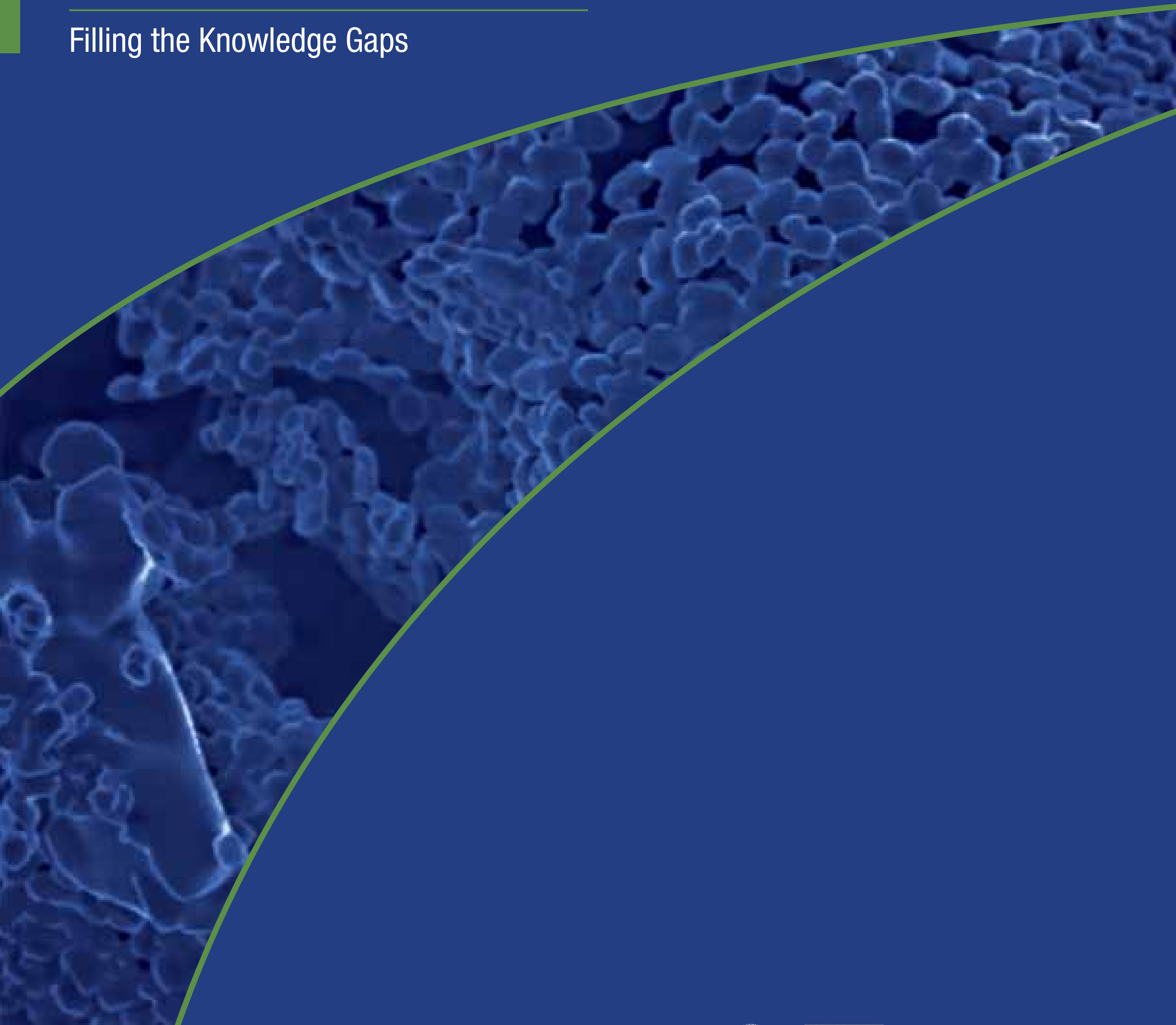
Strategic Plan

for NIOSH Nanotechnology Research and Guidance

Filling the Knowledge Gaps



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

On the cover: Scanning electron microscopy image of “spheres” of agglomerated nanometer sized to TiO_2. Courtesy of Altairnano, Inc. Used with permission.

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Foreword

The National Institute for Occupational Safety and Health (NIOSH) is pleased to present the *Strategic Plan for NIOSH Nanotechnology Research and Guidance: Filling the Knowledge Gaps*. This plan updates the September 2005 strategic plan using knowledge gained from results of ongoing research as described in the 2007 report *Progress Toward Safe Nanotechnology in the Workplace: A Report from the NIOSH Nanotechnology Research Center* and the 2009 report *Progress Toward Safe Nanotechnology in the Workplace: A Report from the NIOSH Nanotechnology Research Center, Project Updates for 2007 and 2008.* The NIOSH nanotechnology research program is a cross-sector program that supports the National Occupational Research Agenda (NORA). Nanotechnology provides many opportunities and challenges for all of us in occupational safety and health. The *Strategic Plan* for the nanotechnology program is the roadmap we are using to advance knowledge about the implications and applications of nanomaterials.

Comments received during external review of the document suggested that NIOSH prioritize goals and projects so as to better understand the feasibility of conducting research based on available resources. In addition, specific suggestions on the scientific direction of the research program were also offered by reviewers, such as the need to understand the role of genetics. We have attempted to acknowledge these issues in finalizing this version of the strategic plan.

This published version of the document will continue to exist on the NIOSH Web site and be updated periodically to reflect new research efforts.

John Howard, M.D. /s
Director, National Institute for
Occupational Safety and Health
Centers for Disease Control and Prevention

Executive Summary

Nanotechnology—the manipulation of matter on a near-atomic scale to produce new materials—has the potential to transform many industries, from medicine to manufacturing, and the products they produce. Research in nanoscale technologies continues to expand worldwide. By 2015, the National Science Foundation estimates that nanotechnology will have a $1 trillion impact on the global economy and employ two million workers, one million of whom will likely reside in the United States. While this emerging technology holds great promise, it also presents unknown risks, especially to the health of workers. Many questions remain about how to best manage and control the potential hazards associated with the safe handling of nanomaterials. Thus for the period 2009–2012, NIOSH will collaborate with stakeholders at home and abroad to fill knowledge gaps related to nanotechnology, to identify and characterize hazards associated with nanomaterials, and to develop guidance for workers exposed to nanomaterials. Protecting the health of workers involved with nanotechnology is a global issue that requires international cooperation, commitment, and collaboration.

Nanotechnology and NIOSH Research

The rapid spread of nanotechnology threatens to outpace knowledge about its attendant safety and health risks. As nanotechnology moves forward into all avenues of commerce, stakeholders from industry, academia, labor, occupational safety and health professions, and government must make a concerted effort to identify and characterize the human health hazards associated with nanomaterials. NIOSH will continue to play an active role in this process. In June 2007, NIOSH reported its progress in conducting nanotechnology research and drafting guidance for the safe handling of nanomaterials [see report *Progress Toward Safe Nanotechnology in the Workplace: A Report from NIOSH Nanotechnology Research Center* at http://www.cdc.gov/niosh/topics/nanotech/, DHHS (NIOSH) Publication No. 2007–123]. An update of the progress report listing project updates from 2007–2008 was published in November 2009 [DHHS (NIOSH) Publication No. 2010–104]. [http://www.cdc.gov/niosh/docs/2010-104/pdfs/2010-104.pdf]

NIOSH Nanotechnology Research Center (NTRC)

Given the rapid growth and global reach of nanotechnology, NIOSH established the Nanotechnology Research Center (NTRC) in 2004 to conduct research and provide guidance to protect workers involved with nanomaterials. The NTRC and its Steering Committee consist of a diverse group of NIOSH scientists charged with overseeing the Institute's scientific and organizational plans in nanotechnology health research.

The main goals of the NTRC are to:

1. Determine whether nanoparticles and nanomaterials pose risks of injuries and illnesses for workers.

2. Conduct research on applying nanotechnology to the prevention of work-related injuries and illnesses.
3. Promote healthy workplaces through interventions, recommendations, and capacity building.
4. Enhance global workplace safety and health through national and international collaborations on nanotechnology research and guidance.

Strategic Plan

With the input of a broad range of stakeholders in government, academia, and the private sector, NIOSH developed a strategic plan for nanotechnology research and guidance. The strategic plan also highlights how NIOSH's critical research and guidance efforts align with and support the National Nanotechnology Initiative's Environmental Health and Safety priorities. For the period 2009–2012, NIOSH will continue to fill information and knowledge gaps in priority areas. Specifically, NIOSH will:

1. Conduct toxicological research on nanoparticles likely to be commercially available.
2. Conduct research to identify long-term health effects of carbon nanotubes (CNT).
3. Develop recommendations for controlling occupational exposure to fine and ultrafine titanium dioxide (TiO_2) including development of recommended exposure limits (RELs). Conduct research on improving sampling and analytical methods, determining the extent of workplace exposures, and controlling airborne exposures below the REL. Identify what medical surveillance is appropriate. Consider to what extent the observed relationship between TiO_2 particle size and toxicity can be generalized to other metal oxides.
4. Develop recommendations for controlling occupational exposures to purified and unpurified single-walled carbon nanotubes (SWCNT) and multi-walled carbon nanotubes (MWCNT) including development of RELs. Conduct research to address gaps in information on sampling, analysis, exposure assessment, instrumentation and controls. Identify what medical surveillance or epidemiological studies are appropriate.
5. Conduct research on how to identify categories of nanoparticles that can be distinguished on the basis of similar physico-chemical properties. Conduct research to develop RELs and ultimately recommended exposure standards for these categories.
6. Conduct research on explosion potential of various nanoparticles.

This plan proposes 38 activities in 10 critical areas to help protect the nanotechnology workforce. It is a large challenge but one that NIOSH is well prepared to accept.

Abbreviations

AIHA	American Industrial Hygiene Association
ACGIH	American Conference of Governmental Industrial Hygienist
ANSI	American National Standards Institute
ASSE	American Society of Safety Engineers
ASTM	American Society for Testing and Materials
ASSE	American Society of Safety Engineers
CAS	chemical abstract system
CDC	Centers for Disease Control and Prevention
CIB	Current Intelligence Bulletin
CNF	carbon nanofibers
CNT	carbon nanotubes
COPD	chronic obstructive pulmonary disease
CPSC	Consumer Product Safety Commission
DART	Division of Applied Research and Technology
DEP	diesel exhaust particulate
DHHS	U.S. Department of Health and Human Services
DOE	U.S. Department of Energy
ECHA	European Chemicals Agency
EHS	environmental health and safety
EPA	U.S. Environmental Protection Agency
ESLI	end-of-service life indicator
EU	European Union
FAQs	frequently asked questions
FMSH	Federal Mine Safety and Health
FY	fiscal year

GIS	geographical information systems
HELD	Health Effects Laboratory Division
HEPA	high-efficiency particulate air
HPS	Health Physics Society
HPV	high production volume
HVAC	heating, ventilation, and air conditioning
IANH	International Alliance for NanoEHS Harmonization
ICON	International Council on Nanotechnology
ID	identification
IEC	International Electrotechnical Commission
IOM	Institute of Occupational Medicine
ILO	International Labor Organization
INRS	Institut National de la Recherchè Scientifique
ISO	International Organization for Standardization
ISPE	International Society for Pharmaceutical Engineering
IRSST	Institut de recherché Robert–Sauvè en santé et en sécurité du travail
MINChar	Minimum Information Needed for Characterization of Nanomaterials
MSDS	material safety data sheet
MSHA	U.S. Mine Safety and Health Adminstration
MWCNT	multi-walled carbon nanotubes
NASA	National Aeronautics and Space Administration
NCER	National Center for Environmental Research
NEHI	Nanotechnology Environmental and Health Implications
NGO	non-governmental organization
NIEHS	National Institute of Environmental Health Sciences
NIL	Nanoparticle Information Library
NIOSH	National Institute for Occupational Safety and Health
NIST	National Institute of Standards and Technology

nm	nanometer(s)
NNI	National Nanotechnology Initiative
NORA	National Occupational Research Agenda
NSET	Nanoscale Science, Engineering, and Technology
NSF	National Science Foundation
NTRC	Nanotechnology Research Center
NSC	National Safety Council
OEP	Office of Extramural Programs
OECD	Organization for Economic Cooperation and Development
OELs	occupational exposure limits
OEP	Office of Extramural Programs
OSH	occupational safety and health
OSHA	U.S. Occupational Safety and Health Administration
PCAST	Presidents Council of Advisors on Science and Technology
POSS	polyhedral oligomeric silsesquioxanes
PPE	personal protective equipment
PPNANSG	Project Planning Nanotechnology Strategic Goal
PPNANIG	Project Planning Nanotechnology Interim Goal
PPNANAOG	Project Planning Nanotechnology Activity/Output Goal
QRA	quantitative risk assessment
r2p	Research to Practice
REL	recommended exposure limit
RFA	request for application
RM	reference material
ROS	reactive oxygen species
SWCNT	single-walled carbon nanotubes
TC	technical committee
TEM	transmission electron microscopy

TiO_2	titanium dioxide
TNO	Netherlands Organisation for Applied Scientific Research
TWA	time weighted average
$\mu g/m^3$	microgram per cubic meter
UN	United Nations
VGCF	vapor grown carbon fibers
WHO	World Health Organization
WPMN	Working Party on Manufactured Nanomaterials
WPN	Working Party on Nanotechnology

Contents

Acknowledgments

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1 Introduction

1.1 Background

Nanotechnology is a system of innovative methods to control and manipulate matter at near-atomic scale to produce new materials, structures, and devices. Nanoparticles are a specific class or subset of these new materials, having at least one dimension that is less than 100 nanometers. They exhibit unique properties because of their nanoscale dimensions. Nanotechnology offers the potential for tremendous improvement and advances in many areas that may benefit society, such as integrated sensors, semiconductors, medical imaging, drug delivery systems, structural materials, sunscreens, cosmetics, coatings, and many other uses. Nanotechnology is one of the most rapidly growing industries across the world. By 2015, the global market for nanotechnology-related products is predicted to reach $1 trillion and employ 1 million workers in the United States alone [Lux 2007]. There are currently over 1,000 commercial products on the market (Figure 1).The properties of nanoparticles (e.g., size, surface area, reactivity) that yield many of the far reaching

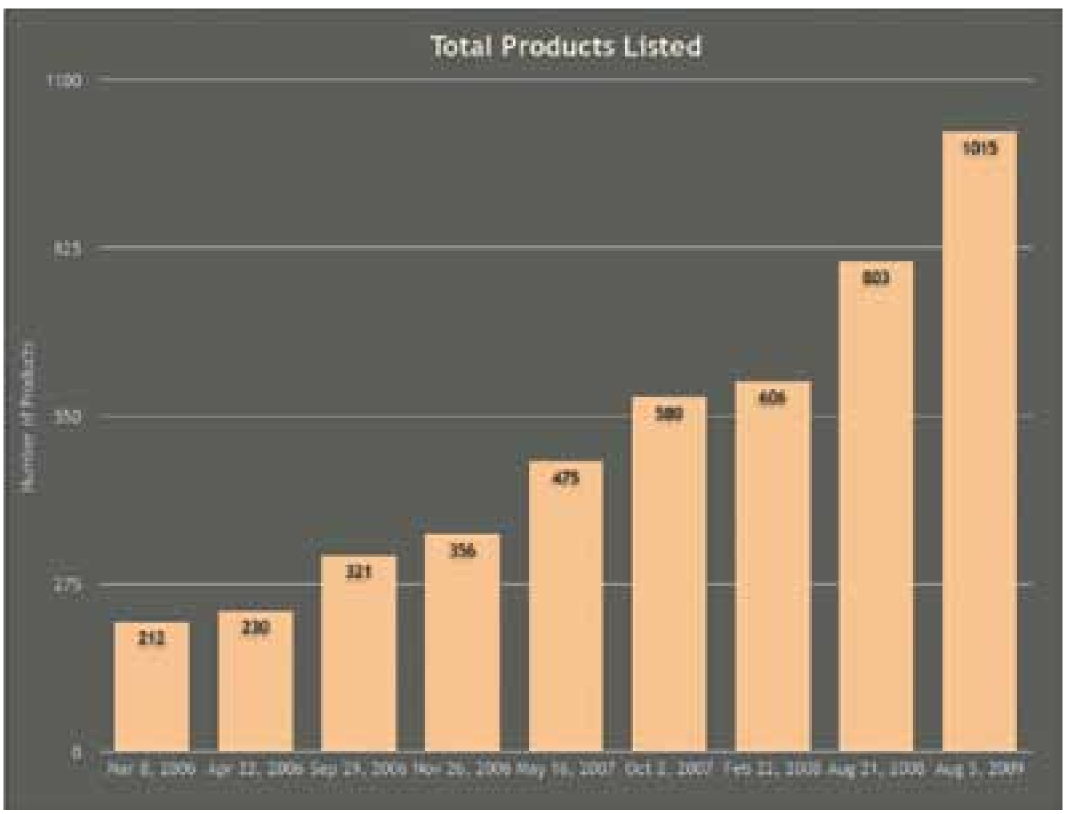


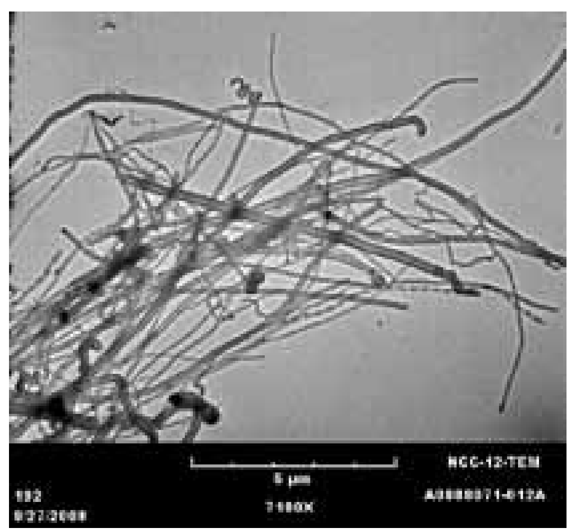
Figure 1. Total nanomaterial containing products in the Wilson Center Consumer Product Inventory (used with permission from Project on Emerging Nanotechnologies Woodrow Wilson International Center for Scholars)

societal benefits may also pose risks. Currently, increasing numbers of workers are potentially exposed to nanomaterials in research laboratories, start-up companies, production facilities, and in operations where nanomaterials are processed, used, disposed or recycled. The challenges are to determine whether the nature of intentionally produced (engineered) nanostructured materials and devices presents new occupational safety and health risks. At the same time, there is a need to address how the benefits of nanotechnology can be realized while proactively minimizing the risk.

Efforts across multiple federal agencies are fostering the development and use of nanotechnology. In 2001, the President's Council of Advisors on Science and Technology collaborated with the interagency National Science and Technology Council to create the National Nanotechnology Initiative [NNI 2001]. This initiative supports basic and applied research and development in nanotechnology to create new nanomaterials and to disseminate new technical capabilities to industry. The purpose of the NNI is to facilitate scientific breakthroughs and maintain U.S. competitiveness in nanoscience. A stated goal of this interagency program is to ensure that nanotechnology research leads to the responsible development of beneficial applications by giving high priority to research on societal implications, human health, and environmental issues related to nanotechnology.

The National Institute for Occupational Safety and Health (NIOSH) is the Federal agency responsible for conducting research and making recommendations to prevent work-related injury, illness, and death. NIOSH is a member of the Nanoscale Science, Engineering and Technology (NSET) Subcommittee of the National Science and Technology Council. As such, NIOSH is active in (1) identifying critical issues related to possible hazards of nanomaterials, (2) protecting worker safety and health in this emerging technology, and (3) developing a strategic plan to address such issues and recommend prevention strategies for the safe handling and use of nanomaterials.

A nanotechnology researcher creating a slurry of carbon nanotubes. (Image courtesy of Mark Methner, NIOSH)



An electron micrograph of the personal breathing zone sample collected from the researcher spraying the carbon nanotube slurry

Because of their small size and large surface area, engineered nanoparticles have chemical, physical, and biological properties distinctly different than fine particles of similar chemical composition. Such properties may include a high rate of pulmonary deposition, the ability to travel from the lung to systemic sites, the ability to penetrate dermal barriers, and a high inflammatory potency per mass. At a time when materials and commercial applications are being conceived, NIOSH is positioned well to proactively identify, assess, and resolve potential safety and health issues posed by nanotechnology. NIOSH has 38 years of experience in conducting research and formulating recommendations for occupational safety and health. During this period, NIOSH has developed considerable expertise in measuring, characterizing, and evaluating new processes and new materials by conducting quantitative exposure assessments and evaluating health effects. NIOSH also has expertise in developing control systems and prevention strategies for incidental nanoparticles (e.g., diesel exhaust, welding fume, smelter fume, and fire smoke particles). NIOSH will reapply this experience to address similar issues for engineered nanoparticles.

In 2004, NIOSH created the Nanotechnology Research Center (NTRC) to identify critical issues, create a strategic plan for investigating these issues, coordinate the NIOSH research effort, develop research partnerships, and disseminate information gained. The NTRC is comprised of nanotechnology-related activities and projects consisting of and supported by more than 30 scientists from various NIOSH divisions and laboratories. Through the NTRC, NIOSH has identified 10 critical research areas for nanotechnology research and communication. These 10 critical research areas are: (1) toxicity and internal dose, (2) measurement methods, (3) exposure assessment, (4) epidemiology and surveillance, (5) risk assessment, (6) engineering controls and personal protective equipment (PPE), (7) fire and explosion safety, (8) recommendations and guidance, (9) communication and information, and (10) applications. By working in these critical research areas, NIOSH has comprehensively begun to address the information and knowledge gaps necessary to protect workers and responsibly move nanotechnology forward so that its far-reaching benefits may be realized. A summary of research projects may be found in Appendix A.

Congruent with the efforts of the NTRC are the efforts of the NIOSH Office of Extramural Programs (OEP). OEP uses several mechanisms (R01, R21, R43/44) for funding research*. OEP funding of nanotechnology-related research has been undertaken to help increase the knowledge of nanotechnology and engineered nanomaterials as they relate to occupational safety and health. Research areas supported by NIOSH OEP include emission and exposure assessment methods for nanoparticles in the workplace, toxicology of engineered nanomaterials, and the use of nanotechnology for improved workplace monitoring.

NIOSH is working strategically to address the 10 critical research areas through active intramural and extramural research programs and collaborations. NIOSH is committed to conducting and supporting studies that will improve scientists' abilities to identify potential occupational health effects of nanomaterials. NIOSH will facilitate the translation of those findings into effective workplace practices.

*NIOSH Office of Extramural Programs: http://www.cdc.gov/oep

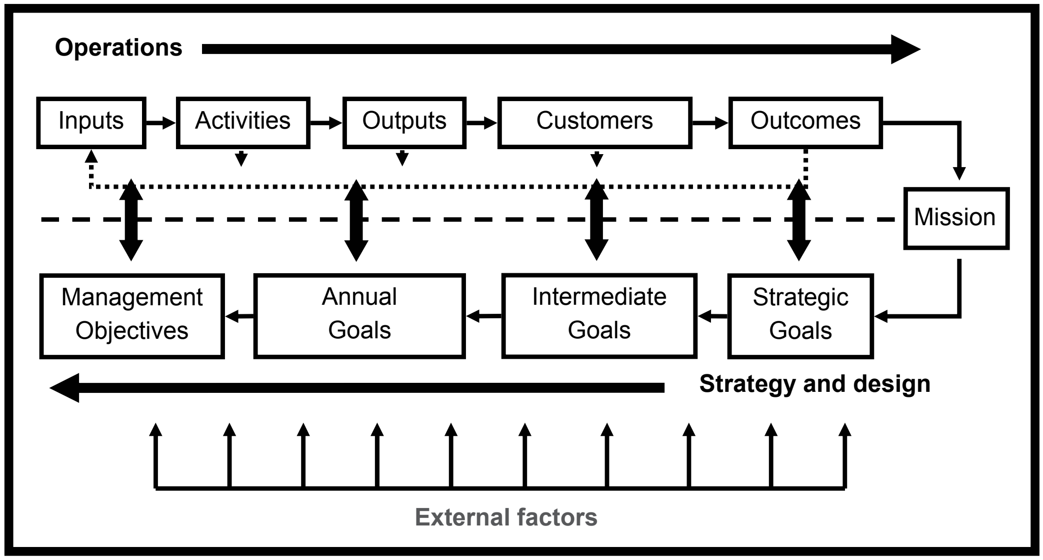


Figure 2. Schematic of the overall NIOSH logic model

1.2 NIOSH Logic Model

Like other scientific organizations, NIOSH can be described by a model of the way it functions to solve identified problems under various conditions. The overall NIOSH logic model is presented in Figure 2. It has a conventional horseshoe shape with the operational upper branch proceeding from inputs to outcomes and with the strategic lower branch proceeding from strategic goals to management objectives. Both branches are correlated vertically and are subject to external factors.

The NIOSH research program begins with an analysis of production and planning inputs and follows the NIOSH operational model (Figure 3). This analysis determines what can and should be done and thereby identifies research priorities. Intramural and extramural researchers present their project proposals which receive appropriate internal and external review and are funded based on proposal merits. Research activities produce outputs such as published materials, oral presentations, training and educational materials, tools, methods, and technologies. NIOSH research outputs are transferred directly to the final customers and partners (who implement improvements in workplace safety and health) or to intermediate customers (who transform further NIOSH outputs and produce intermediate outcomes). These intermediate outcomes such as pilot technologies, training programs, and regulations and standards are forwarded to the final customers. Since NIOSH is not a regulatory agency, it relies heavily on efforts by intermediate and final customers to achieve ultimate outcomes in the form of workplace safety and health improvements. Effectiveness in achieving these ultimate outcomes is influenced at all stages of program operation by both external factors (such as economic and social conditions) and the regulatory environment. Results of NIOSH-funded research and customer feedback (intermediate and final) contribute to the subsequent rounds of program planning.

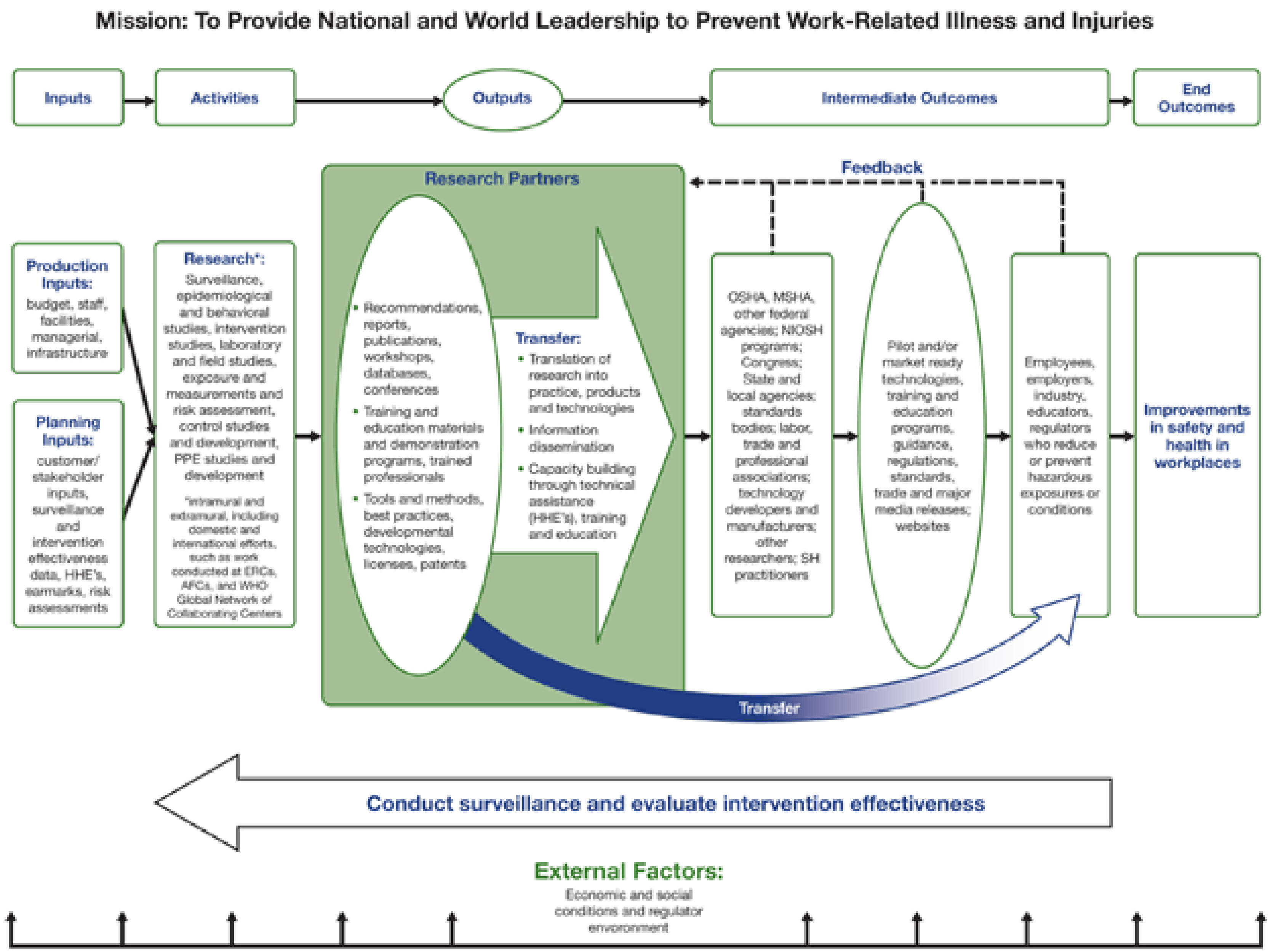


Figure 3. Schematic of the NIOSH operational model

2 Inputs

2.1 Congressional Mandate

In the Occupational Safety and Health Act of 1970 (OSH Act, Public Law 91–596) and the Federal Mine Safety and Health Act of 1977 (FMSH Act, Public Law 95–164), Congress declared that its purpose was to assure, insofar as possible, safe and healthful working conditions for every working man and woman to preserve our human resources. In these Acts, NIOSH is given the responsibility for recommending occupational safety and health standards and describing exposures that are safe for various periods of employment. These include (but are not limited to) the exposures at which no worker will suffer diminished health, functional capacity, or life expectancy as a result of his or her work experience. By means of criteria documents and other publications, NIOSH communicates these recommended standards to regulatory agencies such as the Occupational Safety and Health Administration (OSHA), the Mine Safety and Health Administration (MSHA), and others in the occupational safety and health community. Occupational safety and health research for the mining industry was part of the U.S. Bureau of Mines (Department of the Interior) until 1996 when those functions were transferred to NIOSH as the Office for Mine Safety and Health Research.

Under the OSH Act, NIOSH is charged with conducting "research, experiments, and demonstrations relating to occupational safety and health" and with developing "innovative methods, techniques, and approaches for dealing with [those] problems." The Act specifies target areas of research that include identifying criteria for setting worker exposure standards and exploring problems created by new technology in the workplace. In an amendment to the Act, NIOSH was given responsibility for conducting training and education "to provide an adequate supply of qualified personnel to carry out the purposes of the Act" and for assisting employers and workers with applying methods to prevent occupational injuries and illness (Section 21 of the Act).

2.2 Stakeholders' Input

As it follows from the OSH Act and the FMSH Act, the major stakeholders of NIOSH are the U.S. government (especially OSHA and MSHA), workers, employers, occupational safety and health practitioners and researchers, and the general public. NIOSH receives input through formal committees such as the NIOSH Board of Scientific Counselors, the National Advisory Committee on Occupational Safety and Health, and the Mine Safety and Health Research Advisory Committee and through ad hoc mechanisms such as the NIOSH Web site (www.cdc.gov/niosh), the NIOSH toll-free telephone line (1–800–CDC–INFO), personal contacts with occupational safety and health professionals, and participation in professional conferences and interagency committees. NIOSH also provides stewardship of the National Occupational Research Agenda (NORA) (http://www.cdc.gov/niosh/nora), which is a framework to guide occupational safety and health research into the new millennium—not only for NIOSH but for the entire occupational safety and health community.

The importance of Occupational Safety and Health issues to nanotechnology has been emphasized by the interagency working group on Nanotechnology Environmental and Health Implications (NEHI), under the NSET Subcommittee. NIOSH was formally invited to join the NEHI in 2004, and this interagency effort has consistently encouraged NIOSH to recognize nanotechnology as one of its research priorities.

The importance of research on the occupational safety and health issues for nanotechnology was further stressed at the *National Academies Review of the National Nanotechnology Initiative* held on March 24–25, 2005. Richard Denison (Environmental Defense) and Carol Henry (American Chemistry Council), in their presentations to the National Academies review panel, called for an increase in federal funding of 10%, or $100 million, to address the environmental, safety, and health issues of the nanotechnology industries. These calls were further reiterated in a statement by Fred Krupp (President, Environmental Defense) and Chad Holliday (Chairman and CEO, DuPont) which was published in the June 14, 2005, issue of the *Wall Street Journal*: "An early and open examination of the potential risks of a new product or technology is not just good sense—it's good business strategy. . . . [G]overnment spending on nanotechnology should be reprioritized so that approximately 10% goes to [health and environmental risk]." E. Floyd Kvamme (Co-Chair of the President's Council of Advisors on Science and Technology), who was charged with guiding the NNI, stated in the June 24, 2005, issue of the *Wall Street Journal* that findings "indicated that the primary area for immediate concern is in the workplace, where nanomaterials are being used or manufactured and where there is the greatest likelihood for exposures." In 2008, the President's Council of Advisors on Science and Technology (PCAST) specifically recommended "continuing acceleration of NIOSH funding, particularly for exposure assessment in the context of manufacturing and disposal of nanomaterials and products incorporating relevant quantities of nanomaterials" (PCAST, Addendum to the National Nanotechnology Initiative: Second Assessment and Recommendations of the National Nanotechnology Advisory Panel, July 2008, available at http://www.ostp.gov/galleries/PCAST/PCAST%20Addendum%20Letter.pdf).

Recognizing the importance of this research area and of interagency collaboration, John Marburger (Director of the U.S. Office of Science and Technology Policy) and Joshua Bolten (Director of the Office of Management and Budget) instructed the federal government "to ensure that nanotechnology research leads to the responsible development of beneficial applications, high priority should be given to research on societal implications, human health, and environmental issues related to nanotechnology, and to develop, where applicable, cross-agency approaches to the funding and execution of this research" (July 8, 2005 memorandum for the Heads of Executive Departments and Agencies).

The NEHI working group 2006 publication *Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials* served as the basis for the NNI *2007 Strategy for Nanotechnology-Related Environmental, Health and Safety Research* and identified five priority environmental health and safety research needs: (1) instrumentation, metrology, and analytical methods, (2) nanomaterials and human health, (3) nanomaterials and the environment, (4) health and environmental exposure assessment, and (5) risk management methods (Appendix B) [NNI 2007]. The NIOSH NTRC goals are reflective of these five priority environmental, health and safety areas.

NIOSH has also fostered stakeholder input with trade associations, professional associations, labor, and nongovernmental organizations. These collaborations have provided expertise and resources critical for successfully reviewing research and for developing and disseminating health and safety information on engineered nanoparticles. Some of the ongoing NIOSH NTRC stakeholders include the American Industrial Hygiene Association (AIHA), American Society of Safety Engineers (ASSE), International Safety Equipment Association and National Safety Council (NSC) (Appendix C).

2.3 NIOSH Research Capabilities

The first-class research capability of NIOSH is an integral part of management's inputs to the nanotechnology program. Within its divisions, NIOSH has world renowned researchers who are trained and experienced in the full spectrum of necessary disciplines ranging from epidemiology to intervention effectiveness. Sections 3 and 5 of this document describe current NIOSH research activities including publications on nanomaterials and NIOSH-sponsored meetings and conferences. In addition to their highly qualified research staff, NIOSH has significant laboratory capabilities in particle measurement, collection and characterization, particle surface analysis, measurement of particle surface radicals and activity, and in vitro and in vivo analysis of toxicity and pathogenesis. These laboratories are located in Spokane, Washington; Cincinnati, Ohio; Pittsburgh, Pennsylvania; and Morgantown, West Virginia. NIOSH researchers work closely with a broad range of scientists from industry, academia, and other government agencies. NIOSH involvement in national and international initiatives and programs is an important component of its capacity to address critical occupational safety and health issues in nanotechnology.

2.4 NIOSH Partnerships

NIOSH recognizes both the practical need and the leadership obligation to extend its internal capability by leveraging activities and expertise found in other research institutions, industries, federal agencies, and nongovernmental organizations. These partnerships serve to deliver on multiple objectives; most importantly, they add to the body of knowledge on workplace health and safety issues associated with nanotechnology. Partnerships have taken several forms, ranging from formal letters or memoranda of understanding to informal working agreements on a specific topic. NIOSH will continue to pursue partnerships as a means of achieving the goals of this strategic research plan and as an effective vehicle to develop and disseminate research results that can be translated into practice that will lead to the positive impact of helping nanotechnology move forward responsibly.

NIOSH has successfully used partnerships with industry specific to nanomaterial production, to gain a better understanding of actual workplace exposures, practices, and controls that are in place. The field work that is conducted by NIOSH to assess exposures to engineered nanomaterials represents ongoing partnerships with numerous companies. NIOSH will continue to develop these partnerships in order to receive input on accomplishing its objectives of developing recommendations for the safe handling of nanomaterials; developing methods to measure exposures to nanoparticles; evaluating controls that are, or could be, used in nanomaterial processes; evaluating the need for and the effectiveness of PPE including respiratory protection; and developing communication and information materials that will assist industry in communicating with workers and the public. Several of the industrial partnerships NIOSH has developed have provided opportunities from the beginning of the nanotechnology program to identify areas where additional research was needed.

Collaboration with other research institutes, academia, and government provides NIOSH the opportunity to combine its expertise in workplace health and safety with the capabilities of other organizations that are investigating a specific element of the research that is needed. Developing working relationships with other research institutes provides NIOSH with the information needed to guide its own research and focus its limited resources in the most effective manner. NIOSH has developed partnerships in the areas of toxicology, risk assessment modeling, exposure measurement methods, control technologies, filtration of nanoparticles, and communication of research results and safe work practices.

NIOSH broadens its activities with a wide variety of collaborators and stakeholders by its participation in a number of national and international committees and working groups. This participation provides NIOSH the opportunity to provide and receive input on the key research that is needed to address priority areas.

3 Activities

3.1 NIOSH Nanotechnology Research Center (NTRC)

Vision of the NTRC

The vision of the NTRC is as follows:

Safe nanotechnology by delivering on the Nation's promise—safety and health at work for all people through research and prevention.

Mission of the NTRC

The mission of the NTRC is to provide national and world leadership for research and guidance into the implications of nanoparticles and nanomaterials for work-related injury and illness, and the application of nanoparticles and nanomaterials in occupational safety and health.

3.2 NTRC Steering Committee

The NTRC Steering Committee is responsible for guiding NIOSH scientific and organizational plans in nanotechnology research (including coordination for science and budget) and for developing strategic goals and objectives and performance measures for the NTRC. To ensure the responsiveness, relevance, and impact of NIOSH's nanotechnology program, appropriate representatives of its nanotechnology research program meet in person on an annual basis to update strategic planning for nanotechnology research. At these meetings, the critical occupational safety and health issues arising from nanotechnology are reviewed and updated as appropriate. Regular updates and progress reporting is managed through weekly teleconferences conducted by the NTRC. In addition, meetings are held with appropriate stakeholders at least every other year.

3.3 Current NIOSH Intramural Nanotechnology Research Activities

Current NIOSH research activities in nanotechnology are focused on occupational safety and health implications. NIOSH has expertise in developing control systems and prevention strategies for incidental nanoparticles (e.g., diesel exhaust, welding fume, smelter fume, and fire smoke particles). NIOSH is using this experience to address similar hazard, risk, and control issues for engineered nanoparticles. It appears that nanomaterials that are presently manufactured and subsequently introduced into products have no major physical features that would make them behave differently from fine or ultrafine particles in terms of the ability to control them in the workplace [Methner 2008]. However, the limits of this assumption need continued evaluation. Data from ongoing and proposed studies with engineered nanoparticles are being used to determine nanoparticle exposure concentrations in the workplace, hazards posed by nanomaterials, and the risk of adverse health effects from occupational exposures to nanomaterials. Studies are also providing data on the characteristics of nanomaterials produced and used in the workplace, routes of exposure, work practices, and engineering controls. Findings from these intramural studies are providing scientific data to support the development of occupational safety and health recommendations. The timeline for conducting these research activities with individual research projects is given in Appendix A.

3.4 Current NIOSH Extramural Nanotechnology Research Activities

The NIOSH Office of Extramural Programs (OEP) manages the competitive process for awarding occupational safety and health grants and cooperative agreements to the research community outside the Institute. This process includes peer review, program relevance, and priorities from the National Occupational Research Agenda (NORA), the NIOSH Research to Practice (r2p) initiative, congressional mandates, and sector, cross-sector or coordinated emphasis areas of the NIOSH Program Portfolio (http://www.cdc.gov/niosh/programs).

From 2001 to 2009, the Office of Extramural Programs (OEP) has funded nanotechnology research through Occupational Safety and Health Research Program Announcements (R01) and Small Business Innovation Research Grants (R43/44). Since FY05, OEP has also participated in two joint Requests for Applications (RFAs) for Nanotechnology Research Grants Investigating Environmental and Human Health Issues. The US Environmental Protection Agency's National Center for Environmental Research (NCER) and the National Science Foundation (NSF) participated in FY05. The National Institute of Environmental Health Sciences (NIEHS) joined in FY06. Funding was available to support Research (R01) grants for three years and Exploratory (R21) grants for two years.

In FY07, NIOSH/OEP participated in RFA–ES–06–008 Manufactured Nanomaterials: Physico-chemical Principles of Biocompatibility and Toxicity. This RFA was jointly sponsored by NIEHS, EPA and NIOSH.

In FY09, nanotechnology related research proposals submitted to standing program announcements are being considered for funding by NIOSH/OEP.

From 2001–2009, NIOSH/OEP has committed about $5.2 million dollars to extramural nanotechnology research. Summaries of the projects funded by NIOSH/OEP up through 2006 are included in the 2007 NIOSH *Progress Toward Safe Nanotechnology in the Workplace* [NIOSH 2007a]. Summaries of projects from 2007–2008 are included in the 2009 report *Progress Toward Safe Nanotechnology in the Workplace: A Report from the Nanotechnology Research Center: Project Reports for 2007–2008* [NIOSH 2009c]. NIOSH/OEP plans to continue collaborative efforts with EPA/NCER, NSF, NIH/NIEHS, and other international agencies to support nanotechnology research with occupational safety and health implications. OEP will continue to confer with the NIOSH Nanotechnology Research Center regarding issues, gaps, and future directions.

3.5 Collaborative Workshops

In FY05, NIOSH co-sponsored the 1st International Symposium on Nanotechnology and Occupational Health in Buxton, United Kingdom, and The First International Conference on Nanotoxicology: Biomedical Aspects in Miami, FL. In FY06, NIOSH co-sponsored the 2nd International Symposium on Nanotechnology and Health in

Minneapolis, MN. In FY07, NIOSH collaborated with the International Aerosol Research Assembly and the American Association for Aerosol Research to hold an International Symposium on Nanotechnology and Health in conjunction with the International Aerosol Conference in St. Paul, Minnesota. In FY07, NIOSH and the University of Cincinnati co-sponsored the International Conference on Nanotechnology Occupational and Environmental Health and Safety: Research to Practice, in Cincinnati, OH. In FY07, NIOSH convened a collaborative workshop including representatives from government, academia, labor, and industry in Washington, DC, to review a draft document developed by NIOSH and a cross agency work group, titled *Interim Guidelines on Medical Screening of Workers Potentially Exposed to Engineered Nanoparticles*. In FY07, NIOSH co-sponsored the 3rd International Symposium on Nanotechnology Safety & Health in Taipei, Taiwan. In FY08, NIOSH participated in the planning of the 4th International Congress on Nanotechnology Safety and Health held in August 2009, in Helsinki, Finland. In FY08, NIOSH co-sponsored The Second International Conference on Nanotoxicology in Zurich, Switzerland and Organization for Economic Co-operation and Development workshop on Exposure Assessment and Exposure Mitigation in Frankfurt, Germany. In FY09, NIOSH co-sponsored a National Institute of Standards and Technology Workshop on Enabling Standards for Nanomaterial Characterization in Gaithersburg, MD.

4 Goals

4.1 Goals and the Risk Management Continuum

A complete process for managing occupational safety and health implications during the development of new technologies and materials consists of a set of progressive elements: identifying and characterizing the hazard, assessing the extent of exposure, characterizing the risk, and developing control and management procedures [Schulte et al. 2008]. As exposure assessment data become available, a determination can be made whether or not an occupational risk exists, and if so, the risk can be assessed and characterized. A goal of the risk characterization is to determine whether exposure to a given technology or type of material (in this case, nanomaterials) is likely to result in adverse health effects. Exposure assessment data also provide a means to determine what controls are effective in preventing exposure that could cause adverse health effects. The NIOSH NTRC is involved in answering questions posed in each element in the risk management process. Figure 4 provides a visual representation of the risk management process and the NIOSH research associated with each step.

NIOSH has begun to address its NTRC strategic goals through the initiation of research to address each element of the risk management process as illustrated in Figure 4. The problem is that it is difficult to proceed in a classic step by step research approach in a timely manner to address the elements of hazard identification through risk management because new nanomaterials continue to be introduced into the workplace and the workforce exposed to these materials becomes more diversified. The challenge has been to conduct research to address knowledge gaps while drawing on all available information to provide interim occupational safety and health guidance. Toxicological research is an important element of the risk management paradigm that frequently forms the foundation for occupational safety and health recommendations. NIOSH has identified this as a high priority and will continue to conduct research to identify the critical routes of exposure (respiratory and skin), their targets (lungs, cardiovascular, skin, brain, systemic), health outcomes, and mechanisms of action for specific nanomaterials. Concurrent with this research, research is being conducted on measuring nanoparticles in air, determining what measures are appropriate, and using this information in field assessments to determine what workers are at risk for exposure. Parallel efforts have also been undertaken to address the control of airborne nanoparticles, nanotubes and nanofibers and the strengths and weaknesses of control approaches. Similar efforts are underway for personal protective equipment (PPE) such as respirators and gloves. While the primary focus of research will be to address the elements of "hazard identification" "hazard characterization" and "exposure assessment" of the risk management paradigm, the level of research will be limited by available resources. Thus, the focus of research from year-to-year may change based on available resources and the need to address specific knowledge gaps. As findings of field investigations

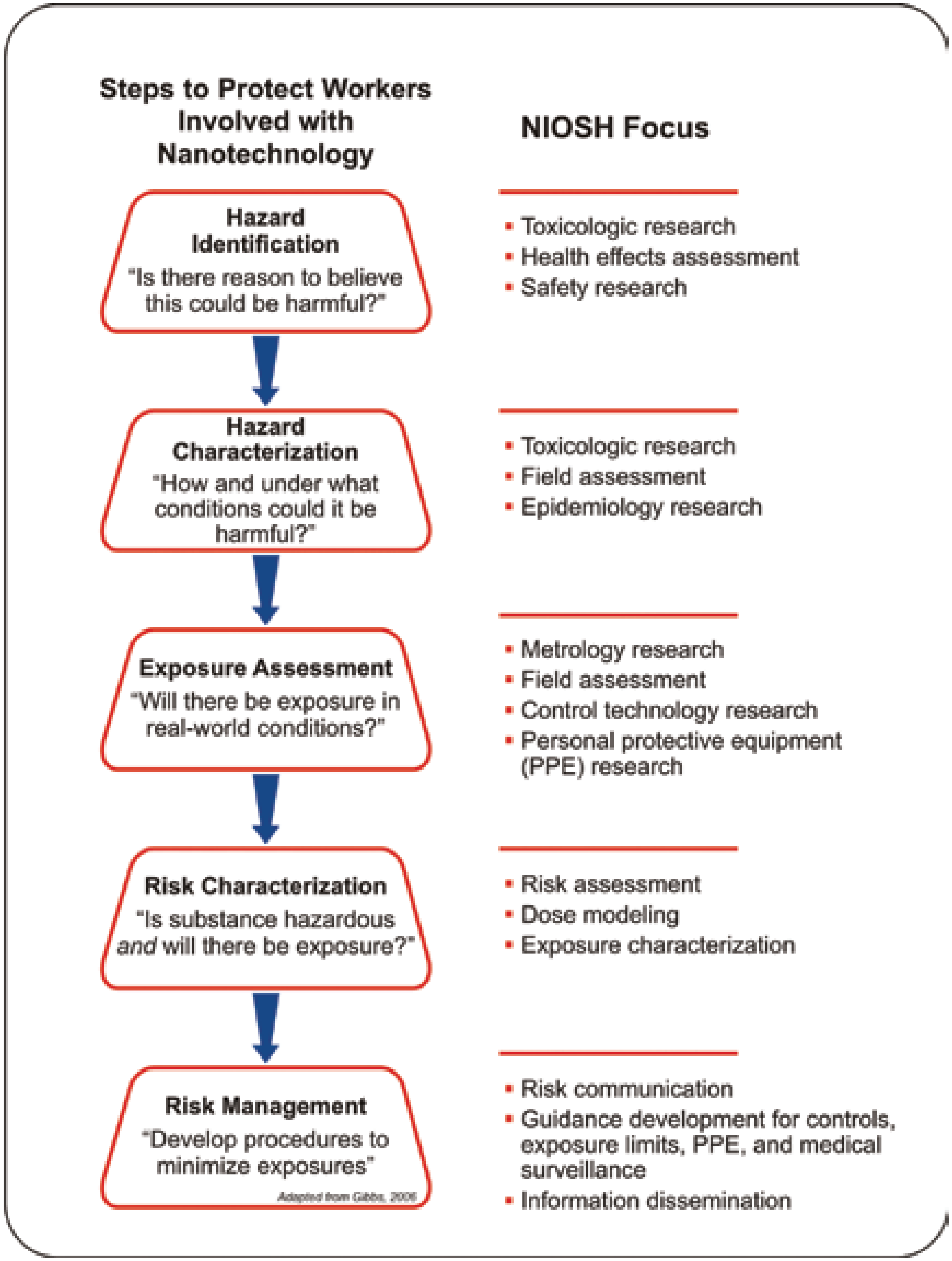


Figure 4. Steps to protect workers involved with nanotechnology

Mixer/sonicator/attrition mill within ventilated enclosure (Image courtesy of Mark Methner, NIOSH)

and laboratory research become available the information will be used to develop and update guidance for evaluating and managing potential nanotechnology risks.

The strategic goals are being addressed by conducting research in the 10 critical research areas identified by the NIOSH NTRC: (1) toxicity and internal dose, (2) measurement methods, (3) exposure assessment, (4) epidemiology and surveillance, (5) risk assessment, (6) engineering controls and PPE, (7) fire and explosion safety, (8) recommendations and guidance, (9) communication and information, and (10) applications. Research conducted in each of the critical areas is intended to address specific intermediate goals and performance measures (see Section 4.3). Additionally, since the fourth strategic goal "Enhance global workplace safety and health through national and international collaborations on nanotechnology research and guidance" cross-cuts all 10 critical research areas, intermediate goals were developed for this area. Ongoing and projected research within each of the 10 critical research areas through 2012 is described in Appendix A. Projected research for 2009–2012 has been coalesced to focus on specific research priorities (see section 4.4). As knowledge gaps are filled and as resources become available these research priorities could change.

4.2 Coordination with the National Nanotechnology Initiative

NIOSH participates in the National Nanotechnology Initiative's (NNI) "Strategy for

Nanotechnology Environmental Health and Safety Research." Table 1 shows the alignment of the four NIOSH NTRC strategic goals and the 10 NTRC critical research areas with the NNI environmental health and safety (EHS) priority research needs (see Appendix B). Planned projects within each of the 10 NIOSH critical research areas meet one or more of the four NIOSH Strategic Goals. A check mark (✓) means that a goal is addressed by projects within the critical research area. Alpha-numerical identifications indicate alignment of the NIOSH critical research goals with the NNI EHS priority environmental health and safety areas.

4.3 Strategic Goals, Intermediate Goals and Activity/Output Goals

The NIOSH Nanotechnology Research Center (NTRC) has developed the following strategic goals based on inputs from stakeholders and partners:

Strategic Goal 1 (PPNANSG1).

Determine if nanoparticles and nanomaterials pose risks for work-related injuries and illnesses.

Intermediate Goal 1.1 (PPNANIG1.1): Conduct research to contribute to the understanding of the toxicology and internal dose of nanomaterials.

NIOSH has studied in great detail the toxicity of incidental exposures to nanoparticles generated from processes involving combustion, welding, or diesel engines. However, less is known about nanoparticles that are intentionally produced (engineered) with diameters or structures smaller than 100 nanometers. Many uncertainties exist as to whether the unique properties of engineered nanomaterials pose occupational health risks. These uncertainties arise because of gaps in knowledge about the potential routes of exposure, movement of nanomaterials once they enter the body, and the interaction of the materials with the body's biological systems. Results from existing studies in animals and humans on exposure to incidental nanoscale and respirable particles provide preliminary information upon which to develop a research strategy to assess the possible adverse health effects from exposures to engineered nanomaterials.

Weighing carbon nanotubes in an exhausted enclosure (Image courtesy of Mark Methner, NIOSH)

Activity/Output Goal 1.1.1 (PPNANAOG1.1.1) Key factors and mechanisms. Systematically investigate the physical and chemical properties of particles that influence their toxicity (e.g., size, shape, surface area, solubility, chemical properties, and trace components). Evaluate acute and chronic effects in the lungs and in other organ systems and tissues. Determine rates of clearance of nanoparticles after pulmonary exposure and translocation to systemic organs; characterize systemic effects. Determine dermal response to exposure to skin and quantitative penetration of nanoparticles into skin. Determine the biological mechanisms for toxic effects

Table 1. Alignment of critical research areas with the four strategic goals of the NIOSH NTRC and the NNI EHS priority environmental health and safety areas

NIOSH NTRC strategic goals	Determine if nanoparticles and nanomaterials pose risks for work-related injuries and illnesses	Conduct research on applying nano-technology to the prevention of work-related injuries and illnesses[1]	Promote healthy workplaces through inter-ventions, recom-mendations, and capacity building	Enhance global workplace safety and health[1]
Toxicity and internal dose	✓[3], A2[4], B1, B2, B3, B4, B5			✓
Measurement methods	✓, A1, A2, A3, A4, A5, B2	✓	✓, E1	✓
Exposure assessment[2]	✓, A1, A2, D1, D4, D5, E1, E2		✓, E2	✓
Epidemiology and surveillance	✓, D1, D2, D3, D4, E4		✓, E4	✓
Risk assessment	✓, A2, B1, B2, D4, E3		✓, E3, E5	✓
Engineering controls and PPE	✓, D5	✓	✓, E1	✓
Fire and explosion safety	✓, A2			✓
Recommendations and guidance			✓, E1, E5	✓
Communication and information			✓, E1, E5	✓
Applications		✓		✓

[1]The NNI EHS plan does not address applications or global activities pertaining to environmental health and safety of nanomaterials. However the NIOSH efforts described herein are consistent with the overall NNI strategy which does identify international opportunities for collaboration.

[2]NIOSH is the lead agency for the NNI EHS Strategic area on human and environmental exposure assessment.

[3]A ✓ indicates that a goal is addressed by projects within the NIOSH critical research area

[4]Alpha-numeric identifications indicate alignment of the NIOSH critical research area with the specific NNI priority research needs (see Appendix B).

(e.g., role of oxidant stress), including from mixed exposures, and how the key chemical and physical factors may influence these mechanisms. Determine if nanoparticles are genotoxic/carcinogenic.

Performance measure 1.1.1 Determine the pulmonary response (dose dependence and time course) to single-walled carbon nanotubes (SWCNT) within the next two years and multi-walled carbon nanotubes (MWCNT) within the next three years. Determine the cardiovascular response to pulmonary exposure to SWCNT and ultrafine titanium dioxide within the next two years. Determine the pulmonary deposition and fate of SWCNT within the next two years and MWCNT and ultrafine titanium dioxide within the next three years. Determine the in vitro effects of SWCNT and metal oxide nanoparticles on skin cells within the next two years and the in vivo effects of topical exposure within the next three years. Determine the genotoxic and carcinogenic effects of SWCNT within the next four years. Determine the central nervous system effects of pulmonary exposure to nanoparticles within the next four years. Determine the pulmonary and systemic effects of other nanoparticles with the next five years. These results will elucidate toxicological mechanisms over the next five years.

Activity/Output Goal 1.1.2 (PPNANAOG1.1.2) Predictive models for toxicity. Integrate mechanistic models (including animal models and in vitro screening tests) for assessing the potential toxicity of new nanomaterials and provide a basis for developing predictive algorithms for structure/function relationships and comparative toxicity analyses for risk assessment. Evaluate the relationship between in vitro and in vivo responses, the relevance of instillation or aspiration exposure to inhalation, and the relevance of animal studies to human response.

Performance measure 1.1.2 Determine the role of oxidant-generating potential in bioactivity of metal oxide nanoparticles and carbon nanotubes over the next three years. Determine the role of shape (nanospheres vs. nanowires) in bioactivity over the next three years. Determine the role of carbon nanotube diameter and length in bioactivity over the next four years. Develop in vitro assays for oxidant generation, fibrogenic potential, and ability to cause endothelial dysfunction over the next four years. These results will address the development of predictive algorithms for toxicity over the next five years.

Activity/Output Goal 1.1.3 (PPNANAOG1.1.3) Metrics of dose. Determine whether (1) particle number, surface area, or other measure of bioavailability or bioactivity is a more appropriate dose metric for toxicity than mass or (2) other measures of bioavailability may be useful (e.g., an integrated measure of retention, solubility, oxidant-generating potential, surface area, and binding reactivity for proteins/lipids).

Performance measure 1.1.3 Determine the pulmonary response to exposure to fine vs. ultrafine particles using both mass and surface area as the dose metric. Determine the role of oxidant generation in the bioactivity of metal oxide nanoparticles and carbon nanotubes. These results will address issues of most appropriate dose metric over the next three years.

Activity/Output Goal 1.1.4 (PPNANAOG1.1.4) Internal dose. Determine the fate, clearance, and persistence of nanomaterials in the body (i.e., pulmonary, lymphatics, blood/systemic, brain) including possible de-agglomeration of nanoparticle agglomerates into primary particles and translocation of nanomaterials from the lung to systemic organs.

Performance measure 1.1.4 Develop methods to label carbon nanotubes and track their pulmonary deposition and fate (i.e., clearance, interstitialization, and translocation) with time post-exposure. Use chemical analysis to track the deposition and fate of metal oxide nanoparticles. These results will address issues of internal dose over the next five years.

Intermediate Goal 1.2 (PPNANIG1.2): Conduct research to evaluate measurement methods for nanomaterials.

Scientifically credible measurement methods are essential in order to effectively anticipate, recognize, evaluate, and control potential occupational exposures from current and emerging nanotechnologies. Traditional measurement approaches, such as determining total and respirable dust concentrations, may not be adequate for analyzing nanomaterials due to their unique physical, chemical, and biological properties.

Activity/Output Goal 1.2.1 (PPNANAOG1.2.1) Extend existing measurement methods. Evaluate current methods for measuring airborne mass concentrations of respirable particles in the workplace and determine whether these mass-based methods can be used as an interim approach for measuring nanomaterials in the workplace and to maintain continuity with historical methods.

Performance measure 1.2.1 Within three years evaluate the correlation between particle number, surface area, mass, and particle size distribution airborne measurement results and provide guidance for sampler selection based on the nanomaterial of interest. Continue to conduct measurement studies of nanoparticles in the workplace over the next five years and establish a suite of instruments and protocols for nanoparticle measurement in the workplace. Continue with refining the NIOSH method 5040 specifications for the collection and analysis of elemental and organic carbon for application to the collection and analysis of carbon nanotubes and nanofibers.

Activity/Output Goal 1.2.2 (PPNANAOG1.2.2) Develop new measurement methods. Expand the currently available instrumentation by developing and field testing methods that can accurately measure workplace airborne exposure concentrations of nanomaterials using metrics associated with toxicity (e.g., particle surface area, particle number).

Performance measure 1.2.2 Support at least three research projects over the next three years with the goal of creating a measurement method that can be correlated with the metrics associated with toxicity. Within five years develop a handheld fast-response nanoparticle monitor and software for spatial mapping of nanoparticles.

Activity/Output Goal 1.2.3 (PPNANAOG1.2.3) Validation of measurement methods. Develop testing and evaluation systems for comparison and validation of nanoparticle sampling instruments and methods.

Performance measure 1.2.3 Within three years publish procedures for validation of nanoparticle sampling instruments and methods.

Activity/Output Goal 1.2.4 (PPNANAOG1.2.4) Standard reference materials. Identify and qualify scientifically credible, nanoscale certified reference materials (RMs) with assigned physical and/or chemical values for use in evaluating measurement tools, instruments, and methods.

Performance measure 1.2.4 Within three years strengthen interactions with the National Institute of Standards and Technology to identify commercially available RMs and perform coherent research to identify, develop, and qualify nanoscale RMs and benchmark materials for evaluating measurement tools, instruments, and methods.

Intermediate Goal 1.3 (PPNANIG1.3): Conduct nanomaterial workplace exposure assessments.

Exposure assessment is a critical component in determining whether nanomaterials pose occupational safety or health risks. Therefore, it is necessary to conduct exposure assessments in the workplace to identify the ways that workers may be exposed to nanomaterials, the amount of exposure that may occur, and the frequency of potential exposure. Without workplace exposure data, it is difficult to accurately characterize the work environment, identify sources that are emitting nanomaterials, or estimate the amount of nanoparticle exposure that workers may receive. In addition, exposure data can be beneficial when making decisions concerning risk management or evaluating the effectiveness of engineering controls and work practices in reducing worker exposures.

Activity/Output Goal 1.3.1 (PPNANAOG1.3.1) Fate of nanomaterials in the work environment. Determine the key factors influencing the generation, dispersion, deposition, and re-entrainment of nanomaterials in the workplace, including the role of mixed exposures.

Performance measure 1.3.1 Support at least 12 research projects (industry exposure assessments) over the next three years to assess the fate of nanomaterials in the work environment.

Activity/Output Goal 1.3.2 (PPNANAOG1.3.2) Worker exposures. Quantitatively assess exposures to nanomaterials in the workplace including inhalation and dermal exposure. Determine how exposures differ by work task or process.

Performance measure 1.3.2 Within three years develop a baseline worker exposure assessment that identifies how exposures differ by work task or process.

Intermediate Goal 1.4 (PPNANIG1.4): Conduct epidemiologic research and evaluate surveillance of nanomaterial workers.

Currently, human studies of exposure and response to engineered nanomaterials are not available. Gaps in knowledge and understanding of nanomaterials must be filled before epidemiologic studies can be performed. For example, improvements in exposure assessment will allow researchers to identify groups of workers likely exposed to nanomaterials. In turn, health studies conducted on these worker-groups can provide useful information about the potential health risks associated with nanomaterials. Until such studies can be conducted effectively, studies of humans exposed to other aerosols (i.e., larger respirable particles) can be used to evaluate the potential health risks to airborne nanomaterials.

Activity/Output Goal 1.4.1 (PPNANAOG1.4.1) Evaluate current knowledge. Critically evaluate existing exposure and health data for workers employed in workplaces where nanomaterials are produced and used. Determine what is known about exposure response to existing nanomaterials, evaluate the applicability of this information to new nanomaterials, and identify data gaps and epidemiological research needs.

Performance measure 1.4.1 Over the next three years, seek input from a collaborative working group made up of representatives from industry, government, academia, and labor concerning the value and utility of establishing exposure registries for workers potentially exposed to engineered nanoparticles.

Activity/Output Goal 1.4.2 (PPNANAOG1.4.2) New epidemiological studies. Evaluate the need for and feasibility of initiating epidemiological or other health studies in workers exposed to existing nanomaterials (e.g., carbon black) or producing and using new (engineered) nanomaterials.

Performance measure 1.4.2 Over the next three years assess the feasibility of industry-wide exposure and epidemiological studies of workers exposed to engineered nanomaterials.

Activity/Output Goal 1.4.3 (PPNANAOG1.4.3) Surveillance. Integrate nanotechnology safety and health issues into existing hazard surveillance mechanisms. Determine whether these mechanisms are adequate or whether additional screening or surveillance methods are needed.

Performance measure 1.4.3 Update within three years the recommendations given in the NIOSH Current Intelligence Bulletin 60 "Interim Guidance for the Medical Screening and Hazard Surveillance of Workers Potentially Exposed to Engineered Nanoparticles" [NIOSH 2009]. Investigate the feasibility of establishing a registry of workers exposed to engineered nanoparticles.

Activity/Output Goal 1.4.4 (PPNANAOG1.4.4) Nanotechnology health information systems. Build on existing public health geographical information systems (GIS) and infrastructure to enable effective and economical development and sharing of nanotechnology safety and health data.

Performance measure 1.4.4 By 2012 create a GIS infrastructure populated with nanotechnology exposure data.

Intermediate Goal 1.5 (PPNANIG1.5): Conduct a risk assessment for high volume nanomaterials.

In the context of occupational safety and health, risk assessment can be described as a scientific evaluation of the potential for adverse health and safety effects to workers exposed to hazardous substances. When assessing risk, it must be determined whether a hazard is present and the extent to which a worker is likely to be exposed to the hazard. Risk involves both the presence of a hazardous agent and the potential for exposure to that agent. Quantitative and qualitative risk assessment methods are used to evaluate risk.

Activity/Output Goal 1.5.1 (PPNANAOG1.5.1). Evaluate current studies. Determine to what extent current exposure-response data (human or animal) for fine and ultrafine particles may be used to identify and assess potential occupational hazards and risks to nanomaterials.

Performance measure 1.5.1 Within three years complete a quantitative risk assessment (QRA) on ultrafine and fine materials from existing studies. Evaluate QRA methods for nanomaterials. Start QRA for nanoparticles using new NIOSH data. Use NIOSH nanoparticle data to calibrate and validate dosimetry models for nanoparticles.

Activity/Output Goal 1.5.2 (PPNANAOG1.5.2) Risk assessment framework. Develop a risk assessment framework for evaluating the hazard and predicting the risk of exposure to nanoparticles.

Performance measure 1.5.2 Within five years develop a risk assessment framework to rank hazard and estimate risk from exposure to selected nanoparticles in the workplace.

Strategic Goal 2 (PPNANSG2). Conduct research to prevent work-related injuries and illnesses by applying nanotechnology products.

Intermediate Goal 2.1 (PPNANIG2.1): Conduct research to evaluate potential applications of nanomaterials for occupational safety and health.

The unique properties and characteristics of nanomaterials may provide the basis for innovative new devices, products, or processes to reduce risks of work-related injuries and illnesses. Such innovations may have properties or capabilities that cannot be created or manufactured using conventional materials.

Activity/Output Goal 2.1.1 (PPNANAOG2.1.1) New devices and uses. Identify uses of nanotechnology in occupational safety and health.

Performance measure 2.1.1 Support at least three projects over the next three years to evaluate the application of nanotechnology in the manufacture of filters, respirators, and respirator cartridge end-of-service indicator.

Activity/Output Goal 2.1.2 (PPNANAOG2.1.2) Dissemination. Evaluate and disseminate effective nanotechnology research findings that may have applications to new sensors, PPE or other nanotechnology health and safety applications.

Performance measure 2.1.2 Within five years publish application findings and disseminate findings to workers, employers, and occupational safety and health professionals.

Strategic Goal 3 (PPNANSG3). Promote healthy workplaces through interventions, recommendations, and capacity building.

Intermediate Goal 3.1 (PPNANIG3.1): Conduct research to better understand engineering controls and personal protective equipment (PPE) for use with nanomaterials.

Currently there are no exposure standards specific to engineered nanomaterials. Therefore, to evaluate the need for and effectiveness of engineering controls an alternative rationale is required. In addition, the success of emerging nanotechnology industries will depend on production and development costs, including the installation of new exposure controls. Minimizing occupational exposure to the lowest possible level is the most prudent approach for controlling materials of unknown toxicity, such as nanomaterials. Typically, these approaches include substituting a less toxic material if possible, enclosing the hazardous process, removing workers from the exposure by automating the process, isolating workers from the hazard, and/or utilizing local exhaust ventilation where nanomaterials are handled. Improved control approaches will become more evident as the risks of exposure to nanomaterials are better understood.

Activity/Output Goal 3.1.1 (PPNANAOG3.1.1) Engineering controls. Evaluate the effectiveness of engineering control techniques for nanoaerosols and develop new approaches as needed.

Performance measure 3.1.1 Conduct field investigations of workplaces where nanoparticles are manufactured and used and evaluate existing engineering controls. Within three years publish updated engineering control guidance.

Activity/Output Goal 3.1.2 (PPNANAOG3.1.2) Personal protective equipment (PPE). Evaluate and improve the effectiveness of PPE for reducing worker exposures to nanomaterials.

Performance measure 3.1.2 Within five years publish updated guidance on the effectiveness of PPE for reducing worker exposures to nanoparticles.

Activity/Output Goal 3.1.3 (PPNANAOG3.1.3) Respirators. Evaluate the effectiveness of NIOSH-approved air purifying respirators to determine whether existing respirator guidelines would still apply for workers exposed to nanoaerosols.

Performance measure 3.1.3 Within five years publish updated respiratory protection guidance.

Activity/Output Goal 3.1.4 (PPNANAOG3.1.4) Work practices. Evaluate the role of work practices and administrative controls in reducing potential exposures to nanomaterials. Make recommendations for appropriate and effective use of these approaches.

Performance measure 3.1.4 Within five years publish updated work practice and administrative control guidance.

Activity/Output Goal 3.1.5 (PPNANAOG3.1.5) Control banding. Evaluate the suitability of a qualitative risk management approach similar to control banding to develop guidance for working with engineered nanomaterials when there is insufficient information available to apply traditional exposure-limit—based control strategies.

Performance measure 3.1.5 Within three years publish a document on the suitability of control banding approaches for nanomaterials.

Activity/Output Goal 3.1.6 (PPNANAOG3.1.6) Substitute materials. Evaluate the feasibility and effectiveness of substitute materials or modification of the engineered nanoparticle in reducing the toxicity of nanomaterials.

Performance measure 3.1.6 Support at least three projects over the next five years to evaluate substitute and modified nanoparticles with toxicological studies.

Intermediate Goal 3.2 (PPNANIG3.2): Conduct research to better define the potential fire and explosion safety hazards of nanomaterials.

The field of nanotechnology is relatively new, and therefore little is known about the potential occupational safety hazards that may be associated with engineered nanomaterials. However, the information that is available about the properties of nanoscale particles indicates that under given conditions, engineered nanomaterials may pose a dust explosion hazard and be spontaneously flammable when exposed to air due to their large surface area and overall small size. Until more specific data become available, NIOSH NTRC is utilizing findings from research studies involving particles smaller than 100 nanometers to evaluate the potential risk for fire and explosion of airborne nanoparticles.

Activity/Output Goal 3.2.1 (PPNANAOG3.2.1) Explosion and fire hazards. Identify physical and chemical properties that contribute to dustiness, combustibility, flammability, and conductivity of nanomaterials. Investigate and recommend appropriate work practices to eliminate or reduce the risk to explosions and fires.

Performance measure 3.2.1 Support at least two projects to evaluate explosion and fire hazards. Within three years publish guidance to eliminate or reduce explosion and fire hazards.

Intermediate Goal 3.3 (PPNANIG3.3): Develop and disseminate recommendations and guidance for the safe use of nanomaterials in the workplace.

NIOSH is responsible for conducting research and making recommendations to OSHA and other regulatory agencies, employers, workers and the general public to protect the health and safety of workers, and for providing guidance to workers and employers on how to control potential occupational health hazards. In addition, NIOSH is dedicated to translating its research findings into recommendations and guidance that are scientifically sound and practical for the workplace.

Activity/Output Goal 3.3.1 (PPNANAOG3.3.1) Guidance documents. Translate research findings into useable guidance documents for nanotechnology owners and workers.

Performance measure 3.3.1 Continue to update the NIOSH document, *Approaches to Safe Nanotechnology: Managing the Health and Safety Concerns Associated with Engineered Nanomaterials* [NIOSH 2009a], as results from research studies become available. Within two years, produce brochures and guidance documents to provide guidance to workers, and laboratory staff. Continue to look for opportunities to translate research from the critical research areas into practice.

Activity/Output Goal 3.3.2 (PPNANAOG3.3.2) Occupational exposure limits (OELs). Evaluate the current mass-based exposure limits for airborne particulates for their effectiveness in protecting workers exposed to nanomaterials. Update the OELs (as needed) to incorporate current scientific information (e.g., particle surface area versus mass as predictor of toxicity, shape, influence of surface properties). Consider development of an OEL for selected carbon nanotubes.

Performance measure 3.3.2 In 2009, complete the Current Intelligence Bulletin (CIB), Evaluation of Health Hazard and Recommendations for Occupational Exposure to Titanium Dioxide, with the OEL for ultrafine titanium dioxide. Support a project over the next three years to evaluate other ultrafine or nanoparticle OELs. Develop a NIOSH Alert by 2010 and a CIB by 2011 on carbon nanotubes.

Activity/Output Goal 3.3.3 (PPNANAOG3.3.3) Classification. Develop a nanoparticle classification system to support a comprehensive nanotechnology safety and health program. Implement criteria based on classification (e.g., chemical abstract system [CAS] number) to determine the need for toxicity testing and hazard and risk assessment of new engineered and existing nanomaterials.

Performance measure 3.3.3 Initiate a project that will develop a classification scheme based on chemical and physical properties. Release this classification scheme within the next three years.

Activity/Output Goal 3.3.4 (PPNANAOG3.3.4) High-production volume (HPV) nanomaterials. Evaluate adequacy of mass-based safety and health criteria developed for bulk chemicals for nanomaterials. Current scientific data indicates greater toxicity of nanomaterials by mass compared to an equal mass of larger particles of similar composition.

Performance measure 3.3.4 Support a project to evaluate existing toxicity information of HPV nanoscale materials.

Activity/Output Goal 3.3.5 (PPNANAOG3.3.5) Material safety data sheets (MSDS). Work with partners to update the MSDS system to incorporate relevant classification, toxicity data, and health and safety recommendations for working with nanomaterials.

Performance measure 3.3.5 Within three years, increase awareness of the need for specific nanomaterial information on MSDS among the target audience by 33% over baseline.

Strategic Goal 4 (PPNANSG4). Enhance global workplace safety and health through national and international collaborations on nanotechnology research and guidance.

Intermediate Goal 4.1 (PPNANIG4.1): Foster the collection, management and dissemination of relevant information to protect nanomaterial workers.

Communication and information are integral components infused throughout the research activities of the NIOSH NTRC and are closely related to the NIOSH Research to Practice (r2p) initiative. Research to Practice is geared towards translating research results into useful health and safety information tailored to various audiences including workers and employers. As a result, communication and information is one of the 10 critical research areas identified to address knowledge gaps, develop strategies, and provide recommendations concerning workplace exposure to engineered nanomaterials/nanoparticles.

Activity/Output Goal 4.1.1 (PPNANAOG4.1.1) Nanoinformatics. Develop a roadmap to create a nanoinformatics database management tool relevant to nanomaterial environmental health and safety information.

Performance measure 4.1.1 Within the next three years create a roadmap that aligns new nanoinformatics with the NIOSH Nanoparticle Information Library (NIL).

Activity/Output Goal 4.1.2 (PPNANAOG4.1.2) Communication. Establish and maintain national and international partnerships with whom knowledge gaps, research needs and priorities, approaches, and results can be shared openly and collaboratively.

Performance measure 4.1.2 Within one year, identify and initiate/establish contact with at least one potential partner from each of the following areas: government, industry, academia, and labor.

Activity/Output Goal 4.1.3 (PPNANAOG4.1.3) Information. Develop and disseminate effective information, education, and training materials to various target audiences such as nanotechnology workers and employers, occupational safety and health professionals, policy-makers, decision-makers, and/or the scientific community.

Performance measures 4.1.3 Within one year, develop at least one informational document tailored to a target audience identified above. Evaluate/assess the reach and effectiveness of the above tailored informational piece within two years. Update progress report on the NIOSH nanotechnology research and communication efforts within two years. Continue to update the NIOSH document, *Approaches to Safe Nanotechnology: Managing the Safety and Health Concerns Associated with Engineered Nanomaterials.*

Intermediate Goal 4.2 (PPNANIG4.2): Enhance global workplace safety and health through international activities.

The international component of NIOSH nanotechnology research aims at achieving the fourth program goal—Enhance global workplace safety and health through national and international collaborations on nanotechnology research and guidance—with two objectives:

1. Develop partnerships for identifying research and for the sharing of research needs, approaches, and results.
2. Develop and disseminate effective educational and training materials for workers and occupational health professionals.

NIOSH international activities crosscut all 10 critical research areas by developing partnerships (first objective) to address critical research gaps and by developing and disseminating occupational safety and health (OSH) documents (second objective). In order to achieve these objectives, NIOSH will continue to engage with a number of international entities at all levels—principle investigator, as well as national, regional, and global organizations.

Activity/Output Goal 4.2.1 (PPNANAOG4.2.1) Improve resource leveraging for research globally.

Performance measure 4.2.1–1 Strengthen coordination of research through government-level organizations (OECD and UN).

Performance measure 4.2.1–2 Expand collaborations to developing nations and emerging powers (Asia-Pacific, Eastern Europe).

Activity/Output Goal 4.2.2 (PPNANAOG4.2.2) Improve sharing critical data globally.

Performance measure 4.2.2–1 Develop global portal for information on nanomaterials relevant to occupational safety and health.

Performance measure 4.2.2–2 If feasible, initiate the development of a global exposure registry database: European countries, ECHA, Asian countries, OECD.

Performance measure 4.2.2–3 Participate in OECD Nanomaterial Safety Testing Program by sponsoring nanomaterial testing and by data exchange.

Activity/Output Goal 4.2.3 (PPNANAOG4.2.3) Produce highest quality products.

Performance measure 4.2.3–1 Facilitate development of government-level exposure mitigation guidance (OECD and UN).

Performance measure 4.2.3–2 Increase utilization of web-based tools for document development (such as wiki-based platforms).

Activity/Output Goal 4.2.4 (PPNANAOG4.2.4) Enhance global dissemination.

Performance measure 4.2.4–1 Increase utilization of emerging information technology mechanisms (e.g., NIOSH science blog, web-based social networks).

Performance measure 4.2.4–2 Establish partnerships for translation of NIOSH publications to other languages.

Activity/Output Goal 4.2.5 (PPNANAOG4.2.5) Increase global acceptance.

Performance measure 4.2.5–1 Strengthen participation in globally recognized organizations.

Performance measure 4.2.5–2 Expand partnerships to international bodies with economic instruments to implement OSH measures such as financial institutions (Inter-American Development Bank, World Bank) and insurance companies (Swiss Re, Munich Re, Lloyds)

4.4 Coalescing Priorities for NIOSH Nanotechnology Research and Guidance for 2009–2012

This strategic plan identifies priorities for NIOSH research and guidance efforts in 10 critical areas. However it is necessary to coalesce the priorities in these areas to align with resources.

NIOSH has limited funds and resources available to re-direct and invest in nanomaterial research. Both the NIOSH Board of Scientific Counselors' review of the NTRC Strategic Plan and the National Academies, in its review of the Nanotechnology section of the Respiratory Disease Research Program, concluded that NIOSH must prioritize its research in nanotechnology. Both reviews stressed the need to focus the Institute resources on applied research that addresses critical needs in the areas of hazard identification, exposure assessment, and exposure control. Both reviews also reinforced the need for timely issuance of recommendations and guidance; a need that has been reinforced by stakeholders.

Figure 5 provides a schema for how NIOSH will focus future nanomaterial research. The ultimate goal of NIOSH research is to prevent adverse effects in workers through the issuance of recommended standards and other guidance for nanomaterials including but not limited to industrial hygiene sampling methods, laboratory analytical methods, and various methods to control exposure in the workplace.

Three factors will contribute to setting the direction of future NIOSH research: production trends of various types of nanomaterials, stakeholder input, and gaps in scientific knowledge as identified by NIOSH investigators. Consideration of these factors will help focus the toxicological and epidemiological research needed to provide data for the conduct of quantitative risk assessments that will serve as the basis for recommended standards and risk management guidance. Research to help develop the other key components of recommended standards will also be needed including research on exposure sampling, analysis, and instrumentation; exposure assessment; control technology; and PPE. Additionally, an on-going effort will be supported to develop medical surveillance guidance for workers exposed to engineered nanoparticles.

Implicit in addressing the ultimate goal of developing recommended standards and guidance for engineered nanomaterials is that NIOSH research will be published in the peer-reviewed scientific literature to inform the scientific and occupational safety and health community. Between 2007 and 2009, NIOSH has initiated nanoparticle research (listed below) that can be depicted in a matrix shown in Table 2. The extent and specificity of that research is identified in the document *Progress Toward Safe Nanotechnology in the Workplace: Project Update 2007–2008.* [http://www.cdc.gov/niosh/docs/2010-104/pdfs/2010-104.pdf]

NIOSH Nanotechnology Specific Projects 2007–2009

Project 1: Nanotechnology Research Center Coordination

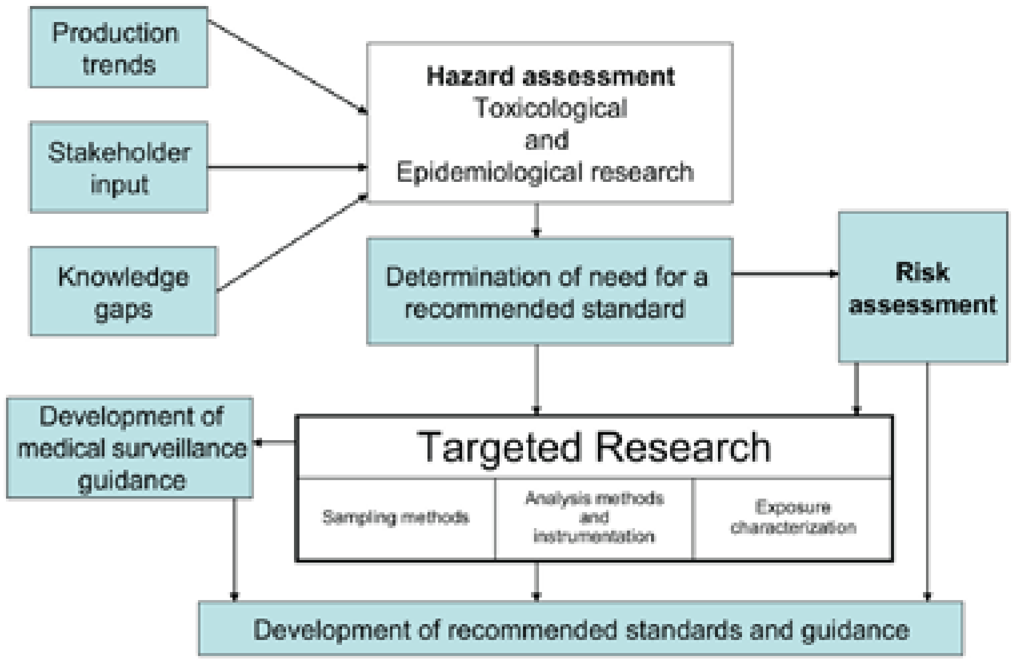


Figure 5. Focus of NIOSH nanomaterial research 2009–2012

Project 2: Nanotechnology Safety and Health Research Coordination

Project 3: Systemic Microvascular Dysfunction: Effects of Ultrafine vs Fine Particles

Project 4: Particle Surface Area as a Dose Metric

Project 5: Role of Carbon Nanotubes in Cardiovascular and COPD-Related Disease

Project 6: Investigations of Multi-Walled Carbon Nanotube Toxicity

Project 7: Pulmonary Toxicity of Metal Oxide Nanospheres and Nanowires

Project 8: WC-Co Nanoparticles in Initiating Angiogenesis by Reactive Oxygen Species

Project 9: Evaluation of the Pulmonary Deposition and Translocation of Nanomaterials

Project 10: Occupational Exposures and Potential Neurological Risks

Project 11: Lung Effects of Resistance Spot Welding Using Adhesives

Project 12: Neurotoxicity after Pulmonary Exposure to Welding Fumes

Project 13: Potential Aneuploidy following Exposure to Carbon Nanotubes

Project 14: Pulmonary Toxicity of Carbon Nanotube Particles

Project 15: Dermal Toxicity of Nanotube Particles

Table 2. NIOSH nanoparticle research projects 2007–2009: Nature of research project number*

Type of particle	Toxicology studies*	Sampling, analysis and instrumentation*	Exposure characterization*	Control and PPE*	Risk assessment*
TiO_2	3*, 4, 7	4, 26, 27, 28, 29, 30, 33	33	—	†
Other metal oxides	7, 18, 20	22, 24, 27, 30, 34	24, 33, 34	34	—
Metals WC-Co B_4C welding fumes	8, 10, 11, 12, 20,	29, 30	34	34	†
SWCNT and MWCNT	5, 6, 9, 10, 13, 14, 15, 16, 21	22, 23, 24, 25, 26, 27, 30, 31	25, 34, 35	34	36
CNF		—	34, 35	34	—
C60		—	32, 35	32	—
Other silica compounds, carbon black, nylon 6, POSS, dioctyl phthalate, NaCl	19	27, 30	34, 35	37, 38, 39	
Diesel exhaust	17, 18	24, 32	32	—	†

*Numbers refer to projects; see list of NIOSH nanotechnology projects 2007–2008 on page 29–32. Note that projects 1, 2, 34, 36–43 are not specific to any one type of engineered nanomaterial.

†The risk assessment for TiO_2, welding fumes and diesel exhaust predates the nanotechnology projects of 2007–2009.

Project 16: Specific Biomarkers for Unusual Toxicity of Nanomaterials

Project 17: Pulmonary Toxicity of Diesel Exhaust Particles

Project 18: Induction of Lung Fibrosis by Cerium Oxide in Diesel Exhaust

Project 19: Potential Effects of Silicon-Based Nanowires on Lung Toxicity

Project 20: Cell-based Assessment for Iron Nanoparticle-Induced Health Risks

Project 21: Assessment of Carbonaceous Materials on Mutagenicity

Project 22: Generation and Characterization of Nanoparticles

Project 23: Dustiness of Nanomaterials

Project 24: Nanoaerosol Monitoring Methods

Project 25: Measurement of Nanoscale Carbonaceous Aerosols

Project 26: Nanoparticle Reference Materials for Health Protection

Project 27: Calm Air Chamber and Wind Tunnel Evaluation of Personal Aerosol Samplers for Nanoparticle Exposure Assessment

Project 28: Ultrafine TiO_2 Surface and Mass Concentration Sampling Method

Project 29: Standard Determination of Nanoparticle Size

Project 30: Development and Evaluation of Nanoaerosol Surface Area Measurement Methods

Project 31: Workplace Monitoring of Carbon Nanofibers/Nanotubes

Project 32: Ultrafine Aerosols from Diesel-Powered Equipment

Project 33: Titanium Dioxide and Other Metal Oxides Exposure Assessment Study

Project 34: Field Research Team

Project 35: Assessing the Feasibility of Industrywide Exposure and Epidemiology Studies of Workers Exposed to Engineered Nanomaterials

Project 36: Nanoparticles—Dosimetry and Risk Assessment

Project 37: Penetration of Nanoparticles through Respirators

Project 38: Nanoparticle Penetration through Protective Clothing

Project 39: Development of PPE Ensemble Test Methods

Project 40: Web-Based Nanoparticle Information Library Implementation

Project 41: Nanoparticles in the Workplace

Project 42: New Sensor Technology Development for end of service-life indicator (ESLI)

Project 43: Global Harmonization of Exposure Measurement and Exposure Mitigation Approaches for Nanomaterials

4.4.1 Gap analysis: basis for additional research beginning in 2009

Titanium dioxide

NIOSH is about to complete a Current Intelligence Bulletin on titanium dioxide (TiO_2) which will provide recommended exposure limits (RELs) for two size ranges of TiO_2; one for particles in the micrometer-diameter range and one for particles in the diameter range below 100 nanometers [NIOSH 2007b]. However, there still remain questions about the specificity of the sampling and analytical method that will be used to evaluate worker exposure to nanoscale TiO_2, as well as about the extent of workplace exposures, and the ability to control exposures at or below the REL (proposed 8-hour TWA in the range of 0.1 μg/m^3). Research to address these questions is a high priority. The assessment of risk for TiO_2 may serve as a model for evaluating the risks to other metal oxide or poorly soluble low toxicity nanoparticles.

Metals and metal oxides

Based on the toxicological literature, it is likely that occupational exposure to a range of nanometer-sized metals and metal oxides may present hazards at a minimum similar to titanium dioxide; namely, increased biologic activity with decreasing particle size. Production trends would lead to the assumption that occupational exposure to nanometals and metal oxides is increasing. Therefore, there is a need for hazard identification, exposure assessment, and control technology research for this class of engineered nanomaterial. This includes development of sampling and analytical methods and other work leading to recommended exposure limits.

Carbon nanotubes (CNT)

NIOSH has conducted extensive toxicological research on carbon nanotubes. Development of recommended occupational standards for CNT will be the objective towards which much of future research will be focused. As part of the first priority of identifying hazards of nanomaterials, NIOSH scientists in the Health Effects Laboratory Division (HELD) have assessed effects of various types of nanoparticles including carbon nanotubes [Shvedoda et al. 2003, 2004, 2005, 2007, 2008, Wang et al. 2008]. The results of HELD research on CNT will provide data sets that NIOSH can use to conduct quantitative risk assessments. This effort will form the basis for developing guidance and occupational standards for CNT. However, developing an effective recommended standard for CNT and other engineered nanoparticles also requires: the ability to quantitatively measure the presence (or concentration) of the material with an acceptable degree of specificity, accuracy, and precision; a characterization of risk by measuring worker exposure; and an understanding of the effectiveness of controls used to control or eliminate exposures [Kuempel et al. 2007, Schulte et al. 2008]. Ideally, information on animal toxicity would be supplemented by epidemiological studies of potential human health effects of exposure to various CNT; however, it is not clear whether the exposed population is large enough and exposure sufficiently well characterized to support such studies [Schulte et al. 2009]. NIOSH is currently collecting data to evaluate the feasibility of industry-wide exposure and epidemiology studies of workers involved in the U.S. manufacture of engineered carbonaceous nanomaterials. This evaluation will impact the utility of future NIOSH epidemiologic studies of this workforce.

A growing number of industrial applications are being developed for CNT, and this class of nanomaterials has shown good potential for developing into a viable economic commodity [Lux 2007]. Moreover, the fibrous-like dimensions of CNT are a source of concern about possible adverse effects. NIOSH investigators have conducted some of the earliest health effects studies in animal models both by pharyngeal aspiration and inhalation of an aerosol of single and multi-walled carbon nanotubes. For the most part, these studies have involved short-term exposure and less than lifetime follow-up; however, these studies have demonstrated the potential for exposures to single-walled carbon nanotubes (SWCNT) and multi-walled carbon nanotubes (MWCNT) to cause lung fibrosis and affect other organs [Shvedova et al. 2007].

It is possible that the data from these NIOSH toxicology studies can be used to conduct a quantitative risk assessment and develop benchmark RELs for the type of CNT used in the studies. It is known that there can be more than tens of thousands of CNT based on various combinations of physicochemical parameters; thus, it may not be possible to assess the risk and develop a REL for each type of CNT. Ultimately, different types of CNT may need to be grouped based on similar physicochemical properties for the purpose of developing recommended exposure limits. Nonetheless, the available toxicity data on specific types of CNT studied by NIOSH, while limited, are compelling and may serve as a starting point and possibly as a benchmark to develop RELs for SWCNT and MWCNT. Table 3 shows four variations of CNT which NIOSH is considering for the development of recommended standards, including RELs. To do this, NIOSH investigators will conduct research to answer specific questions and provide information that can be used by occupational safety and health practitioners in making risk management recommendations. Two types of SWCNT (purified (p) and unpurified (up))† and two types of MWCNT (purified (p) and unpurified (up)) will be the focus of NIOSH research and guidance beginning in 2009. NIOSH research will fill knowledge gaps in four areas: sampling; analysis; exposure assessment; and control (control technology and PPE). Underlying all four of these areas will be issues pertaining to metrology of CNT and workplace factors that affect or influence exposure. Table 3 lists the areas of research that will be needed to develop risk management recommendations for occupational exposure to CNT. The questions listed with Table 3 will be used to identify gaps in information to help formulate research that NIOSH will invest in over the next 3–5 years.

Sampling/analysis‡

Cells 1–8

1. Are there sampling and analytical methods available that can be used to identify and quantitatively measure airborne releases or exposures to SWCNT and MWCNT in the workplace?
2. What experience does NIOSH or others have in attempting to measure CNT?
3. NIOSH Method 5040 was identified in earlier studies as a candidate sampling and analytical method for CNT. What progress has been made in that effort and what is needed to reach an end point?
4. What limitations are placed on the method due to background interference (ambient or process derived contamination) and what impact does purity have?
5. Several groups have reported using TEM-based asbestos fiber counting methods (NIOSH analytical method

†"Purified" describes CNT that have been treated or processed to remove residual catalyst or reaction residue. "Unpurified" describes CNT that have residual catalyst, reaction residue, or mixtures of tube types.

‡Investigations focusing on laboratory-based methods development should be differentiated from field evaluations conducted for the purpose of method evaluations and exposure assessments.

Table 3: Assessment of information that will support a NIOSH REL[*] of 10 μg/m^3[†] (8hr TWA) for SWCNT and MWCNT used in published NIOSH studies[‡].

	SWCNT Purified (p)	SWCNT Unpurified (up)	MWCNT Purified (p)	MWCNT Unpurified (up)
Sampling methods	1[§]	2	3	4
Analysis methods and detection instrumentation	5	6	7	8
Field exposure characterization	9	10	11	12
Exposure control	13	14	15	16

[*]For SWCNT (p), SWCNT (up), MWCNT (p), and MWCNT (up)
[†]This number does not represent a NIOSH recommendation; it is only a target for purposes of discussion
[‡]Studies from NIOSH Health Effects Laboratory Division (e.g. Shvedova et al 2005, Shvedova et al. 2008).
[§]Numbers are used to identify cells that are associated with gap analysis questions that follow.

7402) to evaluate CNT. What is needed to explore that approach?

6. What is the most likely candidate analytical method and when will NIOSH be ready to recommend it?
7. What is the current state of instrument evaluations from prior efforts and what is still needed to demonstrate their utility in evaluating CNT exposures?
8. A critical area is to explore any possible correlation between direct-reading techniques and integrated sampling methods. What progress has been made and what is still needed?
9. What laboratory-based studies are still needed to validate a sampling and analytical method?
10. What is the prognosis for field evaluation trials of methods or instruments and how many of the sites already visited by NIOSH are good candidates?
11. Will the focus of the proposed work be on CNT production only, or will it include CNT-containing product formulations?
12. How can data and observations from current NIOSH field studies be used to guide the proposed work?

Exposure characterization

Cells 9–12

13. Specific to CNT, what are the current trends in production and market applications?
14. What is the extent of production and use of CNT that could result in exposure for the 4 categories of CNT?

15. What do we know from the current NIOSH field investigations: what methods and measurement techniques have been used, and with what degree of success?
16. What job tasks and processes will likely produce the highest exposures?

Control

Cells 13–16

17. Can airborne emissions and potential exposures to CNT be controlled in known processes to at least 10 $\mu g/m^3$ (8hr TWA)?
18. What data might be available to support the answer to Question No. 16?
19. Can pharmaceutical equipment performance guidelines developed for fine powder active ingredient containments be used; for example, International Society for Pharmaceutical Engineering (ISPE) standards for potent compound containment?
20. What is the range and effectiveness of controls already seen by NIOSH field researchers in CNT production and product incorporation processes?
21. What is needed to catalog existing controls and develop initial guidance?
22. Laboratory scale containment devices are already being evaluated by others (U Mass-Lowell). Should NIOSH conduct additional study of laboratory controls?
23. What scale-up, pilot plant, and production processes control strategies are likely candidates given current knowledge of the CNT market?
24. What measurement methods/metrics can be used to validate effectiveness of controls?
25. What surrogate material might be used for qualitative or quantitative control evaluations?
26. Is PPE protective to this level and what data support this?

Exposure metrics for CNT RELs

Ideally, in quantitative risk assessments of nanoscale particulate exposures, response data would be evaluated in relation to mass as well as to other nanoscale metrics such as surface area, particle number concentration, and possibly others. These additional metrics may prove to be a more sensitive measure of the presence, quantity, and nature of CNT. To the extent that these data exist from NIOSH pharyngeal aspiration and inhalation studies, research will be conducted to determine whether there is a correlation between mass, particle number, particle number by size, mass by size, fiber number, and is there any correlation between these metrics and those collected by direct reading instruments for particle number, mass, and size distribution. If these data are available (or can be calculated) and the risk assessment reveals a stronger relationship with some metrics (e.g., surface area, number concentration) other than mass, NIOSH will ascertain the feasibility of recommending an exposure limit based on a nonmass metric.

Additional adverse effect research on CNT

The effort to develop RELs for the CNT used in HELD research will be an interim effort since the research generally involved short-term exposure and follow-up. Ultimately, there will be a need for RELs that protect against long-term (long latency) effects such as cancer and cardiovascular disease. Hence, there will be a need for further toxicological research on such long-term effects.

Generalizing beyond the NIOSH RELs for CNT

Based on the risk assessments of HELD CNT data, NIOSH may recommend 1 to 4 RELs: SWCNT (p), SWCNT (up), MWCNT (p), and MWCNT (up). However, there are tens of thousands of potential single-walled and multi-walled carbon nanotubes, some may be more toxic than the ones HELD studied, some may be less. NIOSH will attempt to ascertain if differences in physicochemical parameters of CNT makes them more or less toxic and whether based on similarities of physicochemical parameters if CNT can be categorized into groups in which specific risk management recommendations can be made. NIOSH will also investigate if different sampling, exposure assessment, and control issues might apply if CNT are categorized into groups.

Investigating other engineered nanoparticles

In conjunction with NIOSH toxicologists, other types of nanoparticles in addition to TiO_2 and CNT will be identified for study. This will be an ongoing effort to ensure early hazard identification through toxicological research and occupational exposure assessment. The NTRC participants and coordinating office will serve to provide information on production trends and stakeholder inputs to identify what nanomaterials are likely to be commercially viable.

Explosion and fire hazards

The history of dust laden atmospheres in confined spaces has shown that various dusts can be explosive. Further research will be conducted on whether moving to nanoscale dimensions with dry powder materials will contribute to the explosion and fire hazard potential of dusts.

Communications

Critical for the effectiveness of NIOSH research and guidance is the ability to provide information and knowledge to various audiences (researchers, workers, employers, government agencies, professional associations, NGOs, the media, and the public). During the period 2009–2012, NIOSH will continue to assess the needs of various audiences and develop an array of communication products.

Summary

The following are NIOSH specific research and guidance priorities for 2009–2012:

1. Develop recommendations for controlling occupational exposure to fine and ultrafine TiO_2 including development of RELs. Conduct research on improving sampling and analytical methods, determining the extent of workplace exposures, and controlling airborne exposures below the REL. Identify what medical surveillance is appropriate. Consider to what extent the observed relationship between TiO_2 particle size and toxicity can be generalized to other metal oxides.

2. Develop recommendations for controlling occupational exposures to

purified and unpurified SWCNT and MWCNT including development of RELs. Conduct research to address gaps in information on sampling, analysis, exposure assessment, instrumentation, and controls. Identify what medical surveillance or epidemiological studies are appropriate.

3. Conduct research on how to identify categories of nanoparticles that can be distinguished on the basis of similar physicochemical properties. Conduct research to develop RELs and ultimately recommended exposure standards for these categories.

4. Conduct research to identify long-term health effects of CNT.

5. Conduct toxicological research on other nanoparticles likely to be commercially viable.

6. Conduct research on explosion potential of various nanoparticles.

5 Outputs

5.1 NIOSH Publications on Nanotechnology

- NIOSH has posted a safety and health topic page, "Nanotechnology," containing accessible information on the safety and health implications of nanotechnology and the related research activities that NIOSH is conducting. Updates of NIOSH activities in nanotechnology research also appear on the topic page. [http://www.cdc.gov/niosh/topics/nanotech/]

- NIOSH has prepared and posted answers to frequently asked questions (FAQs) concerning nanotechnology and NIOSH's involvement with the occupational safety and health research in the field of nanotechnology. [http://www.cdc.gov/niosh/topics/nanotech/faq.html]

- NIOSH published *Safe Nanotechnology in the Workplace* [DHHS (NIOSH) Publication No. 2008–112]. This brochure provides an introduction to nanotechnology in the workplace for employers, managers, and safety and health professionals. It addresses the following questions: Are nanoparticles hazardous to workers? How can workers be exposed? Can nanoparticles be measured? Can worker exposures be controlled?

- NIOSH published *The Nanotechnology Field Research Team Update* [DHHS (NIOSH) Publication No. 2008–120]. This document is an update of the NIOSH Nanotechnology Field Research team's efforts to evaluate work practices and engineering controls used to ensure worker safety and health in the nanotechnology industry. The update includes comments from participating companies interviewed by Nanowerk, LLC who described the collaboration as beneficial and encouraged other companies to take advantage of NIOSH's expertise, service, instrumentation, and unbiased assessments.

Location of personal breathing zone air sampling cassettes (Image courtesy of Mark Methner, NIOSH)

- NIOSH published *NIOSH Fact Sheet: The Nanotechnology Field Research Effort* [DHHS (NIOSH) Publication No. 2008–121]. A description and call for participants for the NIOSH Nanotechnology Field Research team's efforts to evaluate work practices and engineering controls used to ensure worker health and safety in the nanotechnology industry.

- A NIOSH current intelligence bulletin (CIB), *Occupational Exposure to Titanium Dioxide, on fine and ultrafine titanium dioxide (TiO_2)* has undergone stakeholder and peer review and is being finalized for publication in 2009. [http://www.cdc.gov/niosh/review/public/TiO2/default.html]

- NIOSH has prepared the document, *Approaches to Safe Nanotechnology: Managing the Health and Safety Concerns Associated with Engineered Nanomaterials* [DHHS (NIOSH) Publication No. 2009–125]. [http://www.cdc.gov/niosh/topics/nanotech/safenano/]

- NIOSH has developed a web-based Nanoparticle Information Library (NIL) which is a resource on particle information including physical and chemical characteristics. [http://nanoparticlelibrary.net/index.asp]

- NIOSH has published *Progress Toward Safe Nanotechnology in the Workplace: A Report from the NIOSH Nanotechnology Research Center* [DHHS (NIOSH) Publication No. 2007–123], a progress report on the status of nanotechnology research conducted by the NIOSH NTRC through 2006. [http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf]. An updated progress report listing project updates from 2007–2008 was published in November 2009 [NIOSH 2009c] [DHHS (NIOSH) Publication No. 2010–104]. [http://www.cdc.gov/niosh/docs/2010-104/pdfs/2010-104.pdf]

- NIOSH has prepared the document *Guidance for Medical Screening and Hazard Surveillance for Workers Potentially Exposed to Engineered Nanoparticles* [NIOSH 2009b] [DHHS (NIOSH) Publication No. 2009–116]. [http://www.cdc.gov/niosh/docs/2009-116/]

5.2 NIOSH Peer-Reviewed Publications

- NIOSH scientists will publish results of research as the data become available. More than 170 peer-reviewed articles were published through 2008 addressing scientific and technical issues in the field of nanotechnology. For a listing of publications through 2006, see *Progress Toward Safe Nanotechnology in the Workplace: A Report from NIOSH Nanotechnology Research Center* [DHHS (NIOSH) Publication No. 2007–123]. [http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf]. For a listing of publications from 2007–2008, see the 2009 update of the progress report. [http://www.cdc.gov/niosh/docs/2010-104/pdfs/2010-104.pdf]

5.3 Sponsored Conferences

NIOSH will continue to partner with others in sponsoring and conducting conferences on nanotechnology. To date, NIOSH has co-sponsored three international meetings on occupational safety and health involving nanomaterials and has co-sponsored a major occupational safety and health Research to Practice (r2p) conference in Cincinnati, OH, in 2006 which drew over 450 participants from 11 countries. NIOSH staff also participated on several scientific and technical panels convened by government agencies, nongovernmental agencies, and professional associations. For a listing of meetings, panels, and conferences through 2006, see *Progress Toward Safe Nanotechnology in the Workplace: A Report from NIOSH Nanotechnology Research Center* [DHHS (NIOSH) Publication No. 2007–123]. [http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf]. Meetings, conferences, etc. from 2007–2008 may be found on the 2009 update of the progress report [DHHS (NIOSH) Publication No. 2010–104]. [http://www.cdc.gov/niosh/docs/2010-104/pdfs/2010-104.pdf]

5.4 Presentations

NIOSH staff will continue to deliver presentations nationally and internationally concerning occupational safety and health issues associated with nanotechnology, including presentations at scientific conferences, and trade and professional associations. For a listing of presentations, see *Progress Toward Safe Nanotechnology in the Workplace: A Report from NIOSH Nanotechnology Research Center* [DHHS (NIOSH) Publication No. 2007–123]. [http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf]. Presentations from 2007–2008 may be found on the 2009 update of the progress report [DHHS (NIOSH) Publication No. 2010–104]. [http://www.cdc.gov/niosh/docs/2010-104/pdfs/2010-104.pdf]

6 Research to Practice (r2p)

Research to Practice (r2p) involves the translation of research into products, practices, and usable information. The NIOSH nanotechnology research strategic plan reflects the r2p vision to work with partners and stakeholders (see Appendix C) to translate research findings into NIOSH products (e.g., guidance documents, instrumentation, filtration) that will be used to reduce or prevent worker injury and illness from nanotechnology.

6.1 Capacity Building through Technical Assistance

NIOSH is currently collaborating with a number of industries to develop appropriate engineering controls and effective administrative practices for the safe handling of nanomaterials. NIOSH will work with industry in evaluating workplace exposures to nanoparticles and provide recommendations that will minimize worker exposures. For information on the workplace assessments conducted by NIOSH, see *Progress Toward Safe Nanotechnology in the Workplace: A Report from NIOSH Nanotechnology Research Center* [DHHS (NIOSH) Publication No. 2007–123]. [http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf]. An updated progress report listing collaborations on workplace assessments from 2007–2008 may be found on the 2009 update of the progress report [DHHS (NIOSH) Publication No. 2010–104]. [http://www.cdc.gov/niosh/docs/2010-104/pdfs/2010-104.pdf]

NIOSH will continue to make recommendations and provide information based on its research and the published scientific literature. The recommendations will pertain to all areas of the risk management continuum shown in Section 4.1.

7 Intermediate Customers and Intermediate Outcomes

7.1 Federal Government Agencies

NIOSH will conduct and coordinate research with other agencies to foster the responsible development and safe use of nanotechnology as identified by the National Nanotechnology Initiative (NNI).

7.2 Standards Development Organizations

NIOSH actively participates in the development of national and international standards for promoting the health and safety of workers in the nanotechnology industries. NIOSH participates in the American National Standards Institute Nanotechnology Standards Steering Panel, which coordinates the identification and development of critical standards in all areas of nanotechnology.

NIOSH scientists participate in the American Society for Testing and Materials (ASTM) E56 Committee on Nanotechnology, which is developing an integrated family of standards. Committee E56.03 is addressing environmental and occupational safety and health.

NIOSH scientists will continue as members of the U.S. Technical Advisory Group to the International Organization for Standardization (ISO) Technical Committee 229 on Nanotechnologies (ISO TC 229).

7.3 Industry, Labor, and Academia

NIOSH is coordinating input from industry, labor, academics, and a wide range of government agencies in creating guidance for occupational health surveillance. Additionally, NIOSH plans to coordinate input from those same groups of partners and stakeholders with the goal of providing options for the development of standardized data systems for epidemiological research based in workplaces producing and using nanomaterials. Through collaborations with industry, government, and academia, NIOSH developed a "best practices" document, *Approaches to Safe Nanotechnology: Managing the Health and Safety Concerns Associated with Engineered Nanomaterials* [http://www.cdc.gov/niosh/topics/nanotech/], and other communication materials on the safe handling of nanomaterials are in progress. NIOSH is working with industry to characterize occupational exposure to nanoparticles and how to implement effective risk management practices to minimize worker exposure to nanoparticles. In June 2006, NIOSH and E.I. du Pont de Nemours & Co signed an agreement to collaborate on work to evaluate current product performance, test methods, and research gaps related to personal protective equipment used to reduce occupational exposures to nanoparticles.

7.4 Professional Organizations

NIOSH is collaborating with various professional organizations to identify mutual efforts for continuing and developing new worker training programs.

7.5 Research Collaborations

NIOSH has established several national and international collaborations to advance research into the safe use of nanotechnology. NIOSH participates in the National Nanotechnology Initiative (NNI) and has contributed to the nanotechnology strategic plan for the Nation through the working group of Nanotechnology Environmental and Health Implications (NEHI). Occupational Safety and Health is a major priority of the NEHI effort, and NIOSH's strategic research plan and activities have been developed to address most of the major issues in the NEHI plan. NIOSH is also collaborating with the Organization for Economic Cooperation and Development (OECD) to build cooperation, coordination, and communication between the United States and 30 OECD member countries, including the European Union (EU), and more than 180 nonmember economies as well. NIOSH is also working with the World Health Organization Collaborating Centers on global projects of information dissemination and communication.

7.6 International Activities

NIOSH will continue to engage with a number of international entities at all levels—principle investigator, as well as national, regional, and global organizations.

At the national organization levels, NIOSH has been communicating and collaborating with the United Kingdom Institute of Occupational Medicine and the Health and Safety Laboratory, the Netherlands Organization for Applied Scientific Research (TNO), the Finnish Institute of Occupational Health, and the Australian Safety and Compensation Council.

An example of regional level interactions is NIOSH participation in interagency discussions with European communities about establishing a joint U.S./European Union solicitation to fund research looking at nanotechnology health and safety implications. This international solicitation would provide an important venue for leveraging research resources and, as such, is aimed at addressing NIOSH Intermediate Goals 4.1 and 4.2.

At the global organization level, NIOSH will continue to be actively engaged with the Organization for Economic Co-operation and Development (OECD), the UN World Health Organization (WHO), the UN International Labour Organization (ILO), the International Organization for Standardization (ISO), and the International Council on Nanotechnology (ICON).

OECD

NIOSH participation in OECD Working Party on Manufactured Nanomaterials (WPMN) and Working Party on Nanotechnology (WPN) aims at addressing both global objectives by developing international government-level instruments, decisions and recommendations to improve occupational safety and health of nanotechnology globally, and by building cooperation, coordination, and communication between the United States and 30 OECD-member countries including the European Union, and more than 70 nonmember economies.

OECD is government-level organization which is especially effective at conducting economic evaluations, harmonizing test guidelines, exchanging information and data, and facilitating adoption of globally-harmonized voluntary and regulatory programs by governments around the world. It can also provide a mechanism for leveraging research resources by facilitating international government program coordination.

Presently, NIOSH engagement with OECD includes (a) leading an OECD project on Co-Operation on Exposure Measurement and Exposure Mitigation established under the Environmental Directorate, (b) providing expertise in other OECD projects, and (c) exchanging occupational safety and health information through the OECD Working Party on Manufactured Nanomaterials and the Working Party on Nanotechnology. NIOSH Nanoparticle Information Library (NIL) is cross-linked with an OECD database of nanotechnology research projects which are currently under development.

A project on "The analyses and recommendations for exposure measurement and exposure mitigation in nanotechnology occupational settings" was initiated in 2007. The project will deliver a report in 2009 followed by additional reports for specific areas of interest to WPMN.

WHO

NIOSH was instrumental in establishing a 2006–2010 work plan for the World Health Organization Global Network of Collaborating Centers in Occupational Health, and NIOSH's participation in this activity addresses both global objectives. WHO is the directing and coordinating authority for health within the United Nations system, and the "Network" is comprised of key institutions with expertise in occupational safety and health distributed throughout the world.

Since 2006 NIOSH has been leading a nanotechnology project on "Best practices globally for working with nanomaterials" in collaboration with occupational safety and health institutions in Switzerland, the United Kingdom, and Germany.

ILO

NIOSH provides critical assistance in drafting the 5th Edition of the ILO Encyclopaedia of Occupational Safety and Health. The Encyclopaedia will include a chapter on nanotechnology.

ISO

NIOSH scientists are actively involved with the International Organization for Standardization Technical Committee 229 on Nanotechnologies (ISO TC 229) by providing expertise to and leading the development of individual standards and through membership in the U.S. Technical Advisory Group to TC 229. The International Organization for Standardization provides a mechanism for international expertise within the global community to develop the highest quality standards of which are globally accepted. ISO can also serve as a vehicle for global dissemination of NIOSH products.

Since 2006, NIOSH has been leading the development of an ISO TC 229 technical report on safety and health practices in occupational settings relevant to nanotechnologies which is based on the 2006 draft for public comment, *Approaches to Safe Nanotechnology: An Information Exchange with NIOSH*. The technical report ISO/TR 12885:2008 *Nanotechnologies —Health and safety practices in occupational settings relevant to nanotechnologies* was issued in 2008 [ISO 2008].

ICON

The International Council on Nanotechnology is an international multistakeholder organization whose mission is to assess, communicate, and reduce the environmental and health risks of nanotechnology while maximizing its societal benefit. NIOSH experts have been involved in ICON projects related to occupational safety and health since 2006.

Since 2006 ICON has been hosting the development of an internet site on occupational practices for the safe handling of nanomaterials utilizing a wiki software platform "Good Wiki: Good Occupational Practices for the Nanotechnology Industry." NIOSH is a member of a multistakeholder international steering group designing a plan for launching such a novel mechanism for creating and maintaining global occupational safety and health guidance.

8 Outcomes

Nanotechnology is a rapidly developing area of science and technology that promises great benefits. To realize these benefits, it is important to protect workers in nanomaterial research, production, and use from experiencing health problems resulting from the handling of nanomaterials. The NIOSH strategic plan for research is designed to identify and develop information for use in risk management programs that will prevent and control negative impacts to worker health. In addition, research will be conducted to advance the use of nanomaterials in the development of sensors (e.g., detection of harmful chemicals) that can be used in the workplace to ensure an effective control of exposure.

Outcomes of the NIOSH strategic plan include translating research results into products that can be used by the nanotechnology community to advance the technology responsibly and with minimal risk. Specific areas of improvement include sampling/analytical instrumentation and guidance documents. NIOSH will conduct ongoing assessments of the extent to which NIOSH research is used and cited by scientists; scientific, professional, and government agencies; trade associations; unions; nongovernmental organizations; and international communities. NIOSH also will evaluate how research and guidance developed by NIOSH influences others to take action to prevent exposure to hazards related to nanomaterials and ultimately prevent adverse health effects.

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Appendix A

Timeline for NIOSH Nanotechnology Research

Summary of ongoing or initiated research projects in FY05

Critical research area	Projects
Toxicity and internal dose	▪ Begin toxicity testing in laboratory animal and in vitro systems.
Measurement methods	▪ Develop techniques for particle surface area measurement. ▪ Generation and characterization of nanomaterials. ▪ Nanoaerosol monitoring methods. ▪ Ultrafine/respirable particle mapping in automotive manufacturing facilities.
Exposure assessment	▪ Conduct exposure assessment pilot studies of nanoparticles in the workplace.
Epidemiology and surveillance	▪ Surveillance Phase I: Identify and gather information relevant for determining need for worker surveillance. ▪ Conduct studies on wildfire ultrafine aerosol and firefighter exposure studies.
Risk assessment	▪ Quantitative risk assessment on ultrafine and fine TiO_2. ▪ Initiate collaborative research on lung model development and nanoparticle dose estimation.
Engineering controls and PPE	▪ Identify key exposure control issues. ▪ Initiate research on the filtration efficiency of typical respirator filter media for nanoscale particles. ▪ Initiate research on automobile ultrafines.
Fire and explosion safety	▪ Identify key safety issues.
Recommendations and guidance	▪ Develop a draft document on working safely with nanomaterials. ▪ Draft a titanium dioxide (TiO_2) current intelligence bulletin.
Communication and information	▪ Develop a pilot Nanotechnology Information Library (NIL). ▪ Generate a basic set of frequently asked questions (FAQs).

(Continued)

Summary of ongoing or initiated research projects in FY05 (Continued)

Critical research area	Projects
Applications	■ Initiate pilot project on nanofiber-based filter media. ■ Continue a study to investigate nanomaterials for improving sensor technology needed in respirator cartridge end-of-service indicators.
Global activities	■ Co-sponsor the 1st International Symposium on Occupational Health Implications of Nanomaterials in Buxton, UK ■ Contribute to development of ISO technical report on nanoparticle exposure, assessment and characterization in workplace atmospheres.

Summary of ongoing or initiated research projects in FY06

Critical research area	Projects
Toxicity and internal dose	■ Pulmonary toxicity of carbon nanotubes. – determine the oxidant generating potency and cytotoxicity of SWCNT in vitro. – determine the pulmonary response to aspiration of SWCNT in the mouse model; time course and dose-response. ■ Pulmonary toxicity of diesel exhaust particles (DEP). – determine the effects of exposure to DEP on the generation of oxidants in the lung. – determine the role of oxidant generation by DEP on genotoxicity. ■ Nanotechnology safety and health research coordination. – disseminate results of the NIOSH nanotoxicology program through invited presentations. ■ Dermal effects of nanoparticles. – determine the effects of SWCNT on skin cells in vitro.
Measurement methods	■ Develop techniques for particle surface area measurement. ■ Analyze filter efficiency for collecting nanoparticles. ■ Conduct exposure assessment pilot studies of nanoparticles in the workplace with various measurement methods.

(Continued)

Summary of ongoing or initiated research projects in FY06 (Continued)

Critical research area	Projects
Exposure assessment	■ Conduct survey of nanomaterial uses and workers exposed. ■ Conduct exposure assessment pilot studies of nanoparticles in the workplace. ■ Develop study protocol for conducting TiO_2 workplace exposure assessments. ■ Conduct studies to gather hazard ID information about carbon nanotubes.
Epidemiology and surveillance	■ Surveillance Phase I: Continue to ascertain the need for worker surveillance information (e.g., exposure, medical). ■ Conduct studies on wildfire ultrafine aerosol and firefighter exposure studies.
Risk assessment	■ Perform QRA on ultrafine particles from scientific literature. ■ Develop lung deposition model software enhancements.
Engineering controls and PPE	■ Identify key exposure control issues. ■ Evaluate control banding options to reduce worker exposures. ■ Release contract final report on the "Penetration of Nanoparticles through Respirator Filter Media." ■ Initiate intramural research project on "Respiratory Protection against Nanoparticles" to measure the effectiveness of air purifying respirators against nanoparticles. ■ Initiate intramural research on the "Development of PPE Ensemble Test Methods" to better understand the barrier effectiveness of protective clothing and ensembles. ■ Evaluate existing exposure controls and provide recommendations. ■ Continue research of ultrafines in an automotive engine machining and assembly facility .
Fire and explosion safety	■ Identify key safety issues.
Recommendations and guidance	■ Update recommendations on the safe handling of nanomaterials (ongoing). ■ Initiate investigation of qualitative risk assessment and management methods for nanomaterials. ■ Host occupational safety and health Research to Practice (r2p) conference on nanotechnology. ■ Hold public meeting and address external review comments on draft TiO_2 current intelligence bulletin.

(Continued)

Summary of ongoing or initiated research projects in FY06 (Continued)

Critical research area	Projects
Communication and information	■ Update the NIL (ongoing). ■ Develop an expanded set of frequently asked questions (FAQs). ■ Develop a topic page specific to nanotechnology.
Applications	■ Complete pilot project on nanofiber-based filter media. ■ Continue to investigate nanomaterials for improving sensor technology needed in respirator cartridge end of service life indicators.
Global activities	■ Join OECD and begin development of international government-level instruments, decisions, and recommendations to improve occupational safety and health of nanotechnology. ■ Join ISO and develop international consensus-based standards. ISO tech report TC229 initiated. ■ Join WHO work group to develop and disseminate best practices globally. ■ Join ICON to develop and disseminate best practices globally. ■ Co-sponsor the 2nd International Symposium on Occupational Health Implications of Nanomaterials in Minneapolis, MN

Summary of ongoing or initiated research projects in FY07

Critical research area	Projects
Toxicity and Internal dose	■ Define preliminary cardiovascular endpoints. ■ Gather data and develop preliminary dosimetry for diesel exhaust particulate (DEP); determine the role of DEP-induced nitric oxide production on genotoxicity. ■ Determine pulmonary toxicity of carbon nanotubes. – determine the role of lung antioxidants on the pulmonary response to SWCNT. – determine the effect of exposure to SWCNT on susceptibility of the lung to infection. ■ Develop particle surface area as a dose metric. – develop a method to disperse nanoparticles for in vitro and in vivo toxicity testing. – determine if degree to dispersion of a nanoparticle suspension affects bioactivity.

(Continued)

Summary of ongoing or initiated research projects in FY07 (Continued)

Critical research area	Projects
Toxicity and internal dose (Continued)	■ Evaluate systemic microvascular dysfunction effects of ultrafine vs. fine particles. – construct an inhalation exposure system for fine and ultrafine TiO_2. – determine the effects of pulmonary exposure to ultrafine TiO_2 on systemic arteriole function. ■ Evaluate the pulmonary deposition and translocation of nanomaterials. – determine the effect of dispersion on the pulmonary fibrogenic potency of SWCNT. ■ Determine role of carbon nanotubes in cardiovascular inflammation. – determine if pulmonary exposure to SWCNT causes oxidant stress in cardiovascular tissue. – determine if pulmonary exposure to SWCNT causes arterial plaque formation. ■ Disseminate results of the NIOSH nanotoxicology program through invited presentations.
Measurement methods	■ Evaluate surface area–mass metric airborne measurement results. ■ Establish a suite of instruments and protocols for nanomaterial measurements. ■ Continue to conduct exposure assessment/measurement studies of nanoparticles in the workplace. ■ Continue to develop offline and online nanoparticle measurement methods. ■ Evaluate a high flow personal sampler. ■ Evaluate candidate nanomaterials for use in studies of nanoparticle surface area measurement. ■ Evaluate dustiness testing methods for powdered nanomaterials.
Exposure assessment	■ Conduct market surveys of nanomaterial uses and workers exposed. ■ Conduct exposure assessment studies of nanoparticles in the workplace. ■ Initiate ultrafine and fine TiO_2 and metal oxides workplace exposure assessments. ■ Conduct studies to gather hazard ID information about carbon nanotubes.
Epidemiology and surveillance	■ Draft guidelines on occupational health surveillance for nanotechnology workers with assistance from a cross-governmental work group as well as representatives from industry, government, academia, and labor. ■ Conduct studies on wildfire ultrafine aerosol and firefighter exposure studies.

(Continued)

Summary of ongoing or initiated research projects in FY07 (Continued)

Critical research area	Projects
Risk assessment	■ Extend and calibrate rat lung exposure-dose model for nanoparticles. ■ Develop nanoparticle deposition model in rat nasopharyngeal region. ■ Begin developing model for CNT lung deposition in humans.
Engineering controls and PPE	■ Identify key exposure control issues. ■ Evaluate control banding options to reduce worker exposures. ■ Continue developing intramural research project on "Respiratory Protection against Nanoparticles" with an initial focus on filtration efficiency of commercially available respirators. ■ Continue intramural research on the "Development of PPE Ensemble Test Methods."
Fire and explosion safety	■ Identify key safety issues.
Recommendations and guidance	■ Continue updating recommendations on the safe handling of nanomaterials (ongoing). ■ Prepare final draft of TiO_2 document. ■ Develop worker and employer guidelines for safe work practices and proper nanomaterial handling. ■ Draft guidelines on occupational health surveillance for nanotechnology workers with assistance from a cross-governmental work group as well as representatives from industry, government, academia, and labor. ■ Draft interim guidance on the medical screening of workers potentially exposed to engineered nanoparticles.
Communication and information	■ Continue updating the Nanotechnology Information Library (NIL) (ongoing). ■ Develop a progress report on NIOSH nanotechnology research and communication efforts. ■ Cosponsor training courses in safe handling of nanoparticles. ■ Conduct Research to Practice (r2p) activities (ongoing) such as the development of brochures, fact sheets, updating the topic page, etc. ■ Disseminate results of the NIOSH nanotoxicology program through invited presentations.

(Continued)

Summary of ongoing or initiated research projects in FY07 (Continued)

Critical research area	Projects
Applications	■ Develop a method to identify significant emerging nanotechnology products. ■ Research monolayer-protected gold nanoparticles conducted to study whether these nanoparticles can be used in sensors for respirator cartridge end of service life indication. ■ Initiate proposal for FY09 NORA on antibacterial HVAC air filters.
Global activities	■ Continue OECD development of international government level instruments, decisions, and recommendations to improve occupational safety and health of nanotechnology. ■ Continue ISO development of international consensus-based standards; ISO tech report TC229 initiated. ■ Continue with WHO work group to develop and disseminate best practices globally. ■ Continue with ICON to develop and disseminate best practices globally. ■ Establish NIOSH-UK HSL collaboration concerning dustiness testing for nanomaterials and detailed workplace measurements.

Summary of ongoing or initiated research projects in FY08

Critical research area	Projects
Toxicity and internal dose	■ Determine potential aneuploidy following exposure to carbon nanotubes. – determine the effect of in vitro exposure to SWCNT on the mitotic process. ■ Evaluate pulmonary toxicity of carbon nanotubes. – construct an inhalation exposure system for SWCNT. – compare the fibrotic response to inhalation vs. aspiration of SWCNT. ■ Establish particle surface area as a dose metric. – determine the pulmonary response to fine vs. ultrafine TiO_2 and carbon black using mass and surface area dose metrics. – evaluate oxidant generation potential as a predictive in vitro screening test for metal oxide nanoparticles. ■ Evaluate systemic microvascular dysfunction effects of ultrafine vs. fine particles – determine the role of oxidant stress in the microvascular response to pulmonary exposure to ultrafine TiO_2.

(Continued)

Summary of ongoing or initiated research projects in FY08 (Continued)

Critical research area	Projects
Toxicity and internal dose (Continued)	■ Evaluate the pulmonary deposition and translocation of nanomaterials. – determine the rate of translocation of SWCNT from the lung to systemic organs. ■ Evaluate dermal effects of nanoparticles. – determine oxidant generation and cytotoxicity of metal oxide nanoparticles with skin cells in vitro. ■ Determine role of carbon nanotubes in cardiovascular inflammation. – measure blood cytokine levels in response to pulmonary exposure to SWCNT. ■ Evaluate occupational exposures and potential neurological risks. – evaluate markers of brain inflammation and blood/brain barrier damage following pulmonary exposure to MWCNT. ■ Determine neurotoxicity after pulmonary exposure to welding fumes. – determine the pulmonary inflammatory response to inhalation of welding fumes. – determine the effect of welding fumes on the susceptibility of the lung to infection. ■ Conduct nanotechnology safety and health research coordination. – disseminate results of the NIOSH nanotoxicology program through invited presentations.
Measurement methods	■ Evaluate surface area–mass metric airborne measurement results. ■ Establish a suite of instruments and protocols for nanomaterial measurements. ■ Continue to conduct exposure assessment/measurement studies of nanoparticles in the workplace. ■ Continue to develop offline and online nanoparticle measurement methods. ■ Develop a hand held fast response nanoparticle monitor. ■ Develop software for spatial mapping of nanoparticles. ■ Evaluate collection efficiency of personal mass based aerosol samplers. ■ Identify, qualify, and develop nanoscale reference materials for measurement quality control.
Exposure assessment	■ Continue with exposure assessments of nanoparticles in the workplace. ■ Continue ultrafine and fine metal oxides workplace exposure assessments. ■ Conduct studies to characterize size, concentration, and morphology of nanoparticles emitted by various processes. ■ Evaluate the dustiness potential for powdered nanomaterials.

(Continued)

Summary of ongoing or initiated research projects in FY08 (Continued)

Critical research area	Projects
Epidemiology and surveillance	■ Finalize interim guidelines on medical screening for nanotechnology workers. ■ Gather information to assess the feasibility and potential timing of industry-wide exposure and epidemiological studies of workers exposed to engineered carbonaceous nanomaterials. ■ Seek input from a collaborative working group made up of representatives from industry, government, academia, and labor concerning the value and utility of establishing an exposure registry for workers potentially exposed to engineered nanoparticles.
Risk assessment	■ Begin hazard and risk estimates of carbon and metal nanoparticles using new NIOSH toxicity data. ■ Calibrate rat dose-response model for nanoparticles using NIOSH toxicity data. ■ Complete nasopharyngeal deposition model in rats.
Engineering controls and PPE	■ Continue to evaluate the effectiveness of controls to reduce workplace exposures to nanoparticles and metal oxides. ■ Continued research on "Respiratory Protection against Nanoparticles" with a focus on face seal leakage. ■ Continued research on the "Development of PPE Ensemble Test Methods." ■ Evaluate existing exposure control and provide recommendations as part of the exposure assessment/measurement studies in the workplace.
Fire and explosion safety	■ Evaluate the dustiness potential for powdered nanomaterials.
Recommendations and guidance	■ Continue updating recommendations on the safe handling of nanomaterials (ongoing); specifically, information on the field protocol. ■ Continue preparing final TiO_2 document that incorporates peer review comments (ongoing). ■ Develop worker and employer guidelines (brochures) for proper nanomaterial handling and safe work practices. ■ Evaluate control banding options to reduce worker exposures. ■ Conduct a public meeting to discuss interim guidance on the medical screening of workers potentially exposed to engineered nanoparticles.
Communication and information	■ Continue updating the NIL (ongoing). ■ Continue conducting r2p activities (ongoing), such as the development of brochures, fact sheets, updating the topic page, etc.

(Continued)

Summary of ongoing or initiated research projects in FY08 (Continued)

Critical research area	Projects
Communication and information (Continued)	■ Develop a web site highlighting the nanotechnology cross-sector as part of the NIOSH National Occupational Research Agenda (NORA). ■ Draft supplemental strategic plan specific to nanoinformatics and the programs projected communication efforts.
Applications	■ Research monolayer-protected gold nanoparticles used in prototype respirator cartridge end of service indicator (ESLI). ■ Prepare full proposal for NORA on antibacterial HVAC air filters.
Global activities	■ Continue participation with ISO, ICON, OECD, and UN (WHO, ILO). ■ Initiate Good Wiki for good occupational practices for the nanotechnology industry. ■ Participate in nanotech symposium at World Congress on Safety and Health at Work, Seoul, Korea. ■ Participate in 2nd international conf. on nanotoxicology, Zurich, Switzerland.

Summary research planned for FY09–FY10

Critical research area	Projects
Toxicity and internal dose	■ Identify specific biomarkers for unusual toxicity of nanomaterials. Develop an in vitro screening test for fibrogenic potential of nanomaterials. ■ Conduct in vivo investigations of MWCNT; determine time and dose dependence of pulmonary response; compare response to aspirated vs. inhaled MWCNT. ■ Evaluate the potential effect of silicon-based nanowires on lung toxicity; determine the oxidant generating potency and cytotoxicity in vitro. ■ Evaluate systemic microvascular dysfunction effects of ultrafine vs. fine particle pulmonary exposure. ■ Complete studies of nanoparticle translocation in laboratory animals after pulmonary exposure to nanoparticles. ■ Determine the dermal toxicity and penetration potential to the most used nanomaterials. ■ Determine the potential for neurological effects following transport of metal oxide nanoparticles to the brain (e.g., transport by olfactory nerve). ■ Construct and test an inhalation exposure system for spot welding fume; determine lung effects of resistance spot welding using adhesives.

(Continued)

Summary research planned for FY09–FY10 (Continued)

Critical research area	Projects
Toxicity and internal dose (Continued)	■ Determine effects of inhalation of welding fume on markers of brain inflammation and blood/brain barrier damage in a rat model. ■ Conduct cell-based assessment for iron nanoparticle in vitro effects on endothelial cells and the role of ROS. ■ Determine the role of carbonaceous materials on mutagenic and or carcinogenic response in vitro and in vivo. ■ Elucidate mechanisms by which pulmonary exposures to nanoparticles causes brain inflammation; determine dose-response and time course.
Measurement methods	■ Evaluate surface area–mass metric airborne measurement results. ■ Establish a suite of instruments and protocols for nanomaterial measurements. ■ Continue to conduct exposure assessment/measurement studies of nanoparticles in the workplace. ■ Continue to develop offline and online nanoparticle measurement methods. ■ Develop performance results for current nanoparticle measurement instruments and methods. ■ Complete evaluation of viable and practical workplace sampling devices and methods for nanoparticles (affordable, portable, effective). ■ Continue to develop a handheld, fast response nanoparticle monitor. ■ Continue development software for spatial mapping of nanoparticles. ■ Develop a standardized aerosol test method using magnetic passive aerosol samplers. ■ Identify, qualify, and develop nanoscale reference materials for measurement quality control.
Exposure assessment	■ Continue evaluation of workplace exposures to nanomaterials and their potential routes of exposure. ■ Continue evaluation of size, concentration and morphology of nanoparticles emitted by various processes. ■ Focus on collecting personal exposure data for engineered nanoparticles. ■ Develop task-based exposure profiles for engineered nanoparticle processes.
Epidemiology and surveillance	■ Update interim guidelines on medical screening for nanotechnology workers based on input from published literature and collaborative input from representatives of industry, government, academia, and labor. ■ Initiate an industry wide exposure study of workers exposed to specific classes of engineered nanomaterials; for example, a study of workers exposed to carbonaceous engineered nanomaterials.

(Continued)

Summary research planned for FY09–FY10 (Continued)

Critical research area	Projects
Epidemiology and surveillance (Continued)	▪ Assess the feasibility of establishing exposure registries for nanotechnology workers for the purposes of occupational health surveillance and future epidemiologic study.
Risk assessment	▪ Continue hazard and risk assessment of engineering nanoparticles. ▪ Complete the development of model of CNT lung deposition in humans. ▪ Initiate human nanopharyngeal deposition model. ▪ Initiate integrated revision to human dosimetry models.
Engineering controls and PPE	▪ Continue evaluation of respirator filtration performance and continue to evaluate the effectiveness of controls to reduce workplace exposures to nanoparticles. ▪ Produce a summary of control strategies. ▪ Initiate and conduct research on "Nanoparticle penetration through protective clothing" to investigate penetration through non-woven materials used in protective clothing and develop predictive models that can be used to improve and/or develop guidance documents, performance requirements, and test methods.
Fire and explosion safety	▪ Produce a summary of key safety issues and recommendations. ▪ Evaluate the dustiness potential for powdered nanomaterials.
Recommendations and guidance	▪ Develop new or updated recommendations for the safe handling of nanomaterials. ▪ Develop RELs for ultrafine TiO_2 and CNT ▪ Publish respirator selection guide for workers handling nanoparticles.
Communication and information	▪ Publish an updated progress report on NIOSH nanotechnology research and communication efforts. ▪ Continue conducting r2p activities (ongoing), such as the development of brochures, fact sheets, updating the topic page, etc. ▪ Update the web site highlighting the nanotechnology cross-sector as part of the NIOSH NORA program portfolio (ongoing). ▪ Continue updating the NIL (ongoing).
Applications	▪ Evaluate application of nanotechnology for improving antibacterial effect of HVAC filters. ▪ Further develop and refine end-of-service indicators using nanomaterials.

(Continued)

Summary research planned for FY09–FY10 (Continued)

Critical research area	Projects
Global activities	■ Continue participation with ICON, ISO, OECD and UN (WHO, ILO). ■ Continue with development of GoodWiki for good occupational practices for the nanotechnology industry. ■ Participate in ICOH International congress on occupational health in Cape Town, South Africa (2009). ■ Participate in 4th international congress on nanotechnology, Helsinki, Finland (2009). ■ Expand collaborations to developing nations and emerging powers (Asia-Pacific, Eastern Europe). ■ Develop partnerships for translation of NIOSH publications to other languages.

Summary research planned for FY11–FY12 (pending)

Critical research area	Projects
Toxicity and internal dose	■ Evaluate induction of lung fibrosis by cerium oxide and diesel exhaust. ■ Evaluate the potential pulmonary reaction to inhalation of commercial spray containing ultrafine TiO_2. ■ Develop predictive algorithms for nanoparticle bioactivity. ■ Evaluate the predictive value of in vitro screening tests for the fibrogenic potential of carbon nanotubes. ■ Elucidate mechanisms by which carbon nanotubes induce lung fibrosis.
Measurement methods	■ Develop instruments capable of distinguishing process from background nanoparticles. ■ Develop techniques to characterize agglomeration state of nanoparticles.
Exposure assessment	■ Complete evaluation of workplace exposures to nanomaterials and their potential routes of exposure. ■ Complete evaluation of size, concentration, and morphology of nanoparticles emitted by various processes.
Epidemiology and surveillance	■ Assess the feasibility of industry wide health effects studies of workers exposed to engineered nanomaterials. ■ Evaluate occupational exposures and potential neurological risks.

(Continued)

Summary research planned for FY11–FY12 (pending) (Continued)

Critical research area	Projects
Risk assessment	▪ Evaluate/validate nanoparticle exposure-dose-response models. ▪ Investigate models with additional routes of exposure. ▪ Develop risk estimates using models of kinetic and biological activity of nanoparticles. ▪ Characterize risk of nanoparticle exposure in the workplace. ▪ Contribute to OSH recommendation development.
Engineering controls and PPE	▪ Finalize development of a standardized aerosol test method using magnetic passive aerosol samplers for PPE ensemble testing. ▪ Expand particulate penetration project to include different types of fabrics, investigate the use of electrostatic charges, use of a wind tunnel in testing and evaluate bellows effects. ▪ PPE workplace protection factor studies of nanotechnology workers. ▪ Laboratory performance of filter media against carbon nanotubes and/or other key nanoparticle classes.
Fire and explosion safety	▪ Update pertinent safety issues and recommendations.
Recommendations and guidance	▪ Develop RELs for most used nanomaterials ▪ Publish protective clothing selection guide for workers handling nanoparticles.
Communication and information	▪ Publish an updated progress report on NIOSH nanotechnology research and communication efforts. ▪ Continue conducting r2p activities (ongoing), such as the development of brochures, fact sheets, updating the topic page, etc. ▪ Update the Web site highlighting the nanotechnology cross-sector as part of the NIOSH NORA program portfolio (ongoing). ▪ Continue updating the NIL (ongoing).
Applications	▪ Evaluate application of nanotechnology for improving antibacterial effect of HVAC filters and PPE. ▪ Further development and refinement of end-of-service indicators using nanomaterials.
Global activities	▪ Strengthen participation with globally recognized organizations ICON, ISO, OECD and UN (WHO, ILO). ▪ Continue refinement of GoodWiki for good occupational practices for the nanotechnology industry.

Appendix B

NNI Priority Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials

Research categories (A–E)	Research needs
A. Instrumentation, metrology, and analytical methods	1. Develop methods to detect nanomaterials in biological matrices, the environment, and the workplace 2. Understand how chemical and physical modifications affect the properties of nanomaterials 3. Develop methods for standardizing assessment of particle size, size distribution, shape, structure, and surface area 4. Develop certified reference materials for chemical and physical characterization of nanomaterials 5. Develop methods to characterize a nanomaterial's spatio-chemical composition, purity, and heterogeneity
B. Nanomaterials and human health	Overarching Research Priority: Understand characteristics of nanomaterials in relation to toxicity in biological systems. 1. Understand the absorption and transport of nanomaterials throughout the human body 2. Develop methods to quantify and characterize exposure to nanomaterials and characterize nanomaterials in biological matrices 3. Identify or develop appropriate in vitro and in vivo assays/models to predict in vivo human responses to nanomaterials exposure 4. Establish the relationship between the properties of nanomaterials and uptake via the respiratory or digestive tracts or through the eyes or skin, and assess body burden 5. Determine the mechanisms of interaction between nanomaterials and the body at the molecular, cellular, and tissue levels
C. Nanomaterials and the environment	1. Understand the effects of engineered nanomaterials in individuals of a species and the applicability of testing schemes to measure effects 2. Understand environmental exposures through identification of principle sources of exposure and exposure routes

(Continued)

NNI Priority Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials (Continued)

Research category (A-E)	Research needs
C. Nanomaterials and the environment (Continued)	3. Evaluate abiotic and ecosystem-wide effects 4. Determine factors affecting the environmental transport of nanomaterials 5. Understand the transformation of nanomaterials under different environmental conditions
D. Humans and environmental exposure assessment	1. Characterize exposures among workers 2. Identify population groups and environments exposed to engineered nanoscale materials 3. Characterize exposure to the general population from industrial processes and industrial and consumer products containing nanomaterials 4. Characterize health of exposed populations and environments 5. Understand workplace processes and factors that determine exposure to nanomaterials
E. Risk management methods	Overarching Research Priority: Evaluate risk management approaches for identifying and addressing risks from nanomaterials, 1. Understand and develop best workplace practices, processes, and environmental exposure controls 2. Examine product or material life cycle to inform risk reduction decisions 3. Develop risk characterization information to determine and classify nanomaterials based on physical or chemical properties 4. Develop nanomaterial-use and safety-incident trend information to help focus risk management efforts 5. Develop specific two-way risk communication approaches and materials From The National Nanotechnology Initiative, Strategy for Nanotechnology-Related Environmental, Health, and Safety Research, 2008.

Appendix C

Partnerships and Collaborations

Integral to completing this research are the partnerships and collaborations NIOSH has forged with countries, academia, industry, labor, other government agencies, and nongovernmental organizations. These collaborations have provided expertise and resources critical for successfully completing research and for developing and disseminating health and safety information on engineered nanoparticles. Following are some of the ongoing NIOSH NTRC partnerships and collaborations in nanotechnology research:

Universities

- The Ohio State University, evaluating workplaces, controls, and practices in the nanocomposites industry
- University of Cincinnati, translating nanotechnology research into occupational and environmental health and safety activities
- University of Dayton Research Institute, understanding and improving the control of carbon nanotubes
- University of Iowa, measuring airborne levels of ultrafine particles
- University of Nevada at Reno (with Altair Nano), understanding and improving the control of ultrafine metal oxides and engineered nanomaterials
- University of Massachusetts at Lowell, collaborating on the development of good practices for handling nanomaterials in research laboratories and developing exposure assessment methods
- University of Minnesota, measuring airborne concentrations of ultrafine particles
- University of Montana, evaluating the toxicity of nanowires
- University of Pittsburgh, evaluating the toxicity of nanomaterials
- University of Rochester, measuring the ability of nanoparticles to generate radical species
- University of Wisconsin, Madison, developing exposure assessment strategies and characterizing nanoparticles in friction stir welding and micromachining
- Virginia Tech University (with Luna Nano Works), understanding and improving the control of fullerines and other engineered nanoparticles
- West Virginia University Nanotechnology Center, evaluating the toxicity of metal oxide nanowires
- West Virginia University Medical School, evaluating the effects of pulmonary exposure to nanoparticles, including the influence of exposure to titanium dioxide (TiO_2) on systemic microvascular function

Health and Safety Organizations and Expert Groups

- American Industrial Hygiene Association (AIHA)

- American Conference of Governmental Industrial Hygienists (ACGIH)
- American Society of Safety Engineers (ASSE)
- Health Physics Society (HPS)
- National Safety Council (NSC)
- Hamner Institutes for Health Sciences on software modifications for use in lung dosimetry modeling
- International Alliance for Nanotoxicology Harmonization (IAHN)
- International Safety Equipment Association on the respirator filter media work being conducted at the University of Minnesota to assess the filtration efficiency against nanoparticles
- The initiative on Minimum Information Needed for Charaterization of Nanomaterials (MINChar)
- Institute of Occupational Medicine (IOM), Edinburgh, Scotland, on revising rat lung dosimetry models to account for particle size-specific clearance and retention

Federal and Other Government Agencies

- Environmental Protection Agency (EPA)
- Occupational Safety and Health Administration (OSHA) to evaluate the effectiveness of workplace control measures
- Consumer Product Safety Commission (CPSC)
- National Aeronautics and Space Administration (NASA) to evaluate the toxicity of single-walled carbon nanotubes (SWCNT)
- U.S. Air Force
- U.S. Army
- Department of Energy (DOE)
- U.S. Nuclear Regulatory Commission
- National Institute of Environmental Health Sciences/ National Institute of Health and the Department of Defense on nanotoxicology
- National Institute of Standards and Technology (NIST) on evaluating the toxicity of nanoparticles and developing nanoscale reference materials
- National Nanotechnology Initiative (NNI) through active participation in NNI's strategic and budget planning processes, and coordination of research into occupational safety and health of nanotechnology with other government agencies
- National Toxicology Program on field assessments and toxicological research
- Oak Ridge National Laboratory to evaluate the pulmonary toxicity of nanoparticles
- Commonwealth of Massachusetts to promote the safe development of nanotechnology in Massachusetts
- Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST)
- Karolinska Institute on evaluating the effect of nanomaterials on immune cells
- World Health Organization (WHO)
- Organization for Economic Cooperation and Development (OECD)

- International Labour Organization (ILO) to develop information on nanotechnology for a revised edition of the Encylopaedia of Occupational Health and Safety
- International Organization for Standardization (ISO) and the International Electrotechnical Commission (IEC) to develop international standards for terminology, characterization, and safety practices for nanotechnology

Nanotechnology Industries

- DuPont and the Nanoparticle Occupational Safety and Health industry consortium on issues related to the measurement of nanoparticles and the efficiency of filtration materials for engineered nanoparticles
- Mitsui Co. Inc. on evaluating the bioactivity of multi-walled carbon nanotubes (MWCNT).
- IBM on evaluating the bioactivity of silicon nanowires
- Luna Nano Works on understanding and improving the control of fullerines and other engineered nanoparticles
- Altair Nano on understanding the improving the control of ultrafine metal oxides and engineered nanomaterials
- Quantum Sphere on understanding and improving the control of nanoscale metals and metal oxides
- QD Vision on understanding and improving the control of quantum dots
- NanoMech LLC (Fayetteville, Arkansas) to collaborate on a proposed EPA phase I SBIR project related to containment of airborne nanoparticles

Collaborative Workshops

- In FY2005, NIOSH co-sponsored the first *Symposium on Occupational Health Implications of Nanomaterials* in Buxton, United Kingdom
- In FY2006, NIOSH co-sponsored the second *Symposium on Occupational Health Implications of Nanomaterials* in Minneapolis, Minnesota
- In FY2007—
    - — NIOSH collaborated with the International Aerosol Research Assembly and the American Association for Aerosol Research to hold the Second International Symposium on Nanotechnology and Occupational Health in conjunction with the international aerosol conference in St. Paul, Minnesota.
    - — NIOSH and the University of Cincinnati co-sponsored the International Conference on Nanotechnology Occupational and Environmental Health and Safety: Research to Practice, in Cincinnati, Ohio.
    - — NIOSH convened a collaborative workshop that included representatives from government, academia, labor, and industry in Washington, DC to review a draft document developed by NIOSH and a cross-agency work group, titled *Interim Guidelines on Medical Screening of Workers*

Potentially Exposed to Engineered Nanoparticles.

— NIOSH co-sponsored the Third *Symposium on Occupational Health Implications of Nanomaterials* in Taipei, Taiwan.

- In FY2008, NIOSH served as the agency lead to organize the program for the National Nanotechnology Initiative workshop on Human and Environmental Exposure Assessment which was held February 2009, in Bethesda, MD.
- In FY2008, NIOSH began to participate in the planning of the Fourth International Conference on Nanotechnology—Occupational and Environmental Health planned for August 2009, in Helsinki, Finland.
- In FY2009, NIOSH co-sponsored a National Institute of Standards and Technology Workshop on Enabling Standards for Nanomaterial Characterization which was held in October 2008, in Gaithersburg, MD.

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