Continuing to Protect the NANOTECHNOLOGY WORKFORCE:

NIOSH NANOTECHNOLOGY RESEARCH PLAN FOR 2018 – 2025

Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

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Back

1. Destruction of fungus Trichophyton by silver nanoparticles (Photo by ©Dr. Microbe/Getty Images)
2. Hands touching circle global network connection and icon customer (Photo by ©ipopba/Getty Images)

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Department of Health and Human Services
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

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FOREWORD

The National Institute for Occupational Safety and Health (NIOSH) is pleased to present *Continuing to Protect the Nanotechnology Workforce: NIOSH Nanotechnology Research Plan for 2018–2025*. This plan updates the previous, December 2013 strategic plan with knowledge gained from results of ongoing research on the safety and health implications of engineered nanomaterials. The NIOSH Nanotechnology Research Center (NTRC) coordinates the NIOSH nanotechnology research program via a comprehensive, institute-wide plan that supports multiple sectors in the National Occupational Research Agenda (NORA).

NIOSH is using this *Nanotechnology Research Plan for 2018–2025* as a roadmap to advance (1) understanding of nanotechnology-related toxicology and workplace exposures and (2) implementation of appropriate risk management practices during the discovery, development, and commercialization of engineered nanomaterials along their product lifecycle. As researchers explore and characterize potential hazards and risks associated with nanomaterials, the knowledge from that research will serve as a foundation for an anticipatory and proactive approach to the introduction and use of nanomaterials in advanced manufacturing. Although many industries have adopted NIOSH recommendations and guidance on approaches to safe nanotechnology, NIOSH strives to remain at the forefront of developing contemporary guidance that supports and promotes the safe, responsible development of nanomaterials.

John Howard, M.D.
Director
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Centers for Disease Control and Prevention

EXECUTIVE SUMMARY

Nanotechnology—the manipulation of matter on a near-atomic scale (1 to 100 nanometers) to produce new materials and devices—has the ability to transform many industries and their products, from medicine to manufacturing. Even though nanoscale substances such as carbon black or titanium dioxide have been in use for a long time, modern nanotechnology is still an emerging field. The commercial application of newer engineered nanomaterials such as carbon nanotubes began about 20 years ago. Consequently, as is the case with any emerging technology, there are many unanswered questions about the risk management continuum—*hazard, exposure, risk, control*—with regard to nanotechnology. *Hazard* is the driver of that continuum, and the wide use of nanomaterials in commerce possibly means wide worker exposure. Employers, workers, and other decision makers are asking for information on every element of the risk management continuum simultaneously, from hazard identification to control.

Many knowledge gaps remain on how to work safely with these materials. Through strategic planning, research, partnering with stakeholders, and making information widely available, NIOSH is providing national and world leadership to prevent work-related illness and injury.

NANOTECHNOLOGY AND NIOSH RESEARCH

Nanotechnology and the commercialization of products and devices containing engineered nanomaterials could help address critical global problems concerning energy, transportation, pollution, health, and food. The potential benefits of nanotechnology are immense. However, scientists must also address concerns about the potential adverse human health effects of this technology. Timely, targeted research must further define the hazards, exposures, and risks and provide guidance for the safe handling of nanomaterials. A concerted effort by industry, academia, labor, environmental health and safety professionals, and government can fill the knowledge gaps in an accessible process that coincides with development of this new technology.

NIOSH is playing an active part in this process by supporting the development of a broad spectrum of research and prevention strategies for health and safety hazards related to nanotechnology. In a series of reports [NIOSH 2007, 2010, 2012a], NIOSH has summarized its progress in conducting nanotechnology research and recommending risk management strategies (see **http://www.cdc.gov/niosh/topics/nanotech/**). NIOSH investigators have identified adverse health effects in animals exposed to various engineered nanomaterials; assessed worker exposures; initiated epidemiologic research; and provided guidance on occupational exposure limits (OELs), control technologies, and medical surveillance. Yet, there are still many questions. Advanced synthesis techniques yield nanomaterials with a practically limitless combination of physicochemical traits, each of which could have unique toxicology and exposure risks. There is need for an expeditious approach for controlling exposure to the continuously growing number of nanomaterials used both in science and in commerce. Moreover, the advanced nanomaterials under development may have additional potentially hazardous characteristics that will need addressing in the near future [Murashov et al. 2012].

NIOSH NANOTECHNOLOGY RESEARCH CENTER

NIOSH established the Nanotechnology Research Center (NTRC) in 2004 to coordinate nanotechnology research across the institute. Ten critical areas of research (toxicity and internal dose; measurement methods; exposure assessment; epidemiology and surveillance; risk assessment;

engineering controls and personal protective equipment [PPE]; fire and explosion safety; recommendations and guidance; global collaborations; and applications and informatics) have at least one key scientist each, serving as a coordinator. The NTRC and its steering committee of critical area coordinators are responsible for developing and guiding NIOSH scientific and organizational plans in nanotechnology health and safety research.

STRATEGIC PLAN

The development of nanotechnology has reached a point of wide application, and numerous nanomaterials and nano-enabled products are in commerce. Nanotechnology may provide great benefits to society if developed responsibly. This responsibility involves addressing any potential adverse human and environmental impacts of the technology associated with engineered nanomaterials (ENMs). Workers are among the first to have contact with (exposure to) potential health hazards from new technology and products, and their exposure to any new material is often greater than for the general population. Therefore, worker safety and health are at the core of responsible development (Figure 1).

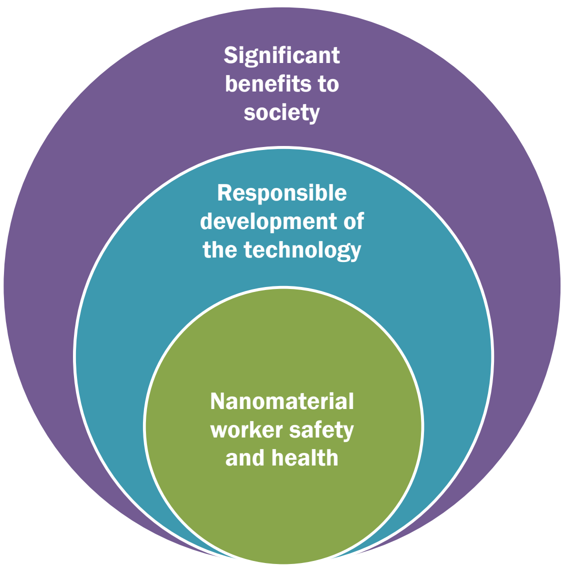

Figure 1. The core of responsible development of nanotechnology.

This document presents the NTRC strategic plan for fiscal year (FY)2018–FY2025. The strategic plan also highlights how the critical research and guidance efforts of NIOSH align with and support the comprehensive Environmental, Health, and Safety Research Strategy needs of the National Nanotechnology Initiative (Section 6). These research needs are consistent with nanotechnology-related research goals included in the NIOSH Strategic Plan for FYs 2019–2023, but offer greater detail (https://www.cdc.gov/niosh/about/strategicplan/).

For the period FY2018–FY2025, NIOSH will continue to fill information and knowledge gaps that address the five NIOSH NTRC strategic goals first defined in the 2013 strategic plan (**http://www.cdc.gov/niosh/docs/2014-106/pdfs/2014-106.pdf**) (NIOSH 2013a):

1. Increase understanding of new nanomaterials and related health risks to nanomaterial workers.
2. Expand understanding of the initial hazard findings on engineered nanomaterials.

3. Support the creation of guidance materials to inform nanomaterial workers, employers, health professionals, regulatory agencies, and decision-makers about hazards, risks, and risk management approaches.
4. Support epidemiologic studies for nanomaterial workers, including medical, cross-sectional, prospective cohort, and exposure studies.
5. Assess and promote national and international adherence with risk management guidance.

Contents

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Abbreviations

AFL-CIO	American Federation of Labor and Congress of Industrial Organizations
AIHA	American Industrial Hygiene Association
AIHce	American Industrial Hygiene conference and exposition
ANSES	The French Agency for Food, Environmental and Occupational Health and Safety
ANSI	American National Standards Institute
ASSP	American Society of Safety Professionals
ASTM	American Society for Testing and Materials (currently ASTM International)
CNF	carbon nanofiber
CNT	carbon nanotube
CPSC	Consumer Product Safety Commission
CPWR	Center for Construction Research and Training
DHHS	Department of Health and Human Services
EHS	environmental, health, and safety
ENM	engineered nanomaterial
EPA	Environmental Protection Agency
ERC	Education and Research Center
FIOH	Finnish Institute of Occupational Health
FMSH	Federal Mine Safety and Health
FY	fiscal year
HSL	Health and Safety Laboratory
IARC	International Agency for Research on Cancer
ICOH	International Commission on Occupational Health
IEC	International Electrotechnical Commission
ILO	International Labour Organization
IOM	Institute of Occupational Medicine
ISEA	International Safety Equipment Association
ISO	International Organization for Standardization
MOU	memorandum of understanding
MSHA	Mine Safety and Health Administration
MWCNT	multi-walled carbon nanotube
NanoBCA	Nanobusiness Commercialization Association
NCER	National Center for Environmental Research
NCRP	National Council on Radiation Protection and Measurements

NEHI	Nanotechnology Environmental and Health Implications
NIEHS	National Institute of Environmental Health Sciences
NIH	National Institutes of Health
NIOSH	National Institute for Occupational Safety and Health
NIST	National Institute of Standards and Technology
NNI	National Nanotechnology Initiative
NORA	National Occupational Research Agenda
NSC	National Safety Council
NSF	National Science Foundation
NSET	Nanoscale Science, Engineering and Technology Subcommittee of the U.S. National Science and Technology Council
NTRC	Nanotechnology Research Center
OECD	Organization for Economic Cooperation and Development
OEP	Office of Extramural Programs
OSH	occupational safety and health
OSHA	Occupational Safety and Health Administration
P3Nano	Public-Private Partnership for Cellulosic Nanotechnology
PAMS	portable aerosol mobility spectrometer
PNS	personal nano-aerosol sizer
PPE	personal protective equipment
PtD	Prevention through Design
QEEN	Quantitative Exposure to Engineered Nanomaterials
QRA	quantitative risk assessment
r2p	Research to Practice
SUNY Poly CNSE	State University of New York Polytechnic Colleges of Nanoscale Science and Engineering
TNO	The Netherlands Organization for Applied Scientific Research
TiO_2	titanium dioxide
UN	United Nations
UNITAR	United Nations Institute for Training and Research
WHO	World Health Organization
WPMN	Working Party on Manufactured Nanomaterials

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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. Whereas nanomaterials have at least one dimension less than 100 nanometers [ISO 2015], nanoparticles are a specific class or subset having *three* dimensions less than 100 nanometers. Nanoparticles may exhibit unique properties because of their nanoscale dimensions.

Nanotechnology offers the potential for tremendous improvement and advances in the development of commercial products that may benefit society, such as integrated sensors, semiconductors, medical imaging equipment, drug delivery systems, structural materials, sunscreens, cosmetics, and coatings. It is one of the most powerful enabling technologies across the world. A review of the 2018 version of the Nanowerk nanomaterials database (**http://www.nanowerk.com/phpscripts/n_dbsearch.php**) revealed about 4,000 commercially available nanomaterials. The inventory at the Project for Emerging Technologies [PEN 2016] shows more than 1,800 nanomaterial-containing commercial products.

The properties of engineered nanomaterials (ENMs) (such as size, surface area, and reactivity) that yield many improvements in commercial products may also pose potential health risks. Increasing numbers of workers are potentially exposed to ENMs in research laboratories, start-up companies, production facilities, and operations where ENMs are processed, used, disposed, or recycled. The challenge is to determine whether intentionally produced ENMs and nano-enabled products present occupational safety and health risks. At the same time, there is a need to address how to realize the benefits of nanotechnology while proactively minimizing the risks.

Efforts across multiple federal agencies and the private and academic sectors 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 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 human health, environmental issues, and societal implications related to nanotechnology.

1.2 Mission of NIOSH

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 the intent of these acts was to ensure, insofar as possible, safe and healthful working conditions for every worker, to preserve our human resources. In these acts, NIOSH has responsibility for recommending occupational safety and health standards and defining exposure levels 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 a work experience.

By means of criteria documents and other publications, NIOSH communicates these recommended standards to the Occupational Safety and Health Administration (OSHA), the Mine Safety and Health Administration (MSHA), and others in the occupational safety and health community.

Under the OSH Act, NIOSH must conduct "research, experiments, and demonstrations relating to occupational safety and health" and develop "innovative methods, techniques, and approaches for dealing with [those related] 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. An amendment to the act states that NIOSH is responsible 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 OSH Act).

1.3 NIOSH Nanotechnology Research Center

In 2004, NIOSH established the Nanotechnology Research Center (NTRC) to identify critical issues relating to nanotechnology, create a strategic plan for investigating these issues, coordinate the NIOSH research effort, develop research partnerships, and disseminate relevant information. The NTRC comprises nanotechnology-related activities and projects supported by approximately 70 scientists in various NIOSH divisions and laboratories (Figure 2).

Through the NTRC, NIOSH has identified 10 critical research areas for nanotechnology research and communication: toxicity and internal dose; measurement methods; exposure assessment; epidemiology and surveillance; risk assessment; engineering controls and personal protective equipment (PPE); fire and explosion safety; recommendations and guidance; global collaborations; and applications and informatics (Figure 3). By researching in these areas concurrently, NIOSH is comprehensively addressing

Figure 2. NIOSH Nanotechnology Research Center Scientists, spring 2016.

the information and knowledge gaps necessary to protect workers and responsibly move nanotechnology forward so that its far-reaching benefits may be realized.

1.4 NIOSH Logic Model

NIOSH receives input on identifying and addressing occupational safety and health problems through a logic model, or process, by which it

1. evaluates the seriousness of the problem or hazard,
2. determines the type and level of research needed, and
3. formulates a plan and process for communicating the research outcomes.

The NIOSH operational logic model (Figure 4) for conducting research depicts the acquisition and analysis of inputs from customers/stakeholders (*production inputs*) and internal/external research capabilities (*planning inputs*) to determine and prioritize research. Intramural and extramural researchers present their project proposals, which receive appropriate internal and external review; funding is according to merit. The conduct of research (*activities*) produces "outputs," such as guidance documents and reports. These address effective risk-management practices, worker and employer education, and new technologies for assessing and controlling workplace hazards. NIOSH outputs are transferred directly to the final customers and stakeholders (who implement improvements in workplace safety and health) or to intermediate customers (who use NIOSH outputs to produce *intermediate outcomes*). These intermediate outcomes, such as training programs, regulations, and occupational standards, advance workplace safety and health.

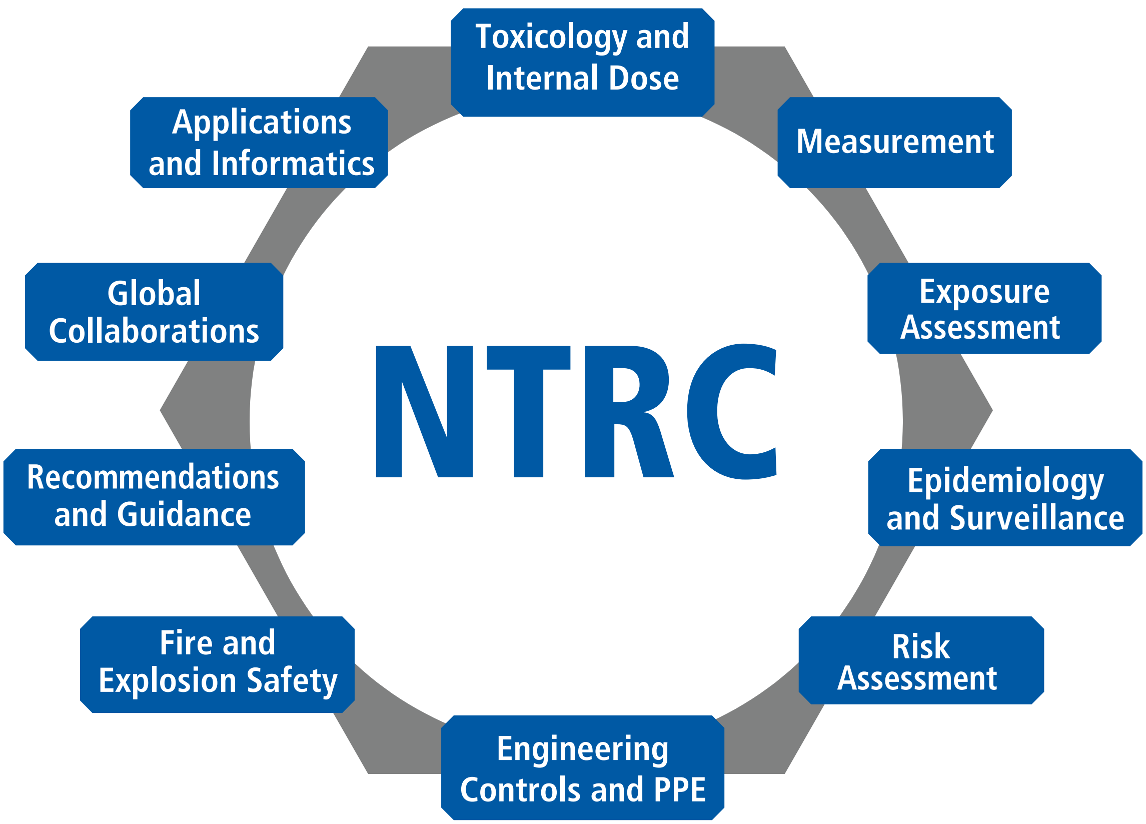

Figure 3. The critical research areas of the NIOSH Nanotechnology Research Center (NTRC).

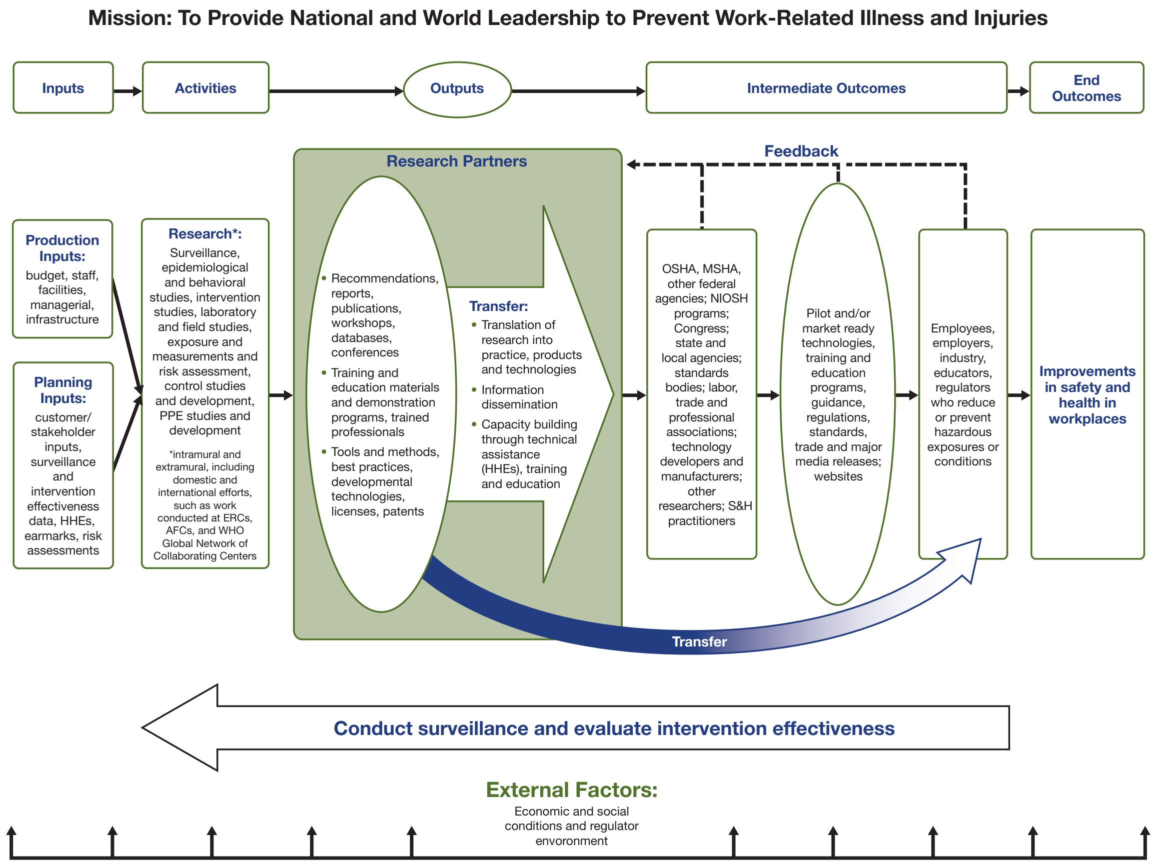

Figure 4. Schematic of the NIOSH operational model.

Because 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. The effectiveness in achieving these outcomes is influenced at all stages of the 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 outcomes and end outcomes) contribute to the subsequent rounds of program planning.

The NIOSH logic model (Figure 5) has a conventional horseshoe shape: the operational upper branch proceeds from inputs to mission-relevant outcomes, and the strategic lower branch supports those operations through measurable goals and management objectives. These two correlated branches are subject to external factors.

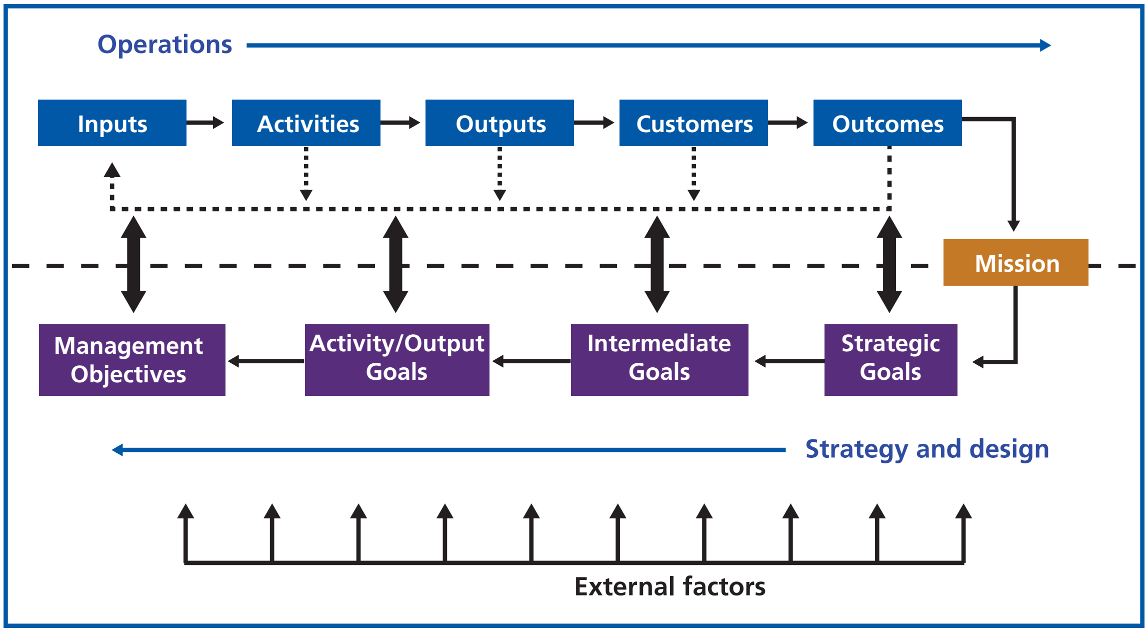

Figure 5. Logic model showing how goals align with the operational model

2 WHERE ARE WE NOW?

2.1 Vision, Mission, and Management

Vision of the NTRC

This is the NTRC vision: 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 on the implications of nanoparticles and nanomaterials for work-related injury and illness, and the application of nanoparticles and nanomaterials in occupational safety and health.

NTRC Steering Committee

The NTRC Steering Committee is co-chaired by the NTRC managers and coordinator. The committee comprises the program managers, program coordinator, program assistant coordinator, and critical area coordinators for each of the 10 research areas (some areas have multiple research coordinators, and some researchers have dual roles). The 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 for the NTRC. Regular updates and progress reports on internal research activities occur through biweekly teleconferences and an annual meeting among members of the NTRC Steering Committee. In addition, to ensure the responsiveness, relevance, and impact of the NIOSH nanotechnology program, all members of the NTRC and appropriate stakeholders meet in person every 2 years at a scientific exchange meeting.

2.2 Accomplishments from 2003 through 2018

The following timeline presents significant outputs and events in the history of the NTRC.

2003: NIOSH published the seminal toxicological study report ***Exposure to Carbon Nanotube Material: Assessment of Nanotube Cytotoxicity Using Human Keratinocyte Cells***. This report has been cited over 1,000 times in the peer-reviewed literature, making it one of the NTRC's most cited publications in nanotoxicology. Additionally, during this time, early fieldwork on carbon nanotubes took place. Results from both the early fieldwork and toxicologic studies indicated a need for a dedicated group within NIOSH to focus specifically on nano-sized materials. NIOSH became a member of the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the National Science and Technology Council.

May 2003: NIOSH Director Dr. John Howard delivered the first information session on NIOSH nanotechnology research, at the American Industrial Hygiene conference and exposition (AIHce). Every year since then at the AIHce, NIOSH has arranged and delivered a dedicated session on progress in nanotechnology research. In 2006, the presentation and discussion expanded to a panel for multiple speakers and nanotechnology-specific topics. In 2015, the nanotechnology update became part of the AIHce Science Symposium track.

March 2004: NIOSH Director Dr. John Howard announced to the Institute Leadership Team the establishment of the Nanotechnology Research Center, now known as the NTRC, to accelerate progress in nanotechnology research across the Institute. Shortly thereafter, NIOSH held the first official meeting of the NTRC.

July 2004 and 2005: NIOSH conducted two of the first NIOSH organized **field efforts** at carbon nanotube (CNT) and carbon nanofiber (CNF) facilities: the first, a university research center making CNTs; the second, a CNF composite pilot lab. These first-ever attempts to evaluate potential sources of emissions from CNT- and CNF-handling processes prompted a more dedicated field effort.

September 2005: NIOSH became the first government agency to publish a strategic plan for nanotechnology research, as the roadmap to advance knowledge about the applications and implications of nanomaterials. Shortly thereafter, the Woodrow Wilson Project on Emerging Nanotechnologies released a webinar providing information on the occupational safety and health applications and implications of nanotechnology. During this time, to ensure its information would reach all interested parties, the NTRC launched the first **nanotechnology topic page** website on the potential hazards of engineered nanomaterials in the workplace.

October 2005: NTRC researchers developed the first comprehensive guidance compendium to inform employers about potential hazards of nanomaterials and the steps they could take to help minimize the health risks from exposure. *Approaches to Safe Nanotechnology: An Information Exchange with NIOSH* has become one of the most widely used nanomaterial occupational safety and health guidance documents throughout the world. NIOSH released an updated version of this **guidance** in 2009 (Figure 6) [NIOSH 2009a].

January 2006: NIOSH formally established the NTRC Field Studies Team to partner with companies that produce or use engineered nanomaterials to assess potential occupational exposure to nanomaterials. To date, NIOSH has performed more than 100 site evaluations (Figure 7). In June 2015, the NIOSH Nanotechnology Field Studies effort won recognition for its technical expertise, technological innovations, and contributions to the science with the Edward J. Baier Award at the AIHce.

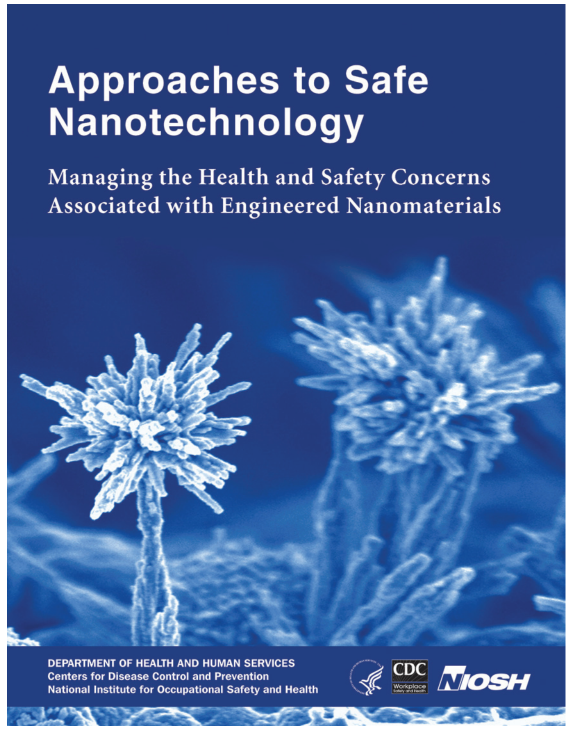

Figure 6. The cover of the updated guidance document, NIOSH Publication No. 2009-125.

February 2006: NIOSH, working with national and international partners, launched the **Nanoparticle Information Library** to help occupational health professionals, industrial users, worker groups, and researchers organize and share information on nanomaterials, including their health and safety–associated properties. Oregon State University is the current administrator of this voluntary database. The database information is also available in the Nanomaterial Registry, sponsored by the NIH. These registries indicate a wide variety of nanomaterial research and use.

June 2006: NIOSH and DuPont signed an agreement under a memorandum of understanding (MOU) to establish a formal partnership to conduct research and increase knowledge and understanding of nanomaterials. This initial agreement focused on measurement of nanomaterials in an occupational environment and determining whether respiratory protection would adequately protect workers with exposure to aerosolized materials.

Figure 7. A sign welcoming the nanotechnology field-studies team to a facility.

Summer 2006: NTRC researchers designed an innovative aerosol exposure system to conduct experimental animal studies with nanoparticles (Figure 8). This system has allowed NTRC researchers to generate airborne exposures to various nanoscale materials such as carbon nanotubes for toxicological studies. The results from these studies have provided the scientific evidence necessary to make recommendations on workplace risk management.

October 2006: NIOSH participated in the inaugural meeting of the international Working Party on Manufactured Nanomaterials (WPMN), Organization for Economic Cooperation and Development (OECD). Since that meeting, NIOSH has served as lead for the Steering Group on exposure, which has developed and published 11 reports on exposure to nanomaterials.

December 2006: NIOSH and the University of Cincinnati co-sponsored the International Conference on Nanotechnology. This conference set the standard by focusing on the impact of nanotechnology on occupational and environmental health and safety from two perspectives: (1) protection of worker safety and health along the entire life cycle of nano-based products and (2) use of emerging technology in prevention and detection/treatment of occupational and environmental diseases.

2007: NTRC researchers were the first to use elemental carbon as a selective marker for quantifying a worker's exposure to carbon nanofibers and carbon nanotubes. This approach, in combination with additional exposure metrics, is

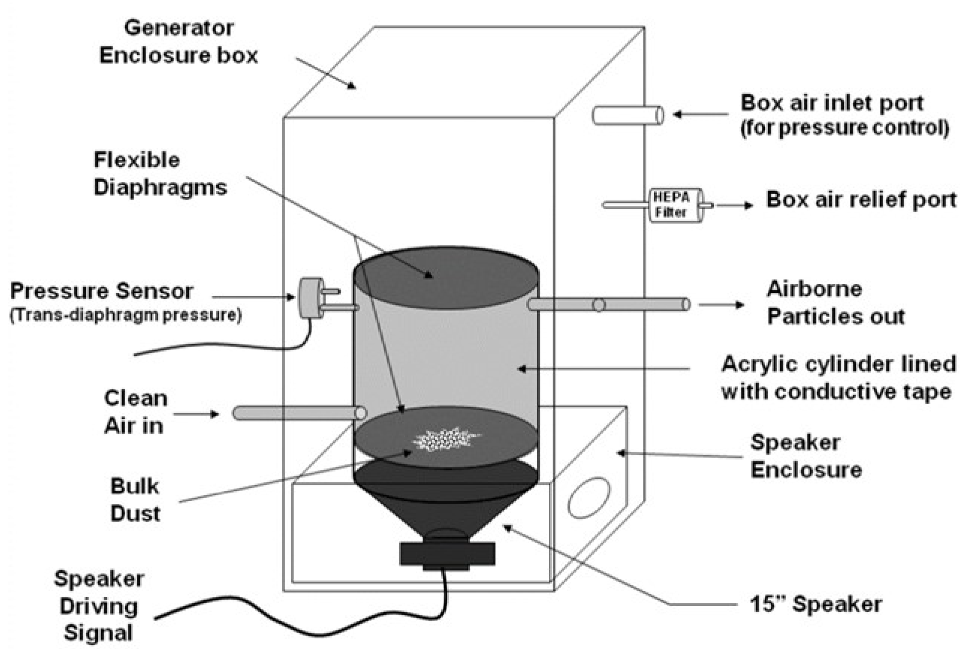

Figure 8. The NIOSH acoustical generator system for aerosolizing nanomaterials [McKinney et al. 2009].

still in use to identify and determine the extent of exposure to carbon-based nanomaterials.

2007: NTRC researchers developed a prototype hand-held sampler to collect airborne nanoparticles that can be directly used for electron microscopy analysis. The prototype was subsequently licensed to a commercial supplier. NTRC researchers have continued to develop innovative sampling methods for engineered nanomaterials, including the Portable Aerosol Mobility Spectrometer (PAMS) and a Personal Nano-aerosol Sizer (PNS).

2008: The International Organization for Standardization (ISO) published the first document on the safety of nanomaterials, TR 12885, *Health and Safety Practices in Occupational Settings Relevant to Nanotechnologies*. This report, developed under the leadership of NIOSH, was based on the NIOSH *Approaches to Safe Nanotechnology*.

June 2008: NIOSH developed and presented the first professional development and training course on nanomaterial worker exposure assessment at AIHce. As methods and recommendations have changed, NIOSH has provided variations of this initial presentation at over 20 different domestic and international conferences, universities, and organizations.

February 2009: NIOSH published the first (interim) **guidance** on medical surveillance and medical screening for workers potentially exposed to engineered nanoparticles (Figure 9) [NIOSH 2009b]. In addition, as part of a national effort to stimulate new research and knowledge, NIOSH collaborated with the NSET Subcommittee to co-sponsor the workshop on Human and Environmental Exposure Assessment of Nanomaterials. This workshop focused on research needed for occupational exposures by measuring and modeling exposure levels and by monitoring biological responses through the product life cycle of a nanomaterial.

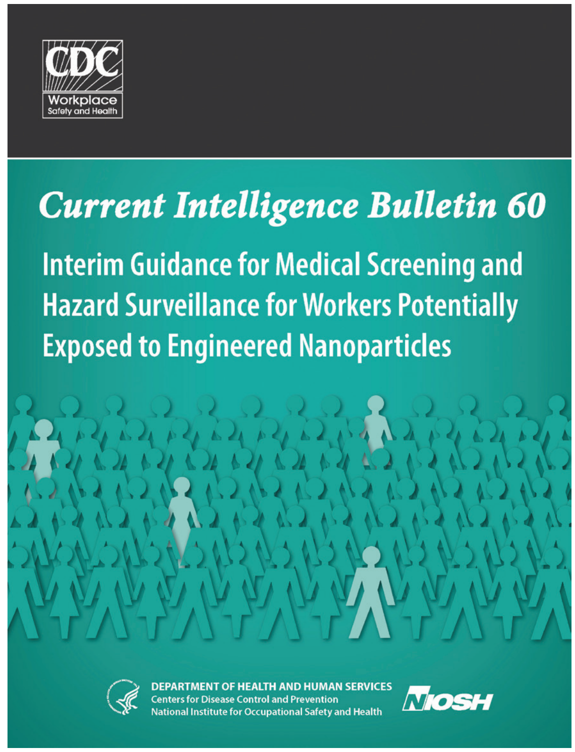

Figure 9. The cover of the first medical screening guidance document, NIOSH Publication No. 2009-116.

March 2010: NIOSH published the **Nanomaterial Emission Assessment Technique (NEAT)**, which established the initial framework for NTRC researchers and others in conducting workplace emission testing and paved the way for more comprehensive exposure assessment techniques [Methner et al. 2009]. This publication was the basis for an international guidance document on nanomaterial exposure assessment techniques issued by the OECD.

April 2010: NIOSH signed an agreement with the United Nations Institute for Training and Research on the critical importance of the world of work in defining sound occupational safety and health prevention policies and interventions in the workplace and implementing strategies for expanding protection to workers and their communities.

July 2010: NIOSH sponsored the first Nanomaterial Workers' Health Conference. This conference addressed three critical, related topics: medical surveillance, formation of exposure registries, and conduct of epidemiologic research. The *Journal of Occupational and Environmental Medicine* dedicated an entire supplement in June 2011 to the publication of 24 peer-reviewed articles from the conference.

October 2010: The World Health Organization approved the development of guidelines on worker safety in nanotechnology workplaces, under the leadership of NIOSH.

April 2011: NIOSH released **guidelines** for occupational exposure to titanium dioxide (TiO_2) (Figure 10). This marked the first time NIOSH had released two separate Recommended Occupational Exposure Limits for the same chemical, based on size. The TiO_2 Current Intelligence Bulletin makes recommendations for occupational exposure limits and suggests techniques for monitoring and controlling worker exposure [NIOSH 2011].

2011: To date, over 400 NIOSH-authored articles had been published, and these had been cited more than 5,000 times in the peer-reviewed literature.

May 2012: NIOSH published the *General Safe Practices for Working with Engineered Nanomaterials in Research Laboratories* (Figure 11). This guidance was the first to address the basic knowledge and guidance needed for handling nanomaterials safely in a research laboratory setting [NIOSH 2012b].

August 2012: NIOSH partnered with the Colleges of Nanoscale Science and Engineering, State University of New York Polytechnic Institute (SUNY Poly CNSE at Albany) to hold a Prevention through Design workshop. This workshop encouraged efforts to develop safer nanoscale molecules that have the same functionality; ways to contain and control processes for minimizing exposure and health risks; and management system approaches for including occupational safety and health in the full product lifecycle.

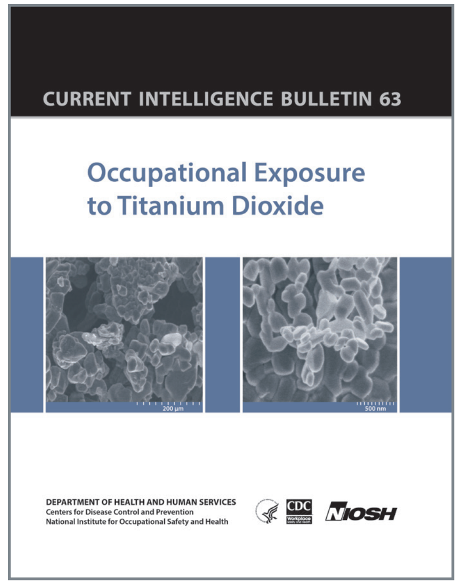

Figure 10. The cover of the TiO2 guidelines, NIOSH Publication No. 2011-160.

2012: NIOSH launched an industry-wide study specifically addressing carbon nanotube and nanofiber worker exposures. It based this study on earlier feasibility and health hazard field studies that indicated an increased population of workers could have exposure to carbon-based nanomaterials.

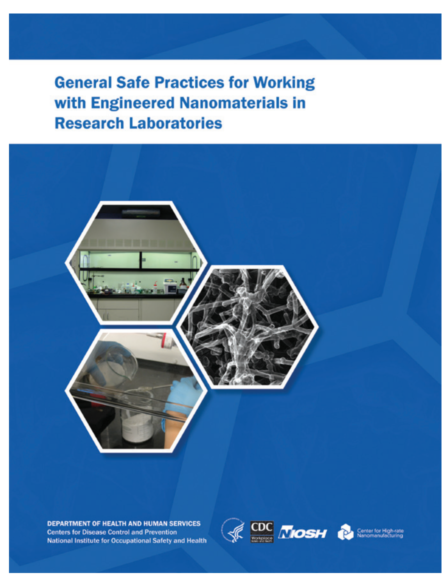

Figure 11. The cover of the document on safe laboratory practices, NIOSH Publication No. 2012-147.

March 2013: At the annual meeting of the Society of Toxicology, NIOSH researchers reported on the first experimental results showing that multi-walled carbon nanotubes (MWCNTs) are a tumor promotor in laboratory animal studies. This study showed that inhalation exposure to MWCNTs increased the risk of cancer in mice concurrently exposed to a known carcinogen. Most significantly, the doses used in the animal study approximated feasible human occupational exposures.

April 2013: NIOSH published a recommended exposure limit (REL) for carbon nanotubes and carbon nanofibers (Figure 12), the first occupational exposure limit for this category of nanomaterials issued by a U.S. government agency. This publication, *CIB 65: Occupational Exposure to Carbon Nanotubes and Nanofibers*, also includes recommendations for medical surveillance and screening of workers potentially exposed to these materials [NIOSH 2013b].

November 2013: NIOSH issued new engineering control recommendations, for controlling worker exposures to engineered nanomaterials during the manufacture and industrial use of those materials (Figure 13). The **recommendations** filled a gap for science-based guidance that employers and workers could apply immediately, while research continued for better understanding of nanomaterial characteristics [NIOSH 2013c].

September 2014: ISO selected NIOSH to lead an international working group on the health, safety, and environmental aspects of nanotechnologies. The working group is part of a larger initiative by ISO to develop standardization in the nanotechnologies field.

October 2014: The International Agency for Research on Cancer (IARC) working group met to evaluate carcinogenicity of carbon nanotubes, fluoro-edinite, and silicon carbide. NIOSH research [Sargent et al. 2014] was integral in the IARC decision to classify MWCNT-7 as a group 2b carcinogen.

January 2015: NIOSH partnered with national and international experts at the convergence of nanotechnology and the nuclear sciences to develop and publish principles and practices for the *Application of an Informatics-Based Decision-Making Framework and Process to the Assessment of Radiation Safety in Nanotechnology* [Hoover et al. 2015].

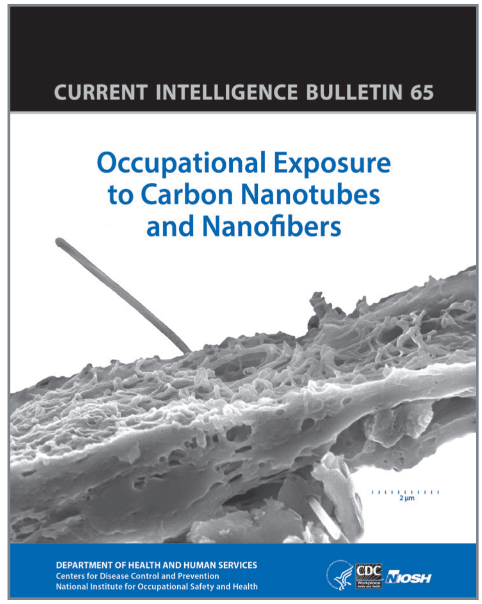

Figure 12. The cover of CNT and CNF guidelines, NIOSH Publication No. 2013-145.

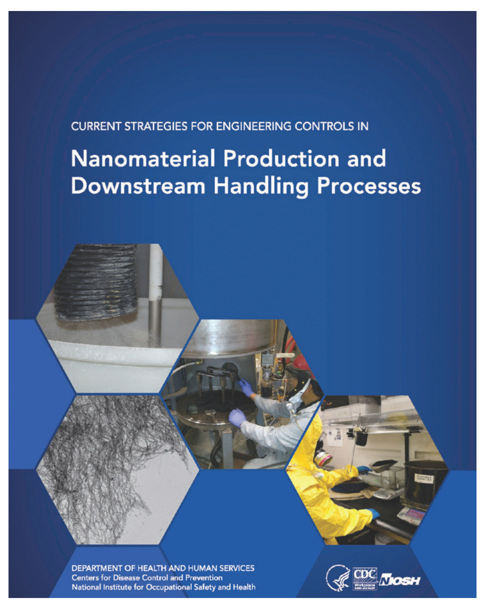

Figure 13. The cover of the document on engineering control recommendations, NIOSH Publication No. 2014-102.

Figure 14. The launching of the Nano Health and Safety Consortium.

May 2015: NIOSH and SUNY Poly CNSE launched the Nano Health and Safety Consortium at a special White House forum sponsored by the National Economic Council and White House Office of Science and Technology Policy (Figure 14).

July 2015: NIOSH provided strategic support to a NNI and Consumer Product Safety Commission (CPSC) co-sponsored workshop on Quantitative Exposure to Engineered Nanomaterials (QEEN). A report from this workshop was subsequently published in March 2016.

2015: To date, the nanotechnology-related literature included more than 1,000 peer-reviewed articles by NIOSH authors.

January 2016: NIOSH released a draft Current Intelligence Bulletin (CIB) entitled *Health Effects of Occupational Exposure to Silver Nanomaterials.* A public meeting followed in March 2016.

March 2016: NIOSH published *Building a Safety Program to Protect the Nanotechnology Workforce: A Guide for Small to Medium-Sized Enterprises* [NIOSH 2016] (Figure 15).

May 2016: The updated *Nanomaterial Exposure Assessment Technique (NEAT 2.0)* was published in the *Journal of Occupational and Environmental Hygiene* [Eastlake et al. 2016]. Unlike the previous method, which focused on emissions, this method encouraged practitioners to focus sampling efforts (as in Figure 16) on integrated full-shift sampling and comprehensive exposure assessment.

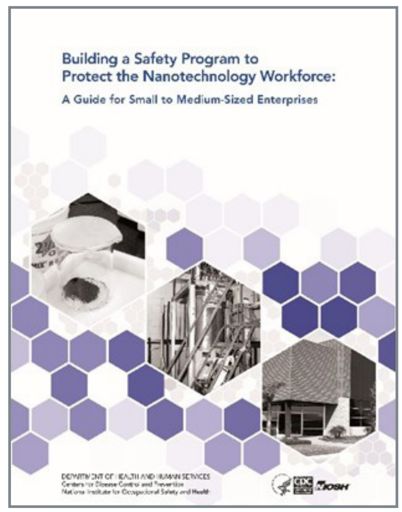

Figure 15. The cover of the small business guide, NIOSH Publication No. 2016-102.

Figure 16. A NIOSH field research team member.

June 2016: NIOSH researchers [Yi et al. 2016] published Emission of Particulate Matter from a Desktop Three-Dimensional (3D) Printer, a preliminary investigation into advanced (additive) manufacturing.

November 2016: NIOSH partnered with the ISO project group in developing the ISO technical report ISO/TR 18637:2016, *Nanotechnologies—Overview of Available Frameworks for the Development of Occupational Exposure Limits and Bands for Nano-Objects and their Aggregates and Agglomerates (NOAAs)*. NIOSH researchers Eileen Kuempel, PhD, and Vladimir Murashov, PhD, were primary authors and co-chairs of the ISO working group on this document.

March 2017: NIOSH provided major contributions to the development and publication of the **National Council on Radiation Protection and Measurements (NCRP) Report No. 176 on Radiation Safety Aspects of Nanotechnology** [NCRP 2017]. NIOSH researcher Mark Hoover, PhD, was the chair of the NCRP committee for this document.

July 2017: NIOSH included a new chapter in its *Manual of Analytical Methods, 5th edition: Analysis of Carbon Nanotubes and Nanofibers on Mixed Cellulose Ester Filters by Transmission Electron Microscopy* [Birch et al. 2017].

July 2017: NIOSH [Stefaniak et al. 2017a] published the Health Hazard Evaluation report *Emission of Particulate Matter from a Desktop Three-Dimensional (3D) Printer*, one of the first field evaluations pertaining to advanced (additive) manufacturing.

August 2017: NIOSH [Bishop et al. 2017] published a seminal document addressing the toxicology of a nanomaterial along its life cycle: *An In-Vivo Toxicity Assessment of Occupational Components of the Carbon Nanotube Life Cycle to Provide Context to Potential Health Effects*.

August 2017: NIOSH researchers and collaborators [Drew et al. 2017] authored a scientific journal article describing a quantitative framework for categorizing nanomaterials by hazard potency. This article contributed to the strategic goals of developing algorithms to derive OELs for nanomaterial groups and predicting potency groups of new nanomaterials from their physicochemical properties.

September 2017: NIOSH [Stefaniak et al. 2017b] published the first NIOSH toxicology paper pertaining to an advanced manufacturing technology, *Inhalation Exposure to Three-Dimensional Printer Emissions Stimulates Acute Hypertension and Microvascular Dysfunction*.

2018: To date (2004-2018), NIOSH authors have published more than 1,400 peer-reviewed articles related to nanotechnology.

Additional information on NIOSH NTRC research outputs and accomplishments from 2004 to 2011 is in the report *Filling the Knowledge Gaps for Safe Nanotechnology in the Workplace* [NIOSH 2012a] (Figure 17).

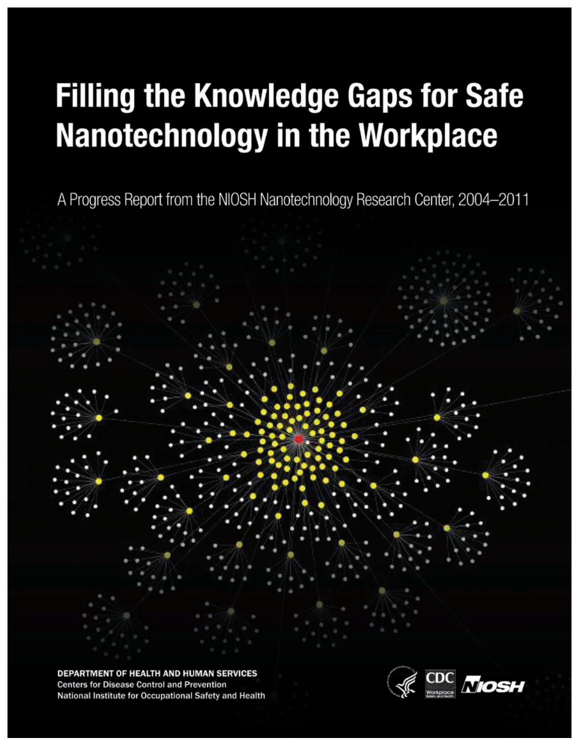

Figure 17. The cover of an early research progress report, NIOSH Publication No. 2013-101.

2.3 Customer and Stakeholder Input

To direct its research and fulfill its responsibilities under the OSH Act and the FMSH Act, NIOSH has relied on input from OSHA and MSHA, workers, employers, trade associations, unions, occupational safety and health practitioners and researchers, and the general public. NIOSH also seeks 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. In addition, NIOSH receives input through ad hoc mechanisms such as the NIOSH website (www.cdc.gov/niosh), a 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/nora**), which is a framework to guide occupational safety and health research—not only for NIOSH but also for the entire occupational safety and health community.

NIOSH continues to be a participating and partnering agency in the NNI and provides occupational health and safety expertise in support of the U.S. Government's Strategic Plan for Nanotechnology Environmental, Health, and Safety Research [NNI 2011]. NIOSH is co-leader of the NNI Nanotechnology Environmental and Health Implications (NEHI) Working Group and contributed to the development of the 2011 NEHI Environmental, Health, and Safety (EHS) Research Strategy. The NNI EHS research strategy focuses on the use of science-based risk analysis and risk management to protect public health and the environment while fostering technological advancements that benefit society. The NNI EHS strategy dovetails into the 2014 NNI Strategic Plan Goal 4: Support the Responsible Development of Nanotechnology. NIOSH has strived to keep the overarching research activities of the NTRC nanotechnology strategic plan consistent with the NNI EHS research strategy (see Section 6 and Appendix A).

The NIOSH NTRC also fosters stakeholder input from trade associations, professional associations, labor, nongovernmental organizations, and private nanomaterial companies. These collaborations have provided expertise and resources critical for reviewing research activities and for developing and disseminating health and safety information on engineered nanoparticles. Some of the ongoing NTRC stakeholders are the American Industrial Hygiene Association (AIHA), American Society of Safety Professionals (ASSP), International Safety Equipment Association (ISEA), National Safety Council (NSC), American Federation of Labor and Congress of Industrial Organizations (AFL–CIO), NanoBusiness Commercialization Association (NanoBCA), and Center for Construction Research and Training (CPWR).

2.4 NIOSH Partnerships

NIOSH recognizes both the practical need and its leadership obligation to extend its internal capabilities 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 important, 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 MOUs to informal working agreements on a specific topic. The NTRC has developed partnerships in the areas of toxicology, risk assessment modeling, exposure measurement methods, epidemiology, industrial hygiene, control technologies, and communication of research results and safe work practices. In addition, the NTRC has successfully used partnerships with industry to gain a better understanding of industrial nanomaterial processes, workplace exposures, work practices, and exposure control techniques. The field research conducted by the NTRC to assess exposures to engineered nanoparticles represents ongoing partnerships with numerous companies. The NTRC will continue to develop these partnerships to:

- better understand how ENMs are being produced and used

- develop recommendations for the safe handling of ENMs
- develop sampling and analytical methods
- evaluate exposure controls that are or could be used in ENM processes
- evaluate the need for and determine the effectiveness of PPE, including respiratory protection
- develop communication and information materials that will assist industry in communicating with workers and the public.

The NTRC participates in a number of national and international committees and working groups. This participation gives NTRC scientists the opportunity to provide and receive input on the key research necessary to address priority areas. NIOSH has entered into MOUs or partnerships with DuPont; the National Science Foundation (NSF); the Center for High-rate Nanomanufacturing (CHN, a collaboration of the University of Massachusetts Lowell, Northeastern University, and the University of New Hampshire); the State University of New York Polytechnic Colleges of Nanoscale Science and Engineering (SUNY Poly CNSE); and the Public-Private Partnership for Cellulosic Nanotechnology (P3Nano).

2.5 Standards Development Organizations

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

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

The NIOSH NTRC will continue leading, as convener, the ISO Technical Committee 229 on Nanotechnologies (ISO TC 229). Work on instrumentation-related standards will continue with committees of the International Electrotechnical Commission (IEC).

NIOSH NTRC scientists will also continue collaborating on the development of nanotechnology-related guidance with authoritative bodies such as the National Council on Radiation Protection and Measurements.

2.6 International Activities

NIOSH will continue to engage with a number of international entities at all levels—as principle investigator as well as a participant in national, regional, and global organizations. At the national organization level, the NIOSH NTRC has been communicating and collaborating with the United Kingdom Institute of Occupational Medicine (IOM) and the Health and Safety Laboratory (HSL); the Netherlands Organization for Applied Scientific Research (TNO); the French Agency for Food, Environmental and Occupational Health and Safety (ANSES); the Finnish Institute of Occupational Health (FIOH); and the Australian Safety and Compensation Council (Safe Work Australia).

NIOSH participates in the OECD's WPMN to build cooperation, coordination, and communication between the United States and the other 34 OECD member countries, the European Union, and participating non-member countries. NIOSH is also working with the UN World Health Organization (WHO); the UN International Labour Organization (ILO); the UN Institute for Training and Research (UNITAR); the International Organization for Standardization (ISO); the International Electrotechnical Commission (IEC); and the International Commission on Occupational Health (ICOH) on global projects of information dissemination and communication.

2.7 NIOSH Extramural Nanotechnology Research Activities

The NIOSH NTRC continues to work strategically to fill knowledge gaps in nanotechnology occupational safety and health through active intramural and extramural research programs and collaborations. 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 involves peer review, program relevance, and priorities of 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**).

Since 2001, the NIOSH OEP has funded nanotechnology research through Occupational Safety and Health Research Program Announcements (R01), Mentored Scientist Grants (K01), Small Research Grants (R03), Developmental Grants (R21), and Small Business Innovation Research Grants (R43/44). During the period 2001 to 2016, the NIOSH OEP committed approximately $20 million to extramural nanotechnology research. Summaries of the projects funded by the NIOSH OEP are included in the document *Filling the Knowledge Gaps for Safe Nanotechnology in the Workplace* [NIOSH 2012a]. Through continued collaboration with the Environmental Protection Agency/National Center for Environmental Research (EPA/NCER), National Science Foundation (NSF), National Institutes of Health/National Institute of Environmental Health Sciences (NIH/ NIEHS), and international agencies, the NIOSH OEP maintains its support of nanotechnology research that focuses on occupational safety and health issues. In addition, the NIOSH OEP routinely confers with the NIOSH NTRC regarding research needs. Research areas supported by the NIOSH OEP include emission and exposure assessment methods for nanoparticles in the workplace, toxicology of ENMs, and use of nanotechnology for the development of sensors.

3 WHERE DO WE WANT TO BE?

3.1 Addressing Each Element in the Risk Management Continuum

Ultimately, the goal of the NTRC is to develop information, knowledge, and guidance to protect the nanotechnology workforce. There are still many gaps in nanomaterial health and safety knowledge, even though nano-enabled products continue to increase in commerce and worker exposure to ENMs is likely occurring. A challenge for the NIOSH NTRC program is to determine how to conduct timely research that addresses the elements of hazard identification through risk management, as the introduction of ENMs to the workplace continues and the workforce exposed to them becomes larger and more diverse. The NTRC approach has been to conduct concurrent, focused research to address knowledge gaps in each step of the risk management process. This enables the NTRC to provide occupational safety and health guidance across the life cycle of ENMs in a predictive manner to avoid health and safety impacts (Figure 18).

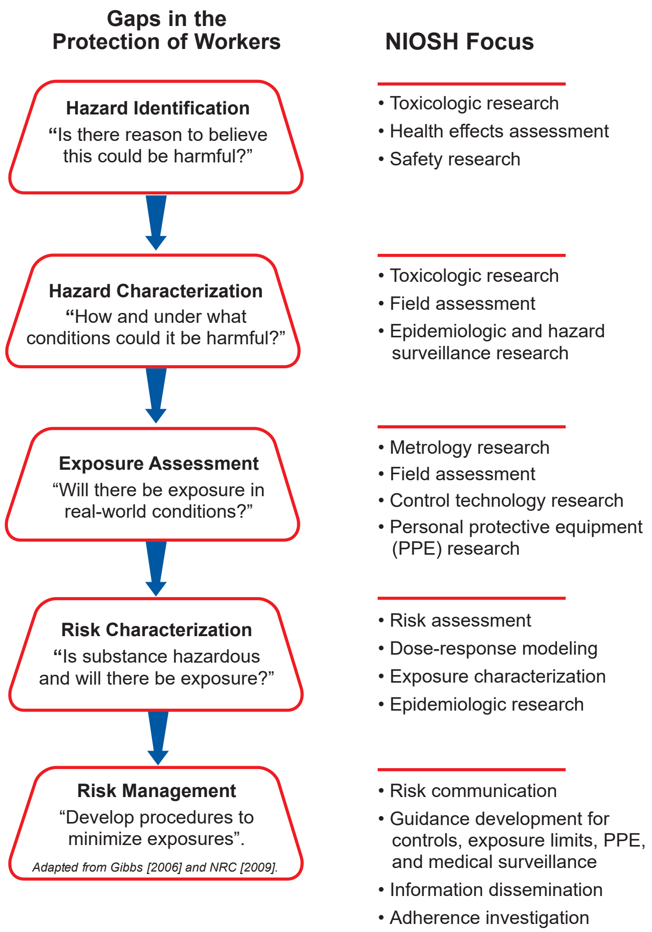

Figure 18. Addressing knowledge gaps in protecting nanomaterial workers.

The process for managing potential workplace exposures to ENMs and ascertaining the appropriate risk management strategy during their synthesis, manufacture, and incorporation into new materials and devices consists of the following steps:

1. identifying and characterizing the health and safety hazard;
1. conducting dose-response risk assessment;
2. assessing the extent of exposure;
3. characterizing the risk on the basis of exposure; and
4. developing control and management procedures [Schulte et al. 2008].

As additional exposure assessment data for ENMs become available, it is possible to determine with greater certainty both the level of occupational risk and the conditions under which exposure to the hazard would be harmful to workers. A goal of NTRC toxicology and risk assessment research is to determine whether exposure to a type of material (in this case, ENMs) used in a given technology is likely to cause adverse health effects. Exposure assessment data provide a means to identify worker exposure and a strategy for preventing it. Epidemiologic research would provide etiologic evidence of new hazards and quantitative exposure–response information for recommended exposure limits. Decisions about which ENMs to study epidemiologically will require information on workforce size, exposure levels, and expected hazard (from toxicological or other data).

In parallel with the ongoing development of ENMs is a new approach to the creation of various objects and products. Many ENM applications are under development for high-volume commercial manufacturing within the U.S. Advanced Manufacturing Initiative (now known as Manufacturing USA) [PCAST 2012]. Advanced manufacturing is the use of technology (including additive manufacturing, nanotechnology, and robotics) to improve products and processes. Continued refinement of nano-manufacturing processes will enable higher production of ENMs and further process and product development. Just as in nanotechnology, good Environmental, Health, and Safety (EHS) research and support are necessary for the flow of ENMs into advanced manufacturing processes. As scientists continue to explore and characterize the hazards and risks associated with ENMs, knowledge from that research will serve as a foundation for an anticipatory and proactive approach to the introduction and use of ENMs in advanced manufacturing.

4 HOW DO WE GET THERE?

4.1 Coalescing Priorities for NIOSH NTRC Research and Guidance for FY2018–FY2025

The NIOSH NTRC has proposed specific research activities (see Section 4.2) for FY2018–FY2025. The overall focus of the strategic plan is to generate data, information, and knowledge to protect the nanotechnology workforce by means of effective risk management techniques and, in particular, by minimizing elemental exposures and keeping exposure below available occupational limits. NIOSH researchers will develop and update good risk-management practices, including categorical and specific recommended exposure limits. Researchers will catalog and share data and information via informatics (resources, devices, and methods required to optimize the acquisition, storage, retrieval, and use of information). Figure 19 shows a schema for how NIOSH will continue to focus its research activities, in accordance with the goals of the NTRC Strategic Plan.

4.2 Proposed NIOSH NTRC Research Goals

The following proposed research for FY2018–FY2025 focuses on specific research needs to fill knowledge gaps and the EHS priority research needs of the NNI (see Section 6). These goals also align with the NIOSH Strategic Plan for FYs 2019-2023, expanding upon NIOSH intermediate goals 1.5, 5.3 and 5.5 (**https://www.cdc.gov/niosh/about/strategicplan/**)

Strategic Goal 1: Increase understanding of new nanomaterials and related health risks to nanomaterial workers.

Intermediate Goal 1.1: Authoritative groups will use NIOSH research to create standards and develop interventions to protect workers from exposures to new, novel ENMs.

Activity Goal 1.1.1: Prioritize high-volume emerging ENMs to identify candidates for toxicological testing and field evaluation of workplace exposures.

Activity Goal 1.1.2: Evaluate acute and chronic effects of emerging ENMs in the lungs and in other organ systems and tissues, using well-characterized ENMs. Determine dose-response and time-course relationships. Determine clearance rates of ENMs after pulmonary exposure and translocation to systemic organs; characterize systemic effects.

Activity Goal 1.1.3: Characterize surface-modified ENMs and evaluate acute and chronic effects in the lungs, organ systems, and tissues. Determine dose-response and time-course relationships, rates of clearance, and translocation to systemic organs relative to the unmodified form of the ENMs.

Activity Goal 1.1.4: Systematically investigate the physical and chemical properties of well-characterized ENMs that influence their toxicity (for example, size, shape, surface area, solubility, chemical properties, and trace components).

Activity Goal 1.1.5: Determine the biological mechanisms of toxic effects (such as oxidant stress, dissolution, fibrogenicity, and hydrophobicity) and how the key chemical and physical factors of ENMs may influence these mechanisms.

Activity Goal 1.1.6: Integrate mechanistic models (including animal models and in vitro screening tests) for assessing the potential toxicity of new ENMs, and provide a basis for developing predictive algorithms for structure/function relationships and

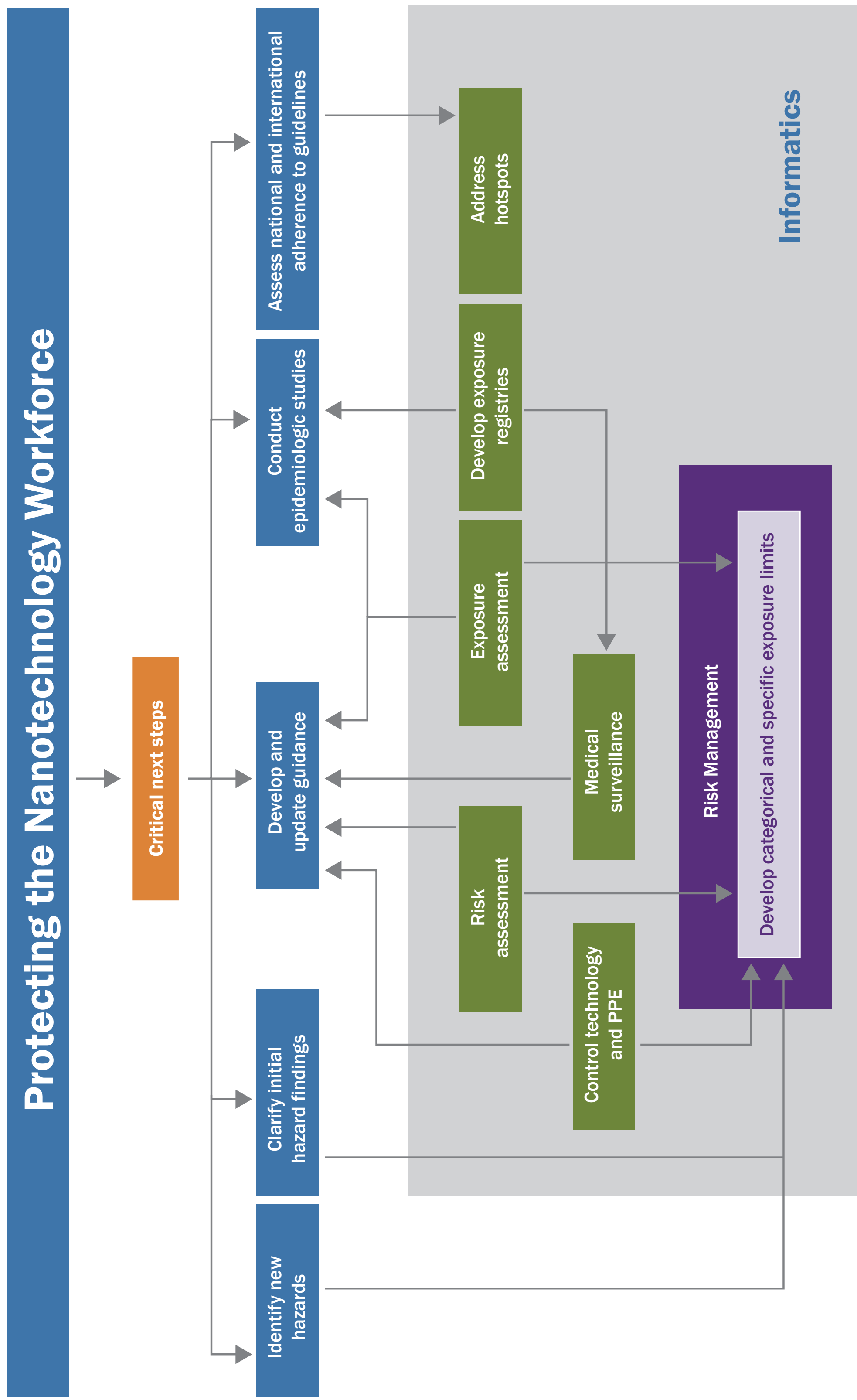

Figure 19. Focus of NIOSH nanomaterial research, 2018–2025.

comparative toxicity analyses for risk assessment. Determine how toxicologic data from new studies might link to existing toxicologic data, to expand the database for assessment.

Strategic Goal 2: Build upon initial data and information to further increase understanding of the initial hazard findings of engineered nanomaterials.

Intermediate Goal 2.1: Authoritative groups will issue guidance based on NIOSH research to prevent pulmonary toxicity from carbon nanotubes and nanofibers, metal, and metal oxides.

Activity Goal 2.1.1: Conduct and publish results from toxicologic testing to determine the potential of various forms of carbon nanotubes and nanofibers, cerium, and other metals to have long-term pulmonary effects (fibrosis, lung cancer, mesothelioma).

Intermediate Goal 2.2: Medical professionals and researchers will use NIOSH information on biomarkers to conduct screening tests to evaluate worker response to inhalation of ENMs.

Activity Goal 2.2.1: Conduct research to determine whether blood, urine, or nasal lavage markers can accurately predict initiation and progression of adverse responses to ENMs.

Activity Goal 2.2.2: Conduct research to determine whether pulmonary responses and systemic responses (such as cardiovascular, neurological, reproductive, or immunological responses) are sensitive indicators of pulmonary exposure to ENMs.

Activity Goal 2.2.3: Evaluate the relationship of deposition patterns and biological responses to pulmonary bolus exposure to ENMs (intratracheal instillation or pharyngeal aspiration) vs. ENM exposure extended over time (inhalation) in rodent models.

Activity Goal 2.2.4: Evaluate predictive *in vitro* screening tests for fibrogenicity, genotoxicity, and/or cell transformation.

Intermediate Goal 2.3: Manufacturers will issue recommendations to protect the health and safety of workers along the product lifecycle of ENMs.

Activity Goal 2.3.1: Characterize particles generated from nano-enabled products during workplace scenarios.

Activity Goal 2.3.2: Characterize emissions and workplace exposures for additive manufacturing processes, including manufacturing of feed materials with ENM additives.

Activity Goal 2.3.3: Evaluate acute and chronic toxicity of particles generated from nano-enabled products containing ENMs during use or application in workplace environments, such as cutting, sanding, grinding, or spraying.

Intermediate Goal 2.4: Health and safety professionals will use standardized measurement methods for evaluating workplace exposure to ENMs.

Activity Goal 2.4.1: Continue interactions with national metrology institutes to identify and qualify needed nanoscale reference materials (RMs) and/or benchmark materials for evaluating measurement tools, instruments, and methods for exposure assessment and toxicology.

Activity Goal 2.4.2: Evaluate relationships between laboratory instrumentation used to characterize aerosols for toxicology studies and field-measurement instrumentation used to characterize workplace atmospheres.

Activity Goal 2.4.3: Conduct further research on determining the advantages and limitations of direct-reading instruments in assessing ENM work-place emissions and exposures.

Activity Goal 2.4.4: Develop and improve methods and approaches (including direct-reading and time-integrated sampling) for assessing workplace exposures to ENMs.

Activity Goal 2.4.5: Evaluate scanning electron microscopy, transmission electron microscopy, and dark-field hyperspectral imaging microscopy as analytical tools for measurement of carbon nanotubes, using *National Institute of Standards and*

Technology (NIST) Standard Reference Material 248: Single-Wall Carbon Nanotubes (Raw Soot).

Activity Goal 2.4.6: Conduct research to advance the use of ENMs in the development of sensors (such as for detection of harmful chemicals) and other health and safety–related applications that can be used in the workplace to ensure effective control of exposure.

Activity Goal 2.4.7: Conduct research to quantify (correlate) the influence of dustiness on the potential for worker inhalation exposure for a range of nanoscale powders and handling tasks.

Intermediate Goal 2.5: Manufacturers will provide information on the potential fire and explosion safety hazards of ENMs on Safety Data Sheets and product labels.

Activity Goal 2.5.1: Identify and publish physical and chemical properties that contribute to dustiness, combustibility, flammability, and explosibility hazards of ENMs.

Intermediate Goal 2.6: Nanomaterial researchers will use informatics to process and communicate information.

Activity Goal 2.6.1: Create a harmonized database to share exposure measurement, control, and epidemiologic data.

Activity Goal 2.6.2: Lead the nanoinformatics community to apply state-of-the-art informatics principles and practices to ENM data analysis and analytics.

Strategic Goal 3: Build upon initial guidance materials to further inform nanomaterial workers, employers, health professionals, regulatory agencies, and decision-makers about hazards, risks, and risk management approaches.

Intermediate Goal 3.1: Authoritative groups will use NIOSH-recommended categorical and specific exposure limits.

Activity Goal 3.1.1: Conduct quantitative risk assessments (QRAs) on specific nanomaterials and groups of nanomaterials by using dose-response data from peer-reviewed published studies and performing comparative potency analyses. Develop and use dosimetry models to describe the deposition and fate of inhaled nanoparticles in rodents and humans.

Activity Goal 3.1.2: Develop a risk-assessment framework for hazard evaluation and predicting the health risk of exposure to ENMs.

Activity Goal 3.1.3: Use a nanomaterial hazard-banding classification scheme to group ENMs.

Intermediate Goal 3.2: Additional employers will adopt NIOSH recommendations for engineering controls and PPE for use with ENMs and additive manufacturing processes.

Activity Goal 3.2.1: Evaluate the effectiveness of engineering-control techniques for ENMs and additive manufacturing processes. Develop and publish new approaches as needed.

Activity Goal 3.2.2: Evaluate the potential for exposure during common dry-powder handling tasks. Develop and publish new approaches as needed.

Activity Goal 3.2.3: Conduct laboratory evaluations of commercially available engineering controls for a variety of common ENM production, handling, and downstream processes.

Activity Goal 3.2.4: Evaluate the effectiveness of PPE (respirators and protective clothing, including gloves) for reducing worker exposures to ENMs.

Activity Goal 3.2.5: Identify and collaborate with businesses that create or use nanomaterials to identify processes that may release nanomaterials during manufacturing or use of ENMs. Evaluate potential exposures and document risk mitigation processes.

Activity Goal 3.2.6: Provide guidance to the Manufacturing USA Initiative and support the responsible commercialization of advanced materials, including ENMs.

Intermediate Goal 3.3: Additional employers will incorporate Prevention through Design (PtD) into ENM health and safety programs.

Activity Goal 3.3.1 (PPNANAOG 3.3.1): Promote PtD principles for ENMs, including development of safer ENMs that have similar industrial uses; containment and control of processes; and system management approaches that include OSH in the synthetic process, development, and manufacture of ENM products.

Intermediate Goal 3.4: International groups such as ISO, OECD, and WHO will include NIOSH research in the collection, management, and dissemination of relevant information to protect ENM workers.

Activity Goal 3.4.1: Develop and disseminate effective information, education, and training materials to target audiences such as nanotechnology workers and employers, occupational safety and health professionals, policy-makers, decision-makers, and the scientific community.

Activity Goal 3.4.2: Establish and maintain national and international partnerships to enable sharing of knowledge gaps, research needs and priorities, approaches, and databases.

Activity Goal 3.4.3: Participate in and lead the development of ISO and WPMN activities and global standards on occupational safety and health for nanotechnology.

Strategic Goal 4: Support epidemiologic studies for nanomaterial workers, including medical, cross-sectional, prospective cohort, and exposure studies.

Intermediate Goal 4.1: Employers, unions, and workers handling ENMs will participate in epidemiologic research and medical surveillance.

Activity Goal 4.1.1: Conduct epidemiological health studies of U.S. workers exposed to CNTs and carbon nanofibers.

Activity Goal 4.1.2: Evaluate the need for and feasibility of initiating registries for workers exposed to existing ENMs (such as titanium dioxide and CNTs) or exposed while producing and using new ENMs.

Activity Goal 4.1.3: Integrate nanotechnology safety and health guidance into existing hazard surveillance systems. Determine whether these systems are adequate by conducting evaluations.

Strategic Goal 5: Assess and promote national and international adherence with risk management guidance.

Intermediate Goal 5.1: Industry will incorporate good risk management guidance for ENMs with their existing management practices.

Activity Goal 5.1.1: Determine whether NIOSH or other precautionary guidance recommendations are adopted by academia and industry.

Activity Goal 5.1.2: Develop a plan for industrial sectors where adherence to good risk-management practices is low.

Activity Goal 5.1.3: Assess the impact of the NTRC outputs.

Activity Goal 5.1.4: Support the International Commission on Occupational Health (ICOH) and other organizations in assessing whether precautionary guidance recommendations are under adoption worldwide.

4.3 Prioritizing Goals by Burden, Need, and Impact

To realize the benefits of nanotechnology, it is important to protect workers potentially exposed to ENMs in research, production, and use [Schulte and Salamanca-Buentello 2007; Nasterlack et al. 2008; Howard and Murashov 2009]. The NIOSH NTRC strategic plan identifies and creates the information needed for risk management programs that will control and prevent adverse health effects in workers. NIOSH will translate NTRC research findings into products that the nanotechnology community will use to develop and implement appropriate risk management practices to minimize worker exposure to ENMs. NIOSH will also evaluate how research results and risk management guidance developed by NIOSH influences others to take action to prevent exposure to hazards related to ENMs. The concepts of burden, need, and impact have always been important considerations in NIOSH project selection and priority-goal-setting processes.

Burden includes estimates at the societal level of analysis of the broad consequences of everything from which all workers suffer, that is, estimates of the total effect of worker injury and illness.

Key components of **Need** involves identification of an information gap that requires filling and a determination of whether (and why) NIOSH is the most appropriate organization to conduct the research to fill the gap. Factors such as intellectual capital, statutory authority, mission relevance, unique infrastructure, and financial capital are a few considerations. NIOSH has a comparative advantage if it can produce something at a lower opportunity cost or more efficiently than its competitors or if no one other than NIOSH would undertake the activity.

Impact is a measure of the significance of contributions and the potential to improve worker health and safety on the basis of evident or anticipated end outcomes or well-accepted intermediate outcomes. A significant factor in demonstrating impact is that the activity will produce or have a clear pathway to produce a substantial effect in one or more of the strategic goals.

Burden

ENMs, at certain concentrations and over certain durations, can affect the lung, cardiovascular, and most organ systems [Donaldson et al. 2000 and 2004; Kreyling et al. 2010; Li et al. 2007; Mercer et al. 2013; Nurkiewicz et al. 2008; Sargent et al. 2014]. Epidemiological analysis of human health effects from air pollution has shown that particles in the nanoscale size range are responsible for excess respiratory and cardiovascular mortality [Dockery et al. 1993]. Recently, air pollution and animal studies have shown that various nanoscale particles are related to adverse neurological changes. Nanoparticles in welding fumes cause toxicological and carcinogenic effects [Sriram et al. 2014; Zeidler-Erdely et al. 2017]. Additionally, nano titanium dioxide has been shown to impact microvascular dysfunction in fetal development of rats [Stapleton et al. 2013]. It is too early to identify the exact burden of ENMs on workers, but we anticipate that health effects from exposure to ENMs can be similar to those from ultrafine air pollution or other dusts and fumes that cause pulmonary and cardiovascular effects. Therefore, it is possible that pneumoconiosis as well as other dust-related conditions could arise. Some engineered nanoparticles (such as titanium dioxide) appear to be 10 times more potent than their bulk counterparts. This higher mass-based potency is associated with the greater surface area [NIOSH 2011]. No one knows the number of potentially ENM-exposed workers. One early estimate, not yet validated, is that 1 to 2 million workers may work with nanomaterials. Still, ENMs are in many product lines and industrial sectors. The Nanowerk nanomaterials database revealed about 4,000 commercially available nanomaterials, and the Woodrow Wilson Project on Emerging Nanomaterials identified more than 1,800 consumer products with ENMs; each product had to involve workers. ENMs are in commercial products, possibly exposing the workers who make, use, or destroy them. Therefore, the burden in terms of morbidity and mortality may be large, significant, and costly. Moreover, failure to develop the technology responsibly, including worker protection, may also place a burden on capital and entrepreneurial investment.

Need

Nanotechnology is continuing to emerge, as commercial application of the technology is only about 20 years old. Consequently, there are many unanswered questions about the risk management continuum of hazard, exposure, risk, and control.

Although hazard is the driver of these actions, the wide use of ENMs in commerce means workers potentially have exposure to them. Employers, workers, and other decision makers are asking for information on all steps of risk management, from hazard identification to control approaches. Consequently, we must address all the steps in the hazard continuum.

Based on Burden, Need, and Impact, the following goals are the top three priorities for the NTRC:

Priority 1—Strategic Goal 1: Increase understanding of new nanomaterials and related health risks to nanomaterial workers.

Impact. This research will contribute to the body of knowledge about the adverse health effects in animals exposed to various ENMs. The findings will have a direct impact on risk assessment of potential outcomes for exposed workers; contribute to epidemiologic research; and provide background that can be used to create guidance on control technologies and medical surveillance.

Priority 2—Strategic Goal 3: Build upon initial guidance materials to inform nanomaterial workers, employers, health professionals, regulatory agencies, and decision-makers about hazards, risks, and risk management approaches.

Impact. Various target audiences such as nanotechnology workers and employers, occupational safety and health professionals, policy-makers, decision-makers, and/or the scientific community in research, manufacturing, construction, mining, oil and gas, and healthcare will begin or continue to apply NIOSH guidance to responsibly develop, handle, and commercialize ENMs. Through strategic planning, research, partnering with stakeholders, and making information widely available, the NTRC will continue supporting the responsible development of nanotechnology by translating research into effective risk management guidance and practices across the lifecycle of ENM-enabled products.

Priority 3—Activity/Output Goal 3.1.3: Use a nanomaterial hazard banding classification scheme to group ENMs.

Impact. This research will investigate the evidence for developing predictive algorithms of structure-activity relationships and comparative toxicity for use in quantitative risk assessment. Findings from this research will provide the scientific basis for developing occupational exposure limits for individual nanomaterials or groups of nanomaterials.

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5 HOW DO WE TRACK PROGRESS AND MEASURE SUCCESS?

The annual project planning effort and the NIOSH Project Planning & Management system (NPPM) are tools used to collect and store project information systematically and consistently. This system allows NIOSH to see the achievements of each individual project but also how projects' achievements work together to create collective impact. Information on outputs and outcomes in particular is used to respond to requests from Congress, the Office of Management and Budget (OMB), Health and Human Services (HHS), the press, and others about NIOSH spending and accomplishments.

Fields updated and tracked in the NPPM system include Activities (such as presentations, webinars, exhibits, field studies, and participation on international committees or as university adjuncts); **Outputs** (such as peer-reviewed journal articles and NIOSH numbered publications); and Intermediate **Outcomes** (for instance, adoption by a non-governmental organization [NGO] or government agency of a NIOSH recommendation, such as use of engineering controls, PPE in industrial processes, or NIOSH-developed measurement methods). These steps ultimately lead to the desired End Outcome (protecting the ENM workforce from adverse health effects and promoting the responsible development of ENMs and advanced manufacturing) (see Figure 4).

Output tracking can be via standard citation metrics (such as the number of citations of an article or a journal impact factor) and alternative metrics. Alternative metrics use data from the social web and can track values such as the number of times a web page is visited, a NIOSH document is downloaded, or a topic is mentioned on a social feed (such as a blog, tweet, or Facebook). Outputs can also include the number of collaborations through initiatives, agreements, MOUs, or field team outreach.

Impact is evident too when NTRC staff interact informally with stakeholders, such as at nanotechnology or occupational, safety, and health conferences. These interactions have led to positive feedback, such as this from a company representative [Mark Banash, PhD, formerly of Nancomp Technologies; verbal communication, 2014]: "NIOSH has been invaluable to us. They bring expertise, they bring workable knowledge, and they have insights as to how to solve technical problems involving the materials, which has been invaluable to us in creating a safe working environment. We continue to look forward to working with NIOSH as we continue our expansion into a full-scale industrial facility."

As the number of industries and occupational settings that use nanotechnology and ENMs expands, the possibility for workers to encounter and be exposed to these materials in the workplace will also likely increase. The expansion of these materials into increasingly diverse products, manufacturing processes, and workplace environments also presents a challenge for assessing the contributions of NTRC to worker safety and health. Trends in advanced manufacturing are redefining manufacturing and enabling access to sophisticated materials and capabilities for an increasing number of smaller companies. This diffusion of materials and capabilities to a growing number of companies and workers may complicate tracking the use of nanotechnologies and ENMs in the workplace, and it may affect the implementation of good practices to reduce worker injuries, illnesses, or exposures. These trends make it more difficult to understand which occupational settings are using ENMs, a difficulty which increases the challenges in understanding the potential risks.

These trends also add to the difficulty of assessing the adoption and efficacy of practices intended to reduce occupational injuries, illnesses, and exposure to nanotechnologies and ENMs. Additionally, although it is relatively straightforward to track and measure an organization's activities and outputs, it is more difficult to track and measure its contributions to desired societal benefits. NIOSH has worked with others, such as the RAND Corporation, for assistance with determining the impact of the NTRC [Landree et al. 2015]. NIOSH also has experience with using a modified version of a contribution analysis approach to determine influence (and impact) by focusing on intermediate outcomes (such as an employer adopting a policy based on NIOSH research) [Downes et al. 2018].

6 ALIGNMENT WITH THE NATIONAL NANOTECHNOLOGY INITIATIVE

6.1 Environmental, Health, and Safety Goals of the NNI

NIOSH research priorities address many of the strategic goals proposed by the NNI Strategy for Nanotechnology Environmental, Health, and Safety Research. The alignment of the five NIOSH NTRC strategic goals and 10 NTRC critical research areas with the NNI EHS priority research needs (Appendix A) is shown in Table 1.

Table 1. Alignment of Critical Research Areas with the Five Strategic Goals of the NIOSH NTRC and the NNI EHS Priority Research Needs (RNs).

NIOSH NTRC Strategic Goal/ Critical Research Area	Increase understanding of new hazards and related health risks to nanomaterial workers	Expand understanding of the initial hazard findings of engineered nanomaterials	Support the creation of guidance materials to inform nanomaterial workers and employers about hazards, risks, and risk management approaches	Support epidemiologic studies for nanomaterial workers, including medical, cross–sectional, prospective cohort, and exposure studies	Assess and promote national and international adherence with risk management guidance
Toxicity and internal dose	√[1] 3-RN12 3-RN2 3-RN3 3-RN4 3-RN5 4-RN1	√ 3-RN12 3-RN2 3-RN3 3-RN4 3-RN5	√		
Measurement methods	√ 1-RN1 1-RN2 1-RN3 2-RN1 3-RN2	√ 1-RN1 1-RN2 1-RN3 2-RN1 3-RN2	√		
Exposure assessment	√ 2-RN1 2-RN3 3-RN2 4-RN1 5-RN2	√ 2-RN1 2-RN3 3-RN2 4-RN1 5-RN2	√		

(Continued)

Table 1 (Continued). Alignment of Critical Research Areas with the Five Strategic Goals of the NIOSH NTRC and the NNI EHS Priority Research Needs (RNs).

NIOSH NTRC Strategic Goal/ Critical Research Area	Increase understanding of new hazards and related health risks to nanomaterial workers	Expand understanding of the initial hazard findings of engineered nanomaterials	Support the creation of guidance materials to inform nanomaterial workers and employers about hazards, risks, and risk management approaches	Support epidemiologic studies for nanomaterial workers, including medical, cross–sectional, prospective cohort, and exposure studies	Assess and promote national and international adherence with risk management guidance
Epidemiology and surveillance	√	√	√	√ 2-RN1 2-RN3 2-RN4 3-RN6 5-RN2	√ 5-RN2
Risk assessment	√ 5-RN1 5-RN2 5-RN5	√ 5-RN1 5-RN2 5-RN5	√ 5-RN3 5-RN4		
Engineering controls and PPE	√ 2-RN1 5-RN1 5-RN2	√ 2-RN1 5-RN1 5-RN2	√		√ 5-RN2
Fire and explosion safety	√ 1-RN5	√ 1-RN5	√		

(Continued)

Table 1 (Continued). Alignment of Critical Research Areas with the Five Strategic Goals of the NIOSH NTRC and the NNI EHS Priority Research Needs (RNs).

NIOSH NTRC Strategic Goal/ Critical Research Area	Increase understanding of new hazards and related health risks to nanomaterial workers	Expand understanding of the initial hazard findings of engineered nanomaterials	Support the creation of guidance materials to inform nanomaterial workers and employers about hazards, risks, and risk management approaches	Support epidemiologic studies for nanomaterial workers, including medical, cross–sectional, prospective cohort, and exposure studies	Assess and promote national and international adherence with risk management guidance
Recommendations and guidance			√ 5-RN3 5-RN4 5-RN5		√ 5-RN2
Global collaborations[3]	√	√	√	√	4
Applications and Informatics[5]			√		

[1]A check mark (✓) indicates that a goal is currently being addressed by projects within the NIOSH critical research area.
[2]Alphanumeric identifications indicate specific NNI priority research needs (see Appendix A) being met by the NIOSH projects in each critical research area.
[3]International engagement is a priority of the NNI and a critical component of the 2011 NNI EHS Research Strategy. However, it is not identified as a research need in the NNI Strategy.
[4]NIOSH will work with other governments to determine global adherence.
[5]The NNI EHS plan does not address applications of nanomaterials for EHS use. However, the NNI strategic plan includes applications as a driving force behind several federal nanotechnology programs, and it has the potential to improve safety and health, such as through the development of advanced sensors or PPE.

REFERENCES

Birch ME, Wang C, Fernback JE, Feng HA, Birch QT, Dozier AK [2107]. Analysis of carbon nanotubes and nanofibers on mixed cellulose ester filters by transmission electron microscopy. In: Ashley K, O'Connor PF, eds. NIOSH manual of analytical methods. 5th ed. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, **www.cdc.gov/niosh/nmam**.

Bishop L, Cena L, Orandle M, Yanamala N, Dahm MM, Birch ME, Evans DE, Kodali VK, Eye T, Battelli L, Zeidler-Erdely PC, Casuccio G, Bunker K, Lupoi JS, Lersch TL, Stefaniak AB, Sager T, Afshari A, Schwegler-Berry D, Friend S, Kang J, Siegrist KJ, Mitchell CA, Lowry DT, Kashon ML, Mercer RR, Geraci CL, Schubauer-Berigan MK, Sargent LM, Erdely A [2017]. An in-vivo toxicity assessment of occupational components of the carbon nanotube life cycle to provide context to potential health effects. ACS Nano *11*(9):8849–8863, **http://dx.doi.org/10.1021/acsnano.7b03038**.

Dockery D, Arden PC, Xu X, Spengler J, Ware J, Fay M, Ferris B Jr., Speizer F [1993]. An association between air pollution and mortality in six U.S. cities. N Engl J Med *329*:1753–1759, **http://dx.doi.org/10.1056/NEJM199312093292401**.

Donaldson K, Stone V, Gilmore P, Brown D, MacNee W [2000]. Ultrafine particles: mechanisms of lung injury. Philos Trans R Soc Lond A *358*(1775):2741–2749.

Donaldson K, Stone V, Tran CL, Kreyling W, Borm PJ [2004]. Nanotoxicology. Occup Environ Med *61*:727–728, **http://oem.bmj.com/content/61/9/727.1**.

Downes A, Novicki E, Howard J [2018]. Using the contribution analysis approach to evaluate science impact: A case study of the National Institute for Occupational Safety and Health. Am J Eval 2018 Apr, 1–13.

Drew NM, Kuempel ED, Pei Y, Yang F [2017]. A quantitative framework to group nanoscale and microscale particles by hazard potency to derive occupational exposure limits: proof of concept evaluation. Regul Toxicol Pharmacol *89*:253–267.

Eastlake A, Beaucham C, Martinez K, Dahm M, Hodson L, Geraci C [2016]. Refinement of the nanoparticle emission assessment technique into the nanomaterial exposure assessment technique (NEAT 2.0). J Occup Environ Hyg *13*(9):708–717.

Hoover MD, Myers DS, Cash LJ, Guilmette RA, Kreyling WG, Oberdörster G, Smith R, Cassata JR, Boecker BB, Grissom MP [2015]. Application of an informatics-based decision-making framework and process to the assessment of radiation safety in nanotechnology. Health Phys J *108*(2):179–194.

Howard J, Murashov V [2009]. National nanotechnology partnership to protect workers. J Nanopart Res *11*:1673–1683.

ISO [2015]. ISO/TS 80004-1:201 Nanotechnologies – vocabulary – part 1: core terms. Geneva, Switzerland: International Organization for Standardization, **https://www.iso.org/standard/68058.html**.

Kreyling WG, Hirn S, Schleh C [2010]. Nanoparticles in the lung. Nat Biotechnol *28*:1275–1276, **http://dx.doi.org/10.1038/nbt.1735**.

Landree E, Miyake H, Greenfield V [2015]. Nanomaterial safety in the workplace: pilot project for assessing the impact of the NIOSH Nanotechnology Research Center. Santa Monica, CA: RAND Corporation, **http://www.rand.org/pubs/research_reports/RR1108.html**.

Li Z, Hulderman T, Salmen R, Chapman R, Leonard S, Young S-H, Shvedova A, Luster M, Simeonova P [2007]. Cardiovascular effects of pulmonary exposure to single-wall carbon nanotubes. Environ Health Perspect *115*:377–382, **http://dx.doi.org/10doi:10.1289/ehp.9688**.

McKinney W, Chen B, Frazer D [2009]. Computer controlled multi-walled carbon nanotube inhalation exposure system. Inhal Toxicol *21*(12):1053–1061.

Mercer R, Scabilloni J, Hubbs A, Wang L, Battelli L, McKinney W, Castranova V, Porter D [2013]. Extrapulmonary transport of MWCNT following inhalation exposure. Part Fibre Toxicol 10:38, **http://dx.doi.org/10.1186/1743-8977-10-38**.

Methner M, Hodson L, Geraci C [2009]. Nanoparticle emission assessment technique (NEAT) for the identification and measurement of potential inhalation exposure to engineered nanomaterials—part A. J Occup Environ Hyg *7*:127–132.

Murashov V, Schulte PA, Howard J [2012]. Progression of occupational risk management with advances in nanomaterials. J Occup Environ Health *9*:D12–D22.

Nasterlack M, Zober A, Oberlinner C [2008]. Considerations in occupational medical surveillance of employees handling nanoparticles. Int Arch Occup Environ Health *81*(6):721–726.

NCRP [2017]. Radiation safety aspects of nanotechnology. Bethesda, MD: National Council on Radiation Protection and Measurements, NCRP Report No. 176.

NIOSH [2007]. Progress toward safe nanotechnology in the workplace. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2007-123.

NIOSH [2009a]. Approaches to safe nanotechnology: managing the health and safety concerns associated with engineered nanomaterials. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2009-125.

NIOSH [2009b]. Interim guidance for medical screening and hazard surveillance for workers potentially exposed to engineered nanoparticles. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2009-116.

NIOSH [2010]. Progress toward safe nanotechnology in the workplace: a report from the NIOSH Nanotechnology Research Center. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2010-104.

NIOSH [2011]. Current intelligence bulletin 63: occupational exposure to titanium dioxide. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2011-160.

NIOSH [2012a]. Filling the knowledge gaps for safe nanotechnology in the workplace: a progress report from the NIOSH Nanotechnology Research Center, from inception in 2004–2011. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2013-101.

NIOSH [2012b]. General safe practices for working with engineered nanomaterials in research laboratories. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2012-147.

NIOSH [2013a]. Protecting the nanotechnology workforce: NIOSH nanotechnology research and guidance strategic plan, 2013–2016. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2014-106.

NIOSH [2013b]. Current intelligence bulletin 65: occupational exposure to carbon nanotubes and nanofibers. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2013-145.

NIOSH [2013c]. Current strategies for engineering controls in nanomaterial production and downstream handling processes. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2014-102.

NIOSH [2016]. Building a safety program to protect the nanotechnology workforce: a guide for small to medium-sized enterprises. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2016-102.

NNI [2001]. National Nanotechnology Initiative: interagency agreement. Washington, DC: United States Executive Office of the President, Office of Science and Technology Policy, http://www.nano.gov/html/about/home_about.html.

NNI [2011]. National Nanotechnology Initiative: environmental, health, and safety research strategy. Washington, DC: United States Executive Office of the President, Office of Science and Technology Policy, Nanotechnology Environmental and Health Implications (NEHI) Working Group.

Nurkiewicz TR, Porter DW, Hubbs AF, Cumpston JL, Chen BT, Frazer DG, Castranova V [2008]. Nanoparticle inhalation augments particle-dependent systemic microvascular dysfunction. Part Fibre Toxicol *5*:1, **https://doi.org/10.1186/1743-8977-5-1**.

PCAST [2012]. Report to the President on ensuring American leadership in advanced manufacturing. Washington, DC: United States Executive Office of the President, President's Council of Advisors on Science and Technology.

PEN [2016]. Project for Emerging Technologies: consumer products inventory, **http://www.nanotechproject.org/cpi**.

Sargent LM, Porter DW, Staska LM, Hubbs AF, Lowry DT, Battelli L, Siegrist KJ, Kashon ML, Mercer RR, Bauer AK, Chen BT, Salisbury JL, Frazer D, McKinney W, Andrew M, Tsuruoka S, Endo M, Fluharty KL, Castranova V, Reynolds SH [2014]. Promotion of lung adenocarcinoma following inhalation exposure to multi-walled carbon nanotubes. Part Fibre Toxicol *11*:3.

Schulte P, Geraci C, Zumwalde R, Hoover M, Kuempel E [2008]. Occupational risk management of engineered nanoparticles. J Occup Environ Hyg *5*:239–249.

Schulte PA, Salamanca-Buentello F [2007]. Ethical and scientific issues of nanotechnology in the workplace. Environ Health Perspect *115*:5–12.

Sriram K, Jefferson A, Lin G, Afshari A, Zeidler-Erdely P, Meighan T, McKinney W, Jackson M, Cumpston A, Cumpston J, Leonard H, Frazer D, Antonini J [2014]. Neurotoxicity following acute inhalation of aerosols generated during resistance spot weld-bonding of carbon steel. Inhal Toxicol *26*(12):720–732.

Stapleton PA, Minarchick VC, Yi J, Engels K, McBride CR, Nurkiewicz TR [2013]. Maternal engineered nanomaterial exposure and fetal microvascular function: does the Barker hypothesis apply? Am J Obstet Gynecol *209*;227:e1–11.

Stefaniak A, Hammond D, Johnson A, Knepp A, LeBouf R [2017a]. Emission of particulate matter from a desktop three-dimensional (3D) printer. Morgantown, WV: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Health Hazard Evaluation Report 2017-0059-3291.

Stefaniak A, LeBouf R, Duling M, Yi J, Abukabda A, McBride C, Nurkiewicz T [2017b]. Inhalation exposure to three-dimensional printer emissions stimulates acute hypertension and microvascular dysfunction. Toxicol Appl Pharmacol *335*:1–72, **https://doi.org/doi:10.1016/j.taap.2017.09.016**.

Yi J, LeBouf RF, Duling MG, Nurkiewicz T, Chen-BT, Schwegler-Berry D, Virji MA, Stefaniak AB [2016]. Emission of particulate matter from a desktop three-dimensional (3D) printer. J Toxicol Environ Health *79*(11):453–465, **http://dx.doi.org/10.1080/15287394.2016.1166467**.

Zeidler-Erdely P, Salmen R, Erdely A, Keane M, Kodali V, Antonini J, Falcone L [2017]. Pulmonary toxicity of gas metal arc-stainless steel welding fume and component metals. Toxicologist *156*(1):265–266.

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APPENDIX A

Comprehensive Chart of the NNI 2011 EHS Research Needs

[National Nanotechnology Initiative: Environmental, Health, and Safety Research Strategy. Washington, DC: United States Executive Office of the President, Office of Science and Technology Policy, Nanotechnology Environmental and Health Implications (NEHI) Working Group, Table D–1.]

Table D–1. The Core EHS Research Categories and their Highest-Priority Research Needs (RNs)

Key Research Needs	Subordinate Research Needs
1. Nanomaterial Measurement Infrastructure Research Needs Develop measurement tools to detect and identify engineered nanoscale materials in products and relevant matrices and determine their physico-chemical properties throughout all stages of their life cycles. Develop measurement tools for determination of biological response and to enable assessment of hazards and exposure for humans and the environment from engineered nanomaterials and nanotechnology-based products throughout all stages of their life cycles.	
RN#1. Develop measurement tools for determination of physico-chemical properties of ENMs in relevant media and during the life cycles of ENMs and NEPs	• Physical dimensions and morphology: size, size distribution, characteristic dimensions, shape • Internal structure: atomic-molecular, core-shell • Surface and interfacial properties: surface charge, zeta potential, surface structure, elemental composition, surface-bound molecular coatings and conjugates, reactivity • Bulk composition: elemental or molecular composition, crystalline phase(s) • Dispersion properties: degree and state of dispersion • Mobility and other transport properties: diffusivity, transport in biological and environmental matrices
RN#2. Develop measurement tools for detection and monitoring of ENMs in realistic exposure media and conditions during the life cycles of ENMs and NEPs	• Sampling and collection of ENMs • Detecting the presence of ENMs • Quantity of ENMs-concentration based on surface area, mass, and number concentrations • Size and size distribution of ENMs • Spatial distribution of ENMs • Discriminating ENMs from ambient NMs such as combustion products and welding fumes • Discriminating multiple types of ENMs such as metals and metal oxides
RN#3. Develop measurement tools for evaluation of transformations of ENMs in relevant media and during the life cycles of ENMs and NEPs	• Agglomeration and de-agglomeration • Dissolution and solubility • Absorption of natural organic matter and bioconstituents • Oxidation and reduction • Deposition of ENMs on surfaces

(continued)

Table D–1 (Continued). The Core EHS Research Categories and their Highest-Priority Research Needs (RNs)

Key Research Needs	Subordinate Research Needs
RN#4. Develop measurement tools for evaluation of biological responses to ENMs and NEPs in relevant media and during the life cycles of ENMs and NEPs	• Adequacy of existing assays • New assays or high-throughput, high content assays • Correlation of biological responses with physico-chemical properties • Surface reactivity at the interfaces between ENMs and biological receptors • Biomarkers of toxicological response
RN#5. Develop measurement tools for evaluation of release mechanisms of ENMs from NEPs in relevant media and during the life cycles of NEPs	• Release by fire, combustion, and incineration • Release by mechanical degradation, such as abrasion, deformation, and impact • Release by dissolution of matrix material • Release by chemical reactions of the matrix material • Release by photo-induced degradation of the matrix material • Release by consumer interactions, such as spraying, mouthing, and swallowing • Release by interactions with biological organisms in the environment
2. Human Exposure Assessment Research Needs Identify potential sources, characterize the exposure scenarios, and quantify actual exposures of workers, the general public and consumers to nanomaterials. Characterize and identify the health outcomes among exposed populations in conjunction with information about the control strategies used and exposures to determine practices that result in safe levels of exposure.	
RN#1. Understand processes and factors that determine exposures to nanomaterials	• Conduct studies to understand processes and factors that determine exposure to engineered nanomaterials • Develop exposure classifications of nanomaterials and processes • Develop internationally harmonized and validated protocols for exposure surveys, sample collection and analysis, and reporting through existing and newly created international frameworks • Develop comprehension predictive models for exposures to a broad range of engineered nanomaterials and processes • Characterize process- and task-specific exposure scenarios in the workplace

(continued)

Table D–1 (Continued). The Core EHS Research Categories and their Highest-Priority Research Needs (RNs)

Key Research Needs	Subordinate Research Needs
RN#2. Identify population groups exposed to engineered nanomaterials	• Systematically collect and analyze information about nanomaterial manufacture, processing, and direct use in commercial and consumer products over time to discern geographic areas where engineered nanomaterials may be emitted into the environment, consumed in the form of ingredients of products, and/or disposed of in solid waste, wastewater, etc. • Conduct population-based surveys to obtain information on use patterns for consumer products • Identify potential subpopulations that are more susceptible to exposure to engineered nanomaterials than others • Develop quantitative assessment methods appropriate for target population groups and conduct assessments of those population groups most likely to be exposed to engineered nanomaterials
RN#3. Characterize individual exposures to nanomaterials	• Expand currently available exposure assessment techniques to facilitate more accurate exposure assessment for engineered nanomaterials at benchmark concentration levels using feasible methods • Develop new tools through national and international surveys to support effective exposure characterization of individuals • Characterize and detect nanomaterials in biological matrices and conduct studies to understand transformations of nanomaterials during transport in the environment and in human bodies • Conduct studies to examine emissions and human contact during normal use and after wear and tear have degraded a product, as well as during repeated exposures • Develop engineered nanomaterials exposure assessment models based on identified critical exposure descriptions • Develop databases to contain the collected data and information
RN#4. Conduct health surveillance of exposed populations	• Establish a program for the epidemiological investigations of physician case reports and reports of suspicious pattern of adverse events • Establish exposure registry and medical surveillance programs for workers • Analyze injury and illness reporting in existing programs

(continued)

Table D–1 (Continued). The Core EHS Research Categories and their Highest-Priority Research Needs (RNs)

Key Research Needs	Subordinate Research Needs
3. Human Health Research Needs Understand the relationship of physico-chemical properties of engineered nanoscale materials to *in vivo* physico-chemical properties and biological response. Develop high-confidence predictive models of *in vivo* biological responses and casual physico-chemical properties of ENMs.	
RN#1. Identify or develop appropriate, reliable, and reproducible *in vitro* and *in vivo* assays and models to predict *in vivo* human responses to ENMs	• Establish a system to develop and apply reliable and reproducible *in vitro* and *in vivo* test methods • Evaluate the degree to which an *in vitro* response correlates with an *in vivo* response • Evaluate the degree to which *in vitro* and *in vivo* models predict human response • Translate structure-activity relationship and other research data into computational models to predict toxicity *in silico*
RN#2. Quantify and characterize ENMs in exposure matrices and biological matrices	• Determine critical ENM measurands in biological and environmental matrices and ensure the development of tools to measure ENMs in appropriate matrices as needed • Determine matrix and/or weathering effects that may alter the physico-chemical characteristics of the ENM measurands • Identify key factors that may influence the detection of each measurand in a particular matrix (e.g., sample preparation, detection method, storage, temperature, solvents/solutions) • Characterize and quantify exposure for all exposure routes using *in vivo* models to identify the most likely routes of human exposure • Identify biomarkers of exposure and analytical methods for their determination
RN#3. Understand the relationship between the physico-chemical properties of ENMs and their transport, distribution, metabolism, excretion, and body burden in the human body	• Characterize ENM physico-chemical properties and link to mechanisms of transport and distribution in the human body • Understand the relationship of the physico-chemical properties of ENMs to the mechanisms of sequestration in and translocation of ENMs out of the exposure organ and secondary organs, and to routes of excretion from the human body • Determine the metabolism or biological transformation of ENMs in the human body

(continued)

Table D–1 (Continued). The Core EHS Research Categories and their Highest-Priority Research Needs (RNs)

Key Research Needs	Subordinate Research Needs
RN#4. Understand the relationship between the physico-chemical properties of ENMs and uptake through the human port-of-entry tissues	• Characterize ENMs at and in port-of-entry tissues, including nontraditional routes of entry such as the ear and eye, and identify mechanisms of ENM uptake into tissues • Determine the relationship of ENM physico-chemical properties to deposition and uptake under acute exposure conditions and under chronic exposure conditions • Translate data on ENM properties and uptake to knowledge that may be used to intentionally redesign ENMs for optimum human and environmental safety and product efficacy
RN#5. Determine the modes of action underlying the human biological response to ENMs at the molecular, cellular, tissue, organ, and whole body levels	• Determine the dose response and time course of biological responses at the primary site of exposure and at distal organs following ENM exposure • Understand the mechanisms and molecular pathway(s) associated with ENM biology within cellular, organ, and whole organism systems • Link mechanisms of response with ENM physico-chemical properties and employ this information in the design and development of future ENMs • Develop translational alternative *in vitro* testing methods for the rapid screening of future ENMs based on mechanism(s) of response that are predictive of *in vivo* biological responses
RN#6. Determine the extent to which life stage and/or susceptibility factors modulate health effects associated with exposure to ENMs and nanotechnology-enabled products and applications	• Determine the effect of life stage and/or gender on biological response to ENMs • Establish the role of genetic and epigenetic susceptibility on the biological response to ENMs in the context of life stage and/or susceptibility factors • Understand mechanistically the influence of preexisting disease on the biological response to ENMs in the context of life stage and other susceptibility factors • Identify exposure conditions that make susceptible individuals more vulnerable to the health effects associated with ENMs and nanotechnology-enabled applications • Establish a database that contains published, peer-reviewed literature, occupational and consumer reports, and toxicological profiles that describe altered responses to ENMs and nanotechnology-enabled applications in susceptible animal models or individuals following exposure

(continued)

Table D–1 (Continued). The Core EHS Research Categories and their Highest-Priority Research Needs (RNs)

Key Research Needs	Subordinate Research Needs
4. Environment Research Needs Understand the environmental fate, exposure, and ecological effects of engineered nanomaterials, with priority placed on materials with highest potential for release, exposure, and/or hazard to the environment.	
RN#1. Understand environmental exposures through the identification of principal sources of exposure and exposure routes	• Manufacturing processes and product incorporation • Life cycle of technology and exposures subsequent to product manufacturing • Analytical approaches to measure temporal changes in nanoparticle properties throughout the life cycle • Models to estimate releases • Environmental receptors for exposure assessment
RN#2. Determine factors affecting the environmental transport of nanomaterials	• Determine key physico-chemical properties affecting transport • Determine key transport and fate processes relevant to environmental media • Develop new tools and adaptation of current predictive tools to accommodate unique properties of nanomaterials
RN#3. Understand the transformation of nanomaterials under different environmental conditions	• Identify and evaluate nanomaterial properties and transformation processes that will reduce environmental persistence, toxicity, and production of toxic products • Determine the rate of aggregation and long-term stability of agglomeration/aggregation and the long-term stability of these aggregates and agglomerates • Develop tools to predict the transformations or degradability of nanomaterials
RN#4. Understand the effects of engineered nanomaterials on individuals of a species and the applicability of testing schemes to measure effects	• Test protocols • Dose-response characterization • Uptake/elimination kinetics, tissue/organ distribution • Mode/mechanism of action, predictive tools • Tiered testing schemes/environmental realism
RN#5. Evaluate the effects of engineered nanomaterials at the population, community, and ecosystem levels	• Population • Community • Other ecosystem-level effects • Predictive tools for population-, community-, and ecosystem-level effects

(continued)

Table D–1 (Continued). The Core EHS Research Categories and their Highest-Priority Research Needs (RNs)

Key Research Needs	Subordinate Research Needs
5. Risk Assessment and Risk Management Methods Research Needs Increase available information for better decision making in assessing and managing risks from nanomaterials, including using comparative risk assessment and decision analysis; life cycle considerations; and additional perspectives such as ELSI considerations, stakeholders' values, and additional decision makers' considerations.	
RN#1. Incorporate relevant risk characterization information, hazard identification, exposure science, and risk modeling and methods into the safety evaluation of nanomaterials	• Characterization, fate, and release of nanoparticles throughout the life cycles of nanotechnology-enabled products • Development of predictive models on accumulation, migration, and release of nanoparticles throughout the life cycles of nanotechnology-enabled products • Safety of nanoparticles throughout the life cycles of the nanotechnology-enabled products • Comprehensive and predictive models to assess the potential risks of nanoparticles during the manufacturing and life cycle of nanoproducts, with inputs from human and environment exposures and on nanomaterial properties
RN#2. Understand, characterize, and control workplace exposures to nanomaterials	• Dissemination and implementation of effective techniques and protocols to measure exposures in the workplace • Identification and demonstration of effective containment and control technologies including for accidents and spills • Development of an effective industry surveillance system • Design and deployment of a prospective epidemiological framework relevant to exposure science • Systematic approaches for occupational risk modeling
RN#3. Integrate life cycle considerations into risk assessment	• Establishment of nanotechnology-specific taxonomy for life cycle stages • Integration of risk assessment, life cycle analyses, and decision-making approaches into regulatory decision making processes • Application of adaptive management tools based on monitoring/implementation to evaluate life cycle analysis implementation • Development of case studies, e.g., green chemistry, nanomaterials selection, nanomaterials acquisition process, illustrating application of these risk management methods

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Table D–1 (Continued). The Core EHS Research Categories and their Highest-Priority Research Needs (RNs)

Key Research Needs	Subordinate Research Needs
RN#4. Integrate risk assessment into decision-making frameworks for risk management	• Development of comparative risk assessment and formal decision-analytical methods as opposed to "absolute" risk assessment strategies • Application of formal decision-analytical methods to prioritize risk management alternatives • Use of gap analyses and value of information analysis to identify research needs • Integration of stakeholder values and risk perceptions into risk management processes • Application of integrated decision framework through case studies in risk management decision making
RN#5. Integrate and standardize risk communication within the risk management framework	• Development and use of standardized terminology in risk communications • Early information-sharing on hazards and risk among Federal agencies • Development of appropriate risk communication approaches for agency-specific needs
Informatics and Modeling Research Need	
RN#1. Develop computational models of ENM structure-property-activity relationships to support the design and development of ENM with maximum benefit and minimum risk to humans and the environment	• Validate the predictive capability of *in vitro* and *in vivo* assays and employ that subset of assays in data generation to establish computational models to predict ENM behavior in humans and the environment • Establish a standard set of physical and chemical characterization parameters, dose metrics, and biological response metrics • Design and establish structures and ontologies for methods development, data capture, sharing, and analysis • Evaluate and adapt as necessary existing computational models by beginning with existing models for exposure and dosimetry and using data generated from validated assays • Use ENM exposure and dosimetry models to develop ENM structure-activity models to predict ENM behavior in humans and the environment • Establish training sets and beta test sites to refine and validate ENM structure-activity models • Disseminate ENM structure-activity models through publicly accessible nanotechnology websites

APPENDIX B

Summary of Proposed NIOSH Nanotechnology Research Projects, 2018–2021 (some projects began prior to 2017)

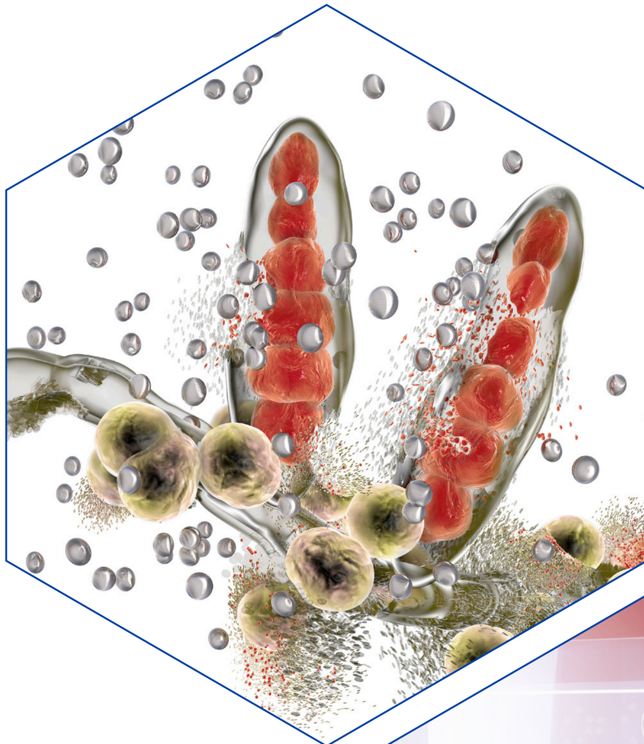
Critical Research Area	Projects
Toxicity and Internal Dose	• Continue evaluation of long-term fibrogenic and carcinogenic potential of carbon nanotubes and carbon nanofibers. • Continue evaluation of immune and cardiovascular responses to pulmonary exposure to CNT, TiO_2, and/or nanosilver. • Continue with identification of biomarkers of response to ENMs. • Develop predictive algorithms for relationships between nanoparticle properties and bioactivity. • Determine the relevance of in vitro and in vivo screening tests. • Evaluate the pulmonary and systemic effects of graphene and nanocellulose. • Evaluate the pulmonary effects of boron nitride nanotubes and metal oxides, including cerium oxide and copper oxide. • Evaluate the toxicity of nanoclay composites and copper-treated lumber dust.
Measurement Methods	• Utilize reference materials and technically sound protocols to improve measurement quality. • Develop techniques to characterize nanoparticles, using advanced microscopy methods. • Assist with round-robin evaluations of ENM reference materials.
Exposure Assessment	• Continue evaluation of workplace exposures to emerging, second-generation, and third-generation ENMs and their potential routes of exposure. • Continue evaluation of size, concentration, and morphology of ENMs emitted by various processes. • Evaluate exposure potential from silver nanoparticles in sprays. • Expand field team efforts into advanced manufacturing, including 3D printing.

(Continued)

Critical Research Area	Projects
Epidemiology and Surveillance	• Analyze biomarker samples from cross-sectional epidemiologic study of carbon nanotube and nanofiber workers. • Analyze data (medical and biomarker with exposure) from cross-sectional epidemiologic study of carbon nanotube and nanofiber workers. • Determine strategy for identifying the next nanomaterial for an epidemiologic study. • Assess feasibility of epidemiologic study of health outcomes among workers exposed to nanomaterials other than carbonaceous nanomaterials.
Risk Assessment	• Develop a comprehensive database of nanotoxicology studies, including dose-response data, physicochemical properties, and experimental factors. • Continue investigating nanomaterial hazard and risk, with consideration of physicochemical properties and biological mode of action. • Perform further comparative analyses of nanomaterials and benchmark materials, and develop hazard potency categories for a broad range of nanoscale and microscale particles. • Contribute to the development and evaluation of dosimetry models and methods to assess internal dose of nanomaterials in workers. • Conduct risk evaluations and contribute to the development of recommended exposure limits for specific nanomaterials or nanomaterial groups.
Engineering Controls and PPE	• Continue to assess engineering controls in the field and develop simplified unit process-based engineering control information sheets. • Continue to evaluate commercially available engineering controls in the lab, and publish test results. • Determine respirator performance against workplace ENMs under laboratory conditions. • Evaluate filtration performance of respirators against various nanoparticle types in the workplace. • Work with PPE manufacturers to provide a protective glove-gown interface that will protect workers when hands are submerged in dry and liquid nanomaterials.
Fire and Explosion Safety	• Continue evaluation of various ENMs for fire and explosion potential. • Evaluate a variety of ENMs for electromagnetic hazard potential. • Correlate dustiness of ENMs with various physical and chemical safety hazards.

(Continued)

Critical Research Area	Projects
Recommendations and Guidance	• Continue r2p activities, such as developing brochures and fact sheets and updating the topic page. Focus on products to educate the worker. • Evaluate market research to maintain and expand knowledge of existing and new materials. • Evaluate how the Globally Harmonized System has affected nanomaterial worker communication. • Continue to encourage and communicate regarding the importance of incorporating PtD into risk management practices. • Maintain and update existing guidance as necessary. • Expand guidance to include advanced manufacturing.
Applications and Informatics	• Further develop and refine end-of-service indicators using nanomaterials. • Evaluate ENM-enabled PPE. • Evaluate the use of nano sensors. • Continue to develop and publish nanoinformatics principles and practices.
Global Activities	• Participate in the US/EU nanomaterial working groups hosted by the NNI. • Lead or co-lead committees with globally recognized organizations: ISO, OECD, and UN (WHO, ILO).



Promoting productive workplaces through safety and health research

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