The National Nanotechnology Initiative

STRATEGY FOR NANOTECHNOLOGY-RELATED ENVIRONMENTAL, HEALTH, AND SAFETY RESEARCH

DRAFT of Jan. 31, 2008

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About this document

This document outlines the NNI strategy for nanotechnology-related environmental, health, and safety (EHS) research. It includes an analysis of the EHS research needs outlined in the previously published NNI document, *Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials* (September 2006) and a summary of the current NNI EHS research portfolio, divided into five primary research categories: (1) Instrumentation, Metrology, and Analytical Methods; (2) Nanomaterials and Human Health; (3) Nanomaterials and the Environment; (4) Human and Environmental Exposure Assessment; and (5) Risk Management Methods. The document also includes an analysis of the strengths, weaknesses, and gaps in the current NNI research portfolio, a recommended framework for addressing the identified research needs, as well as a recommended implementation and adaptive management process. Tables showing research projects funded in 2006 by the NNI agencies in each of the five EHS research categories are included as an appendix.

About the cover

Idealized representation of a scanning tunneling microscope image showing closed chains of C60 molecules, represented by the light-colored lines, around islands of silver on a flat, clean surface of silver. Cover design by Nicolle Rager Fuller, Sayo Arts, Washington, DC.

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National Nanotechnology Initiative

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

Deliberative Draft

31 January 2008

Subcommittee on Nanoscale Science, Engineering, and Technology
Committee on Technology
National Science and Technology Council

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Executive Summary

Nanotechnology encompasses a growing set of activities based on the ability to measure, see, and control matter at the scale of nanometers. Advances in nanotechnology – which depend on the distinct properties of nanoscale materials– are leading to applications in many sectors, including energy, health, and the environment. Due to their size, nanomaterials may also have effects on human health, safety, and the environment that are different than the effects of analogous macroscale or bulk materials. Thus the Federal effort in nanotechnology has included since its inception research and other activities to understand potential risks associated with the manufacture and use of engineered nanoscale materials.

The National Nanotechnology Initiative (NNI), which coordinates and manages nanotechnology research across the Federal government, has invested an estimated $XXX million between Fiscal Year 2006 and 2008 in environmental, health, and safety (EHS) research that is primarily aimed at understanding the risks posed by nanomaterials. Additional relevant research that is not primarily aimed at understanding risk totals another approximately $XXX million in the same period. This research and other NNI activities are coordinated by the Nanotechnology Environmental and Health Implications (NEHI) Working Group under the National Science and Technology Council's Nanoscale Science, Engineering, and Technology (NSET) Subcommittee.

The NEHI Working Group developed the strategy presented in this document to accelerate progress in nanotechnology EHS research, and to fill gaps in and—with the growing level of effort worldwide—avoid unnecessary duplication of such research. This document builds upon previous NEHI reports on EHS research needs and priorities for nanomaterials.

The strategy for addressing the identified research priorities is to strengthen and focus the growing NNI EHS research program through a robust and flexible interagency approach. This strategy builds on the successful aspects of the NNI to date. The approach is driven by the breadth of issues, from transport in the environment and effects on human health to managing risks and the overarching need to measure and characterize nanomaterials in various environments. Addressing such a range of issues requires participation by and coordination among the various NNI agencies.

This report specifies the roles of agencies as contributors to or users of the results of EHS research and identifies the agencies that will act as coordinators in the five previously identified research categories. Coordinating agencies will [insert definition here]. The coordinating agencies for each category are:

- Instrumentation, Metrology, and Analytical Methods—National Institute for Standards and Technology (NIST)
- Nanomaterials and Human Health—National Institutes of Health (NIH)
- Nanomaterials and the Environment—Environmental Protection Agency (EPA)
- Health and Environmental Exposure Assessment—National Institute of Occupational Safety and Health (NIOSH)
- Risk Management Methods—Food and Drug Administration (FDA) and EPA

In order to guide the EHS research program, the NEHI Working Group performed a gap analysis in each research category by comparing existing research vs. the previously identified priorities. The existing portfolio of research is based in large part on detailed data collected for Fiscal Year 2006, which is included as an appendix to this report. Although research categories were not prioritized with respect to each other, there is consensus among members of the NEHI Working Group that instrumentation, metrology, and analytical methods research is cross-cutting, supporting research in every other category, and therefore is generally a high priority. In addition to identifying areas of weakness and gaps, the working group developed timelines and sequencing for key research activities, where appropriate, in order to gain the greatest and most immediate benefit for nanotechnology development broadly and risk management in particular. Recommended sequencing is based on immediacy of needs and whether additional research capacity or prerequisite research is required before a particular research area can be initiated.

To implement the strategy, the NEHI Working Group and NNI agencies individually and jointly will:

- Support a broad base of research that facilitates risk-based decision making and development of nanotechnology-based applications for improving the environment and health.
- Coordinate agency efforts to address priority research needs, with a focus on weaknesses and gaps, identifying opportunities for collaboration and joint development and use of resources, where appropriate.
- Hold workshops to assess progress and evolving needs in each of the five research categories
- Facilitate partnerships with industry.
- Coordinate and support efforts internationally, particularly at the Organisation for Economic Cooperation and Development (OECD) and the International Organization for Standardization (ISO).
- Support development of consensus-based documentary standards.
- Facilitate wide dissemination of research results and other non-proprietary EHS information.

The strategy presented here is based on the state of science today; however, the field of nanotechnology is extremely dynamic. As nanotechnology EHS research and knowledge continue to grow, needs and priorities will evolve. Accordingly, this plan will be reviewed and updated in the future.

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I. Introduction and Background

Environmental Health and Safety Research and the National Nanotechnology Initiative

Nanotechnology encompasses a growing set of activities based on the ability to measure, see, and control matter at the scale of nanometers. Nanoscale circuitry is already in cell phones and other electronic products on the market today. Many applications that are envisioned will take advantage of the fact that at the nanoscale materials have different chemical and physical properties than at larger scales. Also, there is potential for nanosized particles to be transported through cell walls and other biological barriers in ways that are different from their macroscale counterparts. These properties can be used to make better batteries, to deliver drugs where they are needed, and to clean contaminated soil and groundwater.

The National Nanotechnology Initiative (NNI) is the Federal government's multi-agency, multi-disciplinary nanotechnology research and development (R&D) program. Established in Fiscal Year 2001, the NNI serves as a locus for communication, cooperation, and collaboration among the participating Federal agencies, and provides a framework of shared goals, priorities, and strategies. The goals of the NNI are to advance a world-class R&D program; to foster transfer of new technologies into products for commercial and public benefit; to develop and sustain infrastructure, including educational and workforce preparation resources; and to support responsible development of nanotechnology.

Responsible development of nanotechnology includes supporting research and other activities to understand potential risks associated with the manufacture and use of engineered nanoscale materials. The NNI has invested in an expanding portfolio of environmental, health, and safety (EHS) research since its inception. Research is focused in particular on understanding general mechanisms of biological interaction with nanomaterials and on developing broadly useful tools and tests for characterizing and measuring nanomaterials in various environments, including in the body. The relevance of research is in understanding the effects of and mitigating the implications of engineered, incidental, and natural nanomaterials; supporting sustainable development; removing contaminants from soil and water; and preparing for the new generation of nanoproducts. This report is focused on the research to support risk assessment and risk management of engineered nanoscale materials. Development of specific EHS research programs—by NNI agencies singly or jointly—is informed by the research and information needs of agencies with regulatory and oversight responsibilities (Figure 1). Input about the needs of regulatory decision-makers expedites the development of information to support both risk assessment and risk management of nanomaterials. This approach is particularly important due to the multi-agency nature of the NNI EHS research effort.

Understanding the potential risks of nanomaterials to human health and the environment involves research on a number of processes, which are shown schematically in Figure 2. Not every process will be equally important for every situation in which a nanomaterial enters the environment. For example, the processes that affect a nanomaterial that is in a cosmetic will be different from those that affect a nanomaterial that is used in an industrial process, such as polishing, or incorporated into a bicycle frame. This framework is helpful for organizing the variety of research needed to support risk assessment and risk management decisions.

As shown in Figure 2, EHS research must take into consideration the life cycle stage of the nanomaterial—e.g. manufacture, incorporation into an integrated product, consumer use, and recycling or disposal. Nanomaterials released into the environment undergo various forms of transport and transformation, and may cause abiotic effects, such as modification of atmospheric, soil, or water chemistry. The concentration of nanomaterial in the environment depends on factors such as the nature and amount of material released, physical and chemical conditions, and time. Once dispersed, biological or environmental systems may be exposed to the nanomaterial. Once dispersed, exposure of biological or environmental systems to the nanomaterial is possible. Such contact may or may not lead to uptake by the system, resulting in an internal dose that may, in turn, cause a biological response and/or an ecological effect. Collective exposure of individuals leads to effects at the population, community, or ecosystem level. Biological and ecological effects may in turn lead to abiotic effects or may impact further transformation or transport of nanomaterials that are still in the environment or that are newly released.

Research on human health effects of nanomaterials follows a similar framework but has several additional considerations. Exposure to nanomaterials may occur unintentionally in the environment, as described above, or through intentional applications, such as cosmetics, therapeutics or tissue implants, or potentially through ingestion of food. Once in the body, *in vivo* transport and transformation would also be assessed, and biological response would be evaluated in terms of external dose, uptake by route of exposure, and internal dose

Research programs that will help to understand many of the processes outlined above have been established at multiple agencies, based on expertise, information needs, respective missions and priorities, and merit of proposed research. Where appropriate, joint programs among agencies with mutual interests are in place to leverage investments. Moreover, activities other than research are on-going that help to address issues related to EHS of nanomaterials. Examples include development of the cross-agency Food and Drug Administration (FDA) Nanotechnology Task Force report, development of the Environmental Protection Agency (EPA) white paper outlining agency-specific research needs and priorities, and organization of various public meetings, peer review panels, and workshops. Although not included in the research portfolio, these efforts are essential to furthering nanotechnology EHS and are key elements in the overall Federal program.

The Federal government is not the only stakeholder with an interest and a role in research related to understanding potential EHS risks associated with nanomaterials. Businesses that manufacture or use nanomaterials have responsibilities for product and worker safety. Other nations are beginning to invest in this area of research, although the United States appears to have a substantially larger investment to date. NNI research needs to be coordinated with these outside efforts to maximize its value to Federal agencies and to those other entities with needs for the information and knowledge.

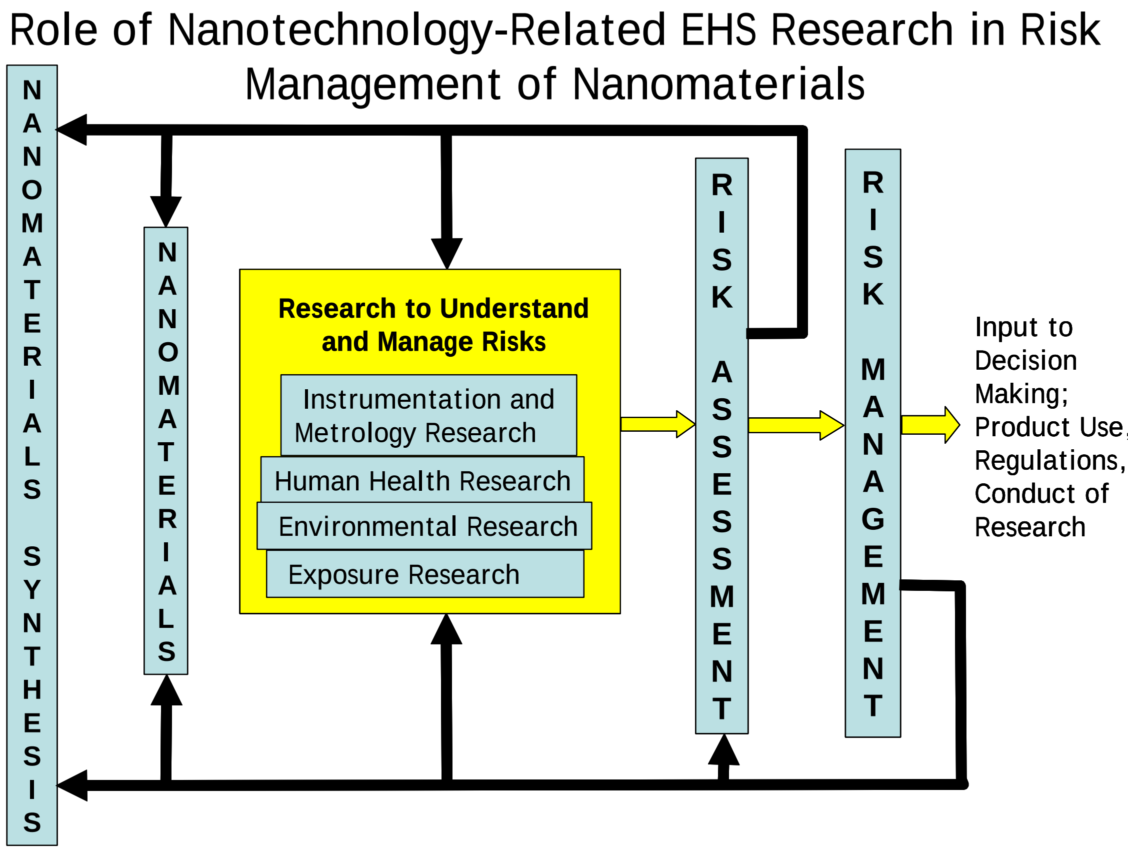

Figure 1. Role of nanotechnology-related EHS research in risk management of nanomaterials

Interagency coordination among the NNI agencies occurs within the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the National Science and Technology Council's Committee on Technology. Under the NSET Subcommittee, the Nanotechnology Environmental and Health Implications (NEHI) Working Group coordinates activities related to understanding potential risks of nanotechnology. The interagency activities are supported by the full-time staff of the National Nanotechnology Coordination Office.

This document has been developed by the NEHI Working Group to accelerate progress in nanotechnology EHS research, avoid gaps and—with the growing level of effort—avoid unnecessary duplication. Section III provides a framework for addressing the research needed to support risk assessment and risk management of nanomaterials. Section IV provides a plan for implementation and for managing the Federal research program given the rapidly evolving state of knowledge. Agencies whose missions support nanomaterial research may use this strategy to better understand where their activities fit into the overall strategy. Moreover, agencies can identify opportunities for collaboration and cooperation, and manage their relationships with other agencies and their research.

Process for Developing a Research Strategy

1. Identify priority needs.

The research strategy described in this document builds upon two earlier NNI reports that identify and prioritize EHS research needs. *Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials*[1], released in

[1] (http://www.nano.gov/NNI_EHS_research_needs.pdf)

2006 and hereafter referred to as the EHS Research Needs document, outlined the research and information needed to support scientifically sound risk assessment and risk management decision making. The needs were identified with input from the Federal agencies with responsibility for oversight of the research, development, manufacture, import, sale, or use of nanomaterials and the products and processes in which they are used. The needs were also informed by input from non-Federal experts on risk assessment issues and by relevant publications on the topic and are grouped in five categories. In August 2007, an interim document[2] that updated and prioritized the top five research needs in each category was released for public comment. The prioritized needs are shown in Table 1.

Table 1. Priority Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials

Research Needs
Instrumentation, Metrology, and Analytical Methods
1. Develop methods to detect nanomaterials in biological matrices, the environment, and the workplace
2. Understand how chemical and physical modifications affect the properties of nanomaterials
3. Develop methods for standardizing assessment of particle size, size distribution, shape, structure, and surface area
4. Develop certified reference materials for chemical and physical characterization of nanomaterials
5. Develop methods to characterize a nanomaterial's spatio-chemical composition, purity, and heterogeneity
Nanomaterials and Human Health
Overarching Research Priority: Understand generalizable characteristics of nanomaterials in relation to toxicity in biological systems.
Broad Research Needs:
• 1. Understand the absorption and transport of nanomaterials throughout the human body
2. Develop methods to quantify and characterize exposure to nanomaterials and characterize nanomaterials in biological matrices
3. Identify or develop appropriate *in vitro* and *in vivo* assays/models to predict *in vivo* human responses to nanomaterials exposure
4. Understand the relationship between the properties of nanomaterials and uptake via the respiratory or digestive tracts or through the eyes or skin, and assess body burden
5. Determine the mechanisms of interaction between nanomaterials and the body at the molecular, cellular, and tissular levels
Nanomaterials and the Environment
1. Understand the effects of engineered nanomaterials in individuals of a species and the applicability of testing schemes to measure effects
2. Understand environmental exposures through identification of principle sources of exposure and exposure routes
3. Evaluate abiotic and ecosystem-wide effects
4. Determine factors affecting the environmental transport of nanomaterials
5. Understand the transformation of nanomaterials under different environmental conditions
Health and Environmental Exposure Assessment
1. Characterize exposures among workers
2. Identify population groups and environments exposed to engineered nanoscale materials
3. Characterize exposure to the general population from industrial processes and industrial and consumer products containing nanomaterials
4. Characterize health of exposed populations and environments
5. Understand workplace processes and factors that determine exposure to nanomaterials
Risk Management Methods
1. Understand and develop best workplace practices, processes, and environmental exposure controls
2. Examine product or material life cycle to inform risk reduction decisions
3. Develop risk characterization information to determine and classify nanomaterials based on physical or chemical properties
4. Develop nanomaterial-use and safety-incident trend information to help focus risk management efforts
5. Develop specific risk communication approaches and materials

[2] http://www.nano.gov/Prioritization_EHS_Research_Needs_Engineered_Nanoscale_Materials.pdf

2. Assess existing research.

In addition to developing a prioritized set of research needs, the NEHI Working Group worked with the Office of Management and Budget (OMB) to collect a "snapshot" of detailed information on research already underway. These data were used to help identify gaps or weaknesses that a research strategy should address.

The agencies reported information for research funded in Fiscal Year 2006 related to the needs listed in the 2006 EHS Research Needs document. The project level information is tabulated in Appendix A and is available online in a searchable format at [insert URL]. Summary and analysis of the research funded in 2006 is in Section II of this report.

It is important to note the difference between the scope of the research included in the data report here for 2006 and that reported as "EHS research" in the NNI budget supplement to the President's Budget for Fiscal Year 2008 . The annual NNI supplement to the President's Budget reports funding for research that is "primarily aimed at understanding risks posed by nanomaterials." Data in this report also include research that is aligned with the research priorities but that is not primarily aimed at understanding risk. The additional research captured by this approach is predominantly of two types: (1) instrumentation and metrology research that enables characterization and measurements vital to development and risk assessment of nanomaterials, and (2) portions of medical application-oriented research that assesses possible toxicity of nanomaterials being considered for use in the body.

The NEHI Working Group established five task force groups, one for each research category, comprising EHS experts from relevant agencies. The task forces reviewed the 2006 data carefully for quality and to ensure that projects were properly categorized.

3. Analyze strengths and weaknesses.

Once the project categorization was final, the task forces analyzed the portfolio of projects in each category to determine the balance of effort among the priority research areas and to identify strengths, weaknesses—i.e., areas that need greater emphasis—and gaps vs. the research category as a whole. In addition to tabulating the number of projects and total funding in each area, the task forces considered the breadth of research, such as variety of nanomaterials or routes of exposure being investigated. The task forces also considered whether the materials being researched are those entering or likely to be used in greatest volume and whether the types of exposures being investigated are relevant to real-world situations. They also analyzed the timing for increased emphasis on particular needs. Delaying greater investment in certain areas is recommended where the research depends on results from, or progress in, other areas, or the need to develop capacity for a specific type of research.

* * *

This document has been developed by the NEHI Working Group in order to accelerate progress in nanomaterials EHS research, to avoid gaps and –with the growing level of effort—to avoid unnecessary duplication. Section II provides a summary and analysis of the existing research portfolio, based largely on detailed information for 2006. Section III describes the framework and strategy for addressing the weaknesses and gaps going forward.

The success of this strategy depends on the collective efforts of the NNI agencies through their individual and joint activities coordinated by the NEHI Working Group and the NSET Subcommittee. Progress will also depend on the availability of resources. The approach that is outlined here is a next step in the ongoing coordination of the NNI EHS research program. With the rapid development of technology and information related to health and environmental exposure and effects, the NEHI Working Group will update the strategy to keep the NNI focused on top priorities and to ensure sound management into the future.

II. Summary of NNI EHS Research: Portfolio Review and Gap Analysis

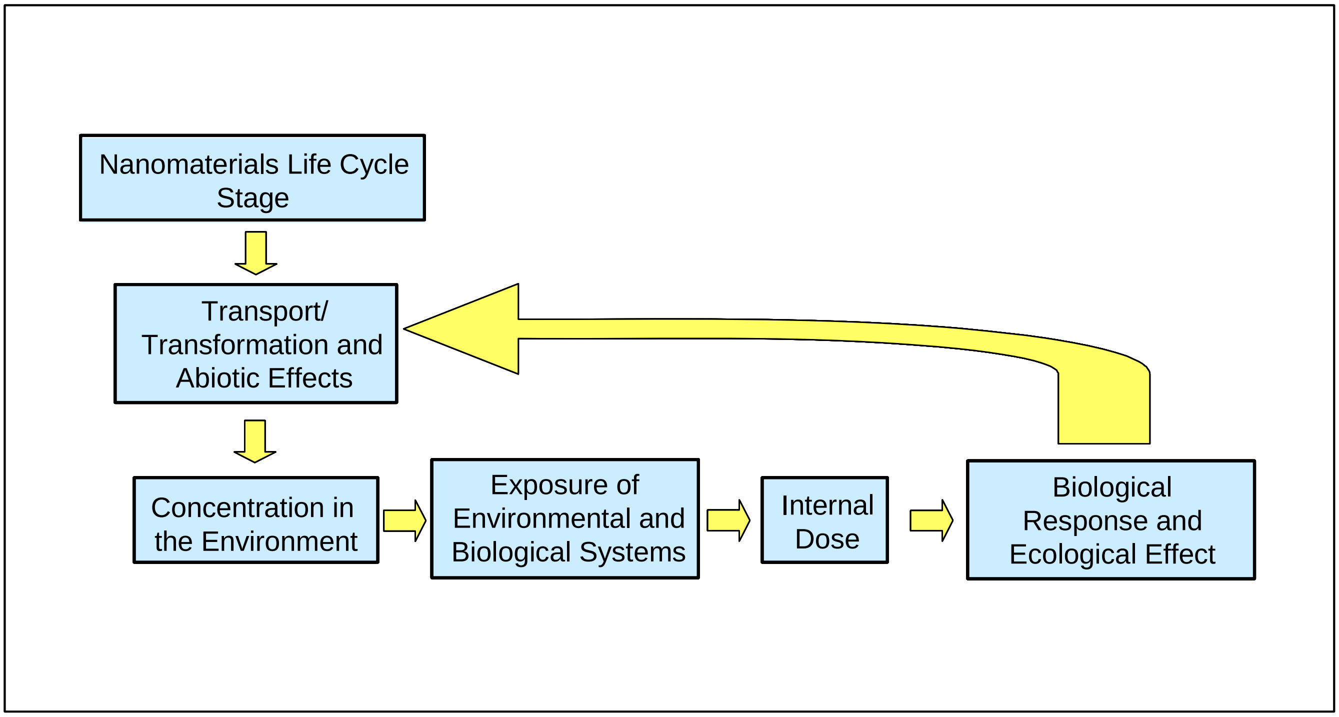

Figure 2. Framework for research related to risk assessment of nanomaterials

A key step in the process for developing the NNI research strategy for nanotechnology-related EHS research is collecting and assessing data on the NNI agencies' current research activities. As described earlier, the Office of Management and Budget (OMB) asked agencies to provide lists of EHS-related projects that were funded or active in 2006 in each of the five research categories outlined in Table 1. The resulting list of projects (both intramural and extramural) is shown in the appendix to this report. This section includes a summary of the data that was reported in response to the OMB data call, analysis of that data (i.e., the types of projects that were reported and the relative levels of investment among the various research priorities), and concludes with a discussion of the strengths, weaknesses, and gaps in the current research portfolio. This in turn informs the strategy for future NNI EHS research that is outlined in later sections of this document.

The section begins with a brief description of the OMB data call and how the resulting data were categorized and analyzed by the NEHI Working Group. It is important to understand that the data gathered for 2006 represent a one-time-only "snapshot" of the NNI agencies' EHS research portfolios in one year. However, these are likely to be indicative of the overall trends in agency investments in more recent years. This is followed by a description of the process for performing analysis of the data, and for identifying the strengths and weaknesses of the current NNI research portfolio as well as any gaps between that portfolio and the NNI EHS research priorities. This analysis of strengths, weaknesses, and gaps will inform agency decisions about the magnitude and balance of future EHS research investments.

The body of this section provides an in-depth analysis of the current research being conducted in each of the five NNI EHS research categories. For each of the categories, a table is included showing the total estimated funding and number of projects, broken down by the prioritized research needs for that category. The table is followed by an overview of the types of projects included in that research category, then by a summary analysis of the projects reported for each research need under that category, including a discussion of strengths, weaknesses, and gaps. Each research category subsection concludes with figures showing:

(a) a graphical representation of the relative emphasis of research as a function of time for each of the priority research needs for the respective category. The timeframes are indicated in terms of near term (1-5 years), medium term (5-10 years), and longer term (more than ten years)

(b) a framework diagram showing how the research in the respective category fits into the overall NNI EHS research strategy outlined in Figure 1, as well as how the different research needs within each respective category relate to each other logically and how the outputs from addressing the research needs will inform the strategy for each respective category of EHS research.

Data for fiscal year 2006 research

Data to support evaluation of current research in EHS priority areas and comparison with previously specified research needs to identify areas of weakness or gaps was supported by a data call issued by the Office of Management and Budget (OMB) for detail regarding funded research for fiscal year 2006 in the EHS-research area (Appendix A). These data enabled an assessment of a snapshot of the Federal research investment in one year in an approach that compared the relative balance of funding across the data needs with respect to the priority of those needs. Priority in this case was considered both in terms of the kind of information developed (some information is of greater relevance to supporting risk management than other) and the appropriate sequencing of research (some research should be timed to occur following other research in order to gain the greatest benefit to risk management needs). Projects relevant to more than one category or need were assigned to the need that was primarily being addressed by the research. In a small number of cases, it was not possible to identify a single primary need and these were categorized as addressing "multiple" needs. In some cases, projects were related to the overarching research category, but did not align with any of the top five priority areas. These projects were categorized as addressing "other" needs.

When analyzing these data and using them for the purposes of a gap analysis with respect to the overarching research needs, the following limitations must be considered.

- The data represent only research funded in 2006. Many projects are multi-year and therefore actual research associated with projects listed may have taken place in earlier or later years. However, projects begun after 2006 are not captured.
- Projects listed are prospective, that is they are planned research not research results. Basic research projects may diverge from the original proposal, based on initial results or as other information becomes available.
- The list represents only Federally funded research. It does not include any research in these areas that is supported by industry, nonprofit organizations, or other countries.

Description of process for performing analysis of gaps between the NNI EHS research priorities and EHS research currently funded by NNI agencies

The gap and priority "balance assessment" using the snapshot of 2006 Federal funding began via a series of inter-agency meetings and discussions by nanotechnology EHS experts across Federal Government agencies. The group of experts representing the NEHI agencies considered available information within the 2006 data call as assigned by funding agencies for a given research category in the September 2007 NNI EHS Research Needs document, and took into account overlaps of individual projects across different research categories and priority needs. The experts also reassigned projects between categories and priority needs in some cases. As such, research funded by the NNI agencies was to a degree validated by the experts according to their application to the NNI EHS research categories and priority research needs. In addition, the overall application of each project with respect to the development of information that enables both protection and beneficial applications of nanotechnology for human and environmental health was considered throughout the review process.

The ability of research to provide results to address current EHS risk management support needs as captured by the prioritized research needs within each category was also considered. When such activities were deemed absent, particularly when activities were absent for entire research needs, "gaps" with respect to desired balance of funding for future funding cycles were noted. In some cases projects were reported for a research need but did not rise to the level of sufficient, either in terms of the amount of funding or the coverage of the funding. These were not necessarily considered as gaps but rather as areas that need greater emphasis in future funding cycles. Summaries of the FY2006 project data for each of the research categories are provided in the next section.

It is important to note that EHS-research planning and project implementation have been taking place simultaneously for several years. The NNI agencies have been funding basic research and technology development and through these activities have been producing information critical to this field. Moreover, the overall analysis of the data call indicates that many of the research areas are already receiving considerable support and that ongoing research is strongly aligned with the priority research needs, needs that were identified prior to the OMB data call. It is also important to note agencies have expended EHS resources through avenues other than research, for example workshops, task forces, white papers, peer reviews, and public meetings. While these more applied efforts are generally not portrayed as research, they are nonetheless essential to furthering nanotechnology EHS and are key elements in the overall Federal EHS portfolio.

Analysis of EHS research by categories In EHS research needs document

Research Category: Instrumentation, Metrology, and Analytical Methods

Total estimated funding in 2006: $26.6 M

Total projects: 78

Agencies supporting research in this category: NIH, NIST, NSF, DOE, NIOSH

Prioritized Research Needs[1]	FY06 funding Estimate $K (% of total)	Number of Projects (% of total)
1. Develop methods to detect nanomaterials in biological matrices, the environment, and the workplace	12396 (47 %)	36 (46 %)
2. Understand how chemical and physical modifications affect the properties of nanomaterials	2845 (11 %)	14 (18 %)
3. Develop methods for standardizing assessment of particle size, size distribution, shape, structure, and surface area	2012 (8 %)	4 (5 %)
4. Develop certified reference materials for chemical and physical characterization of nanomaterials	4319 (16 %)	6 (8 %)
5. Develop methods to characterize a nanomaterial's spatio-chemical composition, purity, and heterogeneity	3650 (14 %)	15 (19 %)
Multiple: Projects that capture multiple needs	1300 (5 %)	2 (3 %)

Other: Not captured in needs above, but with benefit to the research category	50 (0.2 %)	1 (1 %)

Background

The research needs in this research category represent the highest priority research that is essential to understanding, predicting, and quantifying the chemical and physical properties and behavior of nanomaterials. The priorities underpin, and are fundamental to, all five categories of EHS research and information needs. Much of the research also is important for development of nanomaterials for beneficial applications.

Seventy-eight projects were found to be responsive to the research priorities. The majority of the effort focused on priority 1 (to detect nanomaterials in biological matrices, the environment, and the workplace); priority 2 (to understand how chemical and physical modifications affect the properties of nanomaterials); and priority 5 (to characterize a nanomaterial's spatio-chemical composition, purity, and heterogeneity). Work is limited but underway for addressing priority 3, determination of particle size, size distribution, shape, structure, and surface area, with 4 projects. Work on priority 4 to develop reference materials is reported, and is part of work listed in other categories as well. Only one project in this category fell outside the five priority research needs, indicating that even before they were set, agencies have been focusing on top priorities.

As there is a low number of projects for determination of particle size, particularly in complex media such as biological and environmental (air, water), efforts could be stronger in this area. The ability to accurately measure particle size is critical to evaluating potential environmental and human health risks with respect to ambient particulate matter as the role of particle size in such assessments is one that is increasingly realized as important. In addition, the detection of nanomaterials in solid media, such as soil, is not well addressed. This inhibits the ability to monitor and track nanomaterials in the environment or solid waste streams. Work is also apparently sparse for the development of samplers and instruments for monitoring the environment and the workplace, however, environmental and workplace nanomaterial sampling efforts are appropriately reported in the Environmental and Human Health research categories.

A fundamental requirement for assessing the potential impacts of new nanomaterials on both human health and the environment is the ability to make precise, accurate measurements at the nanoscale in multiple, complex mediums. Moreover, unique measurement technology challenges must be met, such as investigating how nanomaterials interact with different environments and effects that may occur at various points of the nano-enabled products' lifecycles including those that may be due to transformations. As such, research to support Instrumentation, Metrology, and Analytical Methods covers all aspects of the human health and environmental framework and is overarching to the other four research categories. In particular, the development of methods to detect nanomaterials in biological matrices, the environment, and the workplace is necessary across the entire framework from the synthesis and use of nanomaterials to the detection and characterization of materials as a function of exposure. Similarly, the development of methods for determining the sizes, shapes, structure, and surface area are essential to assess such metrics from the beginning phases of material production through the characterization of a material that leads to a dose effect.

In addition, the characterizations of materials at various stages of development often do not provide measurements that are reproducible or consistent across disciplines and applications, including assessments of biological response. As such, reference material development plays a key role in these areas by providing a standardized, acceptable approach to study, monitor and potentially track nanomaterials as they are released into the environment or the workplace, and to assess their potential interactions with human and ecological systems. Methods for the determination of the spatial composition, purity, and heterogeneity also play a pivotal role for these areas as single defects or slight changes to surface dimensions or composition can dramatically influence the nanomaterial lifecycle and the biological or environmental effects that may result at any given point. Similarly, methods to support understanding how chemical and physical modifications affect the properties of nanomaterials are critical for assessing nanomaterials beyond external contact as modifications may affect the ability of a material to migrate into or travel within both human and environmental contexts.

Summary of Analysis by Research Need

Research Need #1: Develop methods to detect nanomaterials in biological matrices, the environment, and the workplace

Analytical methods for identifying and measuring the critical parameters related to nanomaterials in biological systems, the environment, and the workplace are not well-developed or readily available. As a result, these important metrics are infrequently or inaccurately reported. Further development of these methods is critical to nanotechnology EHS research.

Thirty-six projects are identified for this priority for which detection and characterization methods, including dimensional and surface metrology efforts, are noted. All of the projects support the four other research categories. Several projects are focused on the development of enhanced microscopic techniques relevant to biological imaging and fluorescence of individual molecules, development of potent magnetic resonance imaging (MRI) contrast agents and probes vital to achieving cellular and molecular imaging with MRI for improved detection capabilities including a safe and sensitive imaging probe for in-vivo molecular imaging, and the synthesis of new ceramic nanoprobes for bio-imaging that are highly fluorescent, bio-compatible and non-toxic. Quantum optical measurement approaches are under development. Issues determining the complete cycle of nanoparticles within biosystems and capabilities to predict how readily nanoparticles may enter tissues and cross membranes are also under investigation, including characterizations of particle dimensions in two- and three-dimensions to obtain structural information on nanoparticle shape and size using image enhancing simulations. This latter work overlaps with the Research Need #5 in this category.

Several projects have specific nanotechnology application foci with an emphasis on the characterization of nanomaterials in tissues, cells, or subcellular levels. Such studies can provide insight into mechanisms of nanoparticle transport in tissue. Enhanced capabilities for detection of nanomaterials may result from some of these application studies as well, for example the development of biological or chemical sensors and in/ex-vivo biomedical diagnostics and therapies may result. To realize such applications it is important to note fundamental properties do not necessarily scale from macro to nano regimes. Therefore, progress toward applications requires developing new quantitative nanoscale metrologies and databases of properties to support these and further investigations (structural, chemical, electronic, optical, transport). The use of nanomaterials for multi-functional sensors and characterization of nanocomposite thin-films for device applications is one area of work that supports this notion, as well as work to enable rapid, accurate imaging of thermal and mechanical properties nanometer length scales to understand and control the thermal and mechanical behavior of materials at the nanoscale. This latter activity targets photoacoustic and photothermal measurement capabilities for the noncontact and nondestructive imaging of surface properties and subsurface defects at the nanoscale, a critical area for detection of nanomaterials.

Development of detection capabilities that can be applied to cellular biophysics, biosensing, nanoscale devices, and translational applications in medicine and environmental sciences is underway. Nanoparticle research on enabling computational and characterization tools with a focus on materials, devices, and the environment also supports such efforts. Innovations in these areas will likely benefit research applications beyond those described and may apply to many aspects of detecting and characterizing nanomaterials in biological and environmental media and possibly the workplace environment.

Research Need #2: Understand how chemical and physical modifications affect the properties of nanomaterials

In the development of products, nanomaterials may undergo any number of modifications including coatings to reduce oxidation, addition of molecular groups to induce or diminish biological activity, or functionalization to enable integration of materials into final products. Research in this area provides information on such changes or modifications to nanomaterials may affect their behavior including their degradation and their uptake by biological materials. Modifications may also affect the chemical and physical properties of nanomaterials and the methods necessary to detect the nanomaterials in human and environmental media.

There are fourteen projects within this priority research need. In particular, interactions at the single-molecule level are under study. Such investigations lead to understanding interactions with complex systems such as molecular aggregates, proteins in biological membranes, or semiconductor nanostructures. The ability to detect a single molecule in a complex environment with a spatial resolution in the order of 10-20 nm may be realized. This work largely overlaps with Research Need #1. Research toward understanding and controlling the chemical properties of reactive metal nanoparticles is also underway; this includes characterization of their surface and bulk composition. Such research on shells or coatings plays a major role in determining reaction pathways. It is noted that relationships of such pathways to toxicity and environmental health are lacking and are essential to understand how chemical and physical modifications affect the properties of nanomaterials.

Quantitative investigations of the effects of size, surface composition, proximity, and dopants on semiconductor nanoparticle properties are underway. Such work provides insight into methods of particle synthesis that allow control over these parameters. The use of synchrotron radiation-based characterization methods that provide element-specific atomic and electronic structure information enhances this effort by refining our understanding of quantum dot structure/property relationships. In addition, other work focused on the diffraction of glasses, liquids, and nanoclusters is providing data on the structure of nanophase clusters in zeolites in distinct environments to correlate molecular structure with electronic structure of caged semiconductors. Such information provides insight into how modifications, such as changing their environment, affect the properties of nanomaterials; a main concern for this research priority.

New methods and instrumentation for the study of magnetic materials and nanostructures using soft X-ray spectroscopies enables the study of engineering materials for applications as sensors, actuators and spintronic devices. A theoretical component of this provides support for applying spectroscopies to the problems of complex materials, including understanding chemical and physical modifications. Theory and prediction studies on the chemical properties of nanostructures are also underway. Additional work on magnetic properties includes the use of spin-polarized positron beams for the measurement process. Electron energy loss spectroscopy to determine the physical and mechanical properties of nanoscale materials provides data on mechanical properties, such as bulk, shear and elastic properties. It is very difficult to obtain such property data for nanomaterials by other techniques. Nano-porous alumina tubes have gained significant interest in drug delivery and gas separation technologies. As such, their use as membranes for hemodialysis is under investigation which includes characterization efforts on porosity and pore size distribution, chemical and thermal degradation, and mechanical properties.

Three projects provide application foci. One provides insight into the processes occurring on or near ZVI surfaces. Techniques designed to probe the surface, such as potentiometry, surface enhanced Raman spectroscopy and electrochemical quartz microbalance methods are under investigation. This work strongly overlaps with the Nanomaterials and Environment Category. The other two projects with focuses on applications overlap with Nanomaterials and Human Health. One is focused on bladder tissue engineering through nanotechnology, and the other makes use of nanotechnology to develop the basic science of nanoparticle thin films which could lead to the novel nanotechnology based sensors for biomaterials with an affinity for gold (i.e homocysteine, cysteine) and other functionalized surfaces. Characterizations of the nanomaterials, which are modified and engineered for specific applications, in all of these projects support this research need.

Research Need #3: Develop methods for standardizing assessment of particle size, size distribution, shape, structure, and surface area

This need seeks to provide rapid, statistically valid, standardized methods for measuring particle size, size distribution, shape, structure, and surface area of nanomaterials. Four projects support this research need.

One project includes nanoparticle and nanomaterial metrology research. Nanoparticle projects are focused on the determination of particle size and particle size distributions with additional efforts focused on the determination of shape, structure, and surface area using various techniques. A second project consists of an instrument development project. Specifically, the development of a laser-based instrument to measure both particle size and electrostatic charge distributions in real time and on a single particle basis for particles in the size range 10 to 1000 nm is underway. This instrument will support many aspects of the other research categories. A third project provides research to enable development of a comprehensive yet practical method for sampling, quantification, and characterization of carbon nanotube (CNT) particles in air. This method will be capable of classifying sampled particles into categories of carbon nanotubes and measuring for each type the number concentrations, size distributions, and the shape characters (diameter, length, aspect ratio and curvature). The fourth project for this research priority is an investigation of size-exclusion-based separation techniques. While the study is focused on an application, it may provide information to support the development of non-conventional particle size analyzers.

As there are a low number of projects for this research need, it appears efforts could be stronger in this area. However, the fundamental work reported is essential to furthering our ability to accurately measure nanoparticle size, size distribution, shape, structure, and surface area. Beneficial enhancements that could augment these efforts include the development of automated microscopic methods for the screening of a large number of nanomaterials, investigations on the correlations of microscopic methods with other methods, such as techniques based on light scattering, and the improvement of size methods for the reproducible determination of particle sizes < 5 nm. Critical biological (and possibly environmental) processes occur in this size range and the ability to measure particles at this scale is necessary for accurately assessing nanomaterial EHS aspects. It is noted one project in the Health and Environmental Exposure Assessment category provides funding for research to identify and evaluate methods to measure airborne nanoparticle concentrations and the development of methods to characterize nanoparticles using a complementary suite of techniques to assess their surface and bulk physical and chemical properties. Two projects in the Nanomaterials and Human Health category also have components supporting the development of methods that meet metrology priority research need #3.

Research Need #4: Develop certified reference materials for chemical and physical characterization of nanomaterials

This research need seeks the development of reference materials for the chemical and physical characterizations of nanomaterials. Reference materials are beneficial for calibration of instruments or analytical processes used to assess the chemical or physical properties of nanomaterials. They are also needed to assess the quality or comparability of results from tests or assays designed to determine the toxicity of health-benefit or drug-related materials. Six projects support this research need

Specific materials under development include carbon nanotubes, nanoparticles that are non-carbon based such as metal oxides, nanostructured powders, fibers, and engineered tissue substitutes. The latter could be useful for the next generation of natural-matrix frozen tissue materials designed to mimic nanomaterials used for bioengineering and tissue engineering studies such as polymer hydrogels or materials with nanoparticles embedded within the matrix for functional, stability or antioxidant capabilities.

While efforts in this area are limited to six projects, the reported work supports a fundamental start for the development of nanoscale reference materials. Efforts could be stronger for the development of materials that are tailored specifically for toxicology and environmental studies as these are currently lacking.

Research Need #5: Develop methods to characterize a nanomaterial's spatio-chemical composition, purity, and heterogeneity

At the nanoscale single defects and slight changes to surface dimension and composition can dramatically influence reactivity. Hence, proper characterization of spatial composition is critical. This research need seeks methods to characterize a nanomaterial's spatial composition, the identification of possible defects or impurities, and batch-to-batch variation in nanomaterial production or biological activity. Fifteen projects support this research need.

Projects provide information on the chemical, energetic, crystallographic, and structural composition of nanomaterials and 3D imaging is evident. Chemical projects range from characterizing reactions at solid/gas and solid/liquid interfaces to probing details of heterogeneous chemical reactions and of chromatographic processes. Atomic-scale 3D chemical imaging of interfaces in nanostructures uses a combination of electron tomography, energy-filtered transmission electron microscopy and aberration correction. Aberration correction may improve the resolution in energy-filtered imaging to the atomic level. Currently such imaging is limited to ~1nm for many applications. This combination improves resolution, sensitivity and validity of data interpretation beyond what is available.

The study of energy interactions with surfaces provides a basis for modifying, patterning and analyzing surfaces/nanoscale materials. Mass based analysis of materials with nm scale lengths may be realized. Studies focused on property sensitive nanoscale structure and defects are underway where quantitative electron microscopy techniques, such as coherent diffraction, atomic imaging, column-by-column spectroscopy, and phase retrieval methods, including electron holography, are a focus in combination with simulations and theoretical modeling.

The development of a wide range of microscopic and spectroscopic techniques is noted and are applicable to a broad range of nanomaterials. These likely can be implemented in many existing research facilities. In addition, two application projects support this research need. One uses a powder X-ray diffractometer for environmental, materials science, and chemical research. Topical areas overlap with the Nanomaterials and Environment category, for example chemistry and mobility of contaminants. The second application project employs extreme UV in a variety of applications to efforts such as high-resolution imaging, spectroscopy, elemental- and bio-microscopy, and nano-fabrication.

Projects in this Research Need overlap with Research Need #1, the development of methods to detect nanomaterials in biological, environmental, and the workplace. Efforts on imaging of nanomaterials in biological media with an emphasis on the co-determination of a material's spatio-chemical composition, purity, and heterogeneity could be stronger. Such work would greatly assist nano-EHS studies as the determination of these metrics are essential to understanding toxicological effects of nanomaterials.

Projects Classified as "Multiple" or "Other": Two projects are placed in the "multiple" category as it appears that multiple priority needs are being met via activities on characterization of nanomaterials and the development of tools, techniques, and web and computational infrastructure development. One additional project is placed in the "other" category as this is targeted to using nanostructured thin films for improving the performance of sorbents in gas chromatography for improving gas analysis, with applications in homeland security, monitoring food freshness, industrial process control, biomedical diagnostics, and surveying environment quality. This is an application of nanomaterials for improving measurements in environmental and occupational safety, but it is not captured in the five priority needs.

Summary of Balance Assessment for Instrumentation, Metrology, and Analytical Methods

There is fundamental, solid research activity in this category. Much of the research reported for 2006 is focused on the development of either adapted or new technologies to measure the amount or type of nanomaterial in a given space or time and these efforts contribute substantially to our overall ability to understand and manage potential risks of engineered nanomaterials. Mechanistic studies of broad classes of nanomaterials are underway. Integration of these across media that are indicative of exposure would enhance nanomaterial health and safety research and as such, should be a near term focus for the development of methods, as detailed in Figure 3 where relative timing of research needs is indicated. In addition, as the availability of a universal air sampler is lacking, research to develop such an instrument should begin right away. Evaluations of nanomaterials with respect to solubility in lipids and aqueous environments are needed in the near term as well to assess nanomaterial correlations with transport phenomena across membranes or in aqueous environments. Such activity would provide datasets for risk assessment and management that can build upon existing research whose primary focus is predictive toxicology or environmental modeling.

> Based on the analysis of the range of needs in the research need categories, research emphasis diagrams have been developed to show the relative timeframes and sequence in which the task forces felt the five research areas within this category should take place. The timing of each area depends on the immediacy of the need for the results and whether other research or information is needed before the subject research can be undertaken. Color shades correlate with relative level of emphasis (i.e., darker shades representing greater emphasis). Changes in level of emphasis through time in a given research area will presumably correlate with variation in level of spending. Within a given research area, changes in level of emphasis through time will presumably correlate with variation in level of spending. However, the color shades do not indicate levels of funding relative to other research categories or research needs. The estimated time required to carry out a particular area of research will depend to some extent on the level of funding and, in some cases, on progress in related areas of research. Therefore, the starting time and the duration of high intensity activity shown in this and other diagrams in this section are estimates and may be subject to modification.

Mid term efforts should focus on technology developments for the monitoring of nanomaterials in water. This technology would then support studies on understanding the effect of surface function on the behavior of nanomaterials in water (Figure 3). Reference materials developed for these types of studies in the mid term would also greatly facilitate such investigations and provide a basis to build modeling platforms to predict environmental behavior of nanomaterials, a longer term research activity not present on the agenda but one with existing activity that can be built upon.

Figure 4 represents the conceptual framework for the relationship between instrumentation, metrology, and analytical methods research needs and the sequence of events for decision making with respect to nanomaterial use. A fundamental requirement for assessing the potential impacts of new nanomaterials on both human health and the environment is the ability to make precise, accurate measurements at the nanoscale in multiple, complex mediums. Moreover, unique measurement technology challenges must be met, such as investigating how nanomaterials interact with different environments and effects that may occur at various points of the nano-enabled products' lifecycles including those that may be due to transformations. As such, research to support instrumentation, metrology, and analytical methods covers all aspects of the human health and environmental framework andprovides a foundation for work in the other four research categories. In particular, the development of methods to detect nanomaterials in biological matrices, the environment, and the workplace is necessary across the entire framework from the synthesis and use of nanomaterials to the detection and characterization of materials as a function of exposure. Similarly, the development of methods for determining the sizes, shapes, structure, and surface area are essential to assess such metrics from the beginning phases of material production through the characterization of a material that leads to a dose effect. In addition, the characterizations of materials at various stages of development often do not provide measurements that are reproducible or consistent across disciplines and applications, including assessments of biological response. Hence, reference material development plays a key role in these areas by providing a standardized, acceptable approach to study, monitor and potentially track nanomaterials as they are released into the environment or the workplace, and to assess their potential interactions with human and ecological systems. Methods for the determination of the spatial composition, purity, and heterogeneity also play a pivotal role for these areas as single defects or slight changes to surface dimensions or composition can dramatically influence the nanomaterial lifecycle and the biological or environmental effects that may result at any given point. Similarly, methods to support understanding how chemical and physical modifications affect the properties of nanomaterials are critical for assessing nanomaterials beyond external contact as modifications may affect the ability of a material to migrate into or travel within both human and environmental contexts.

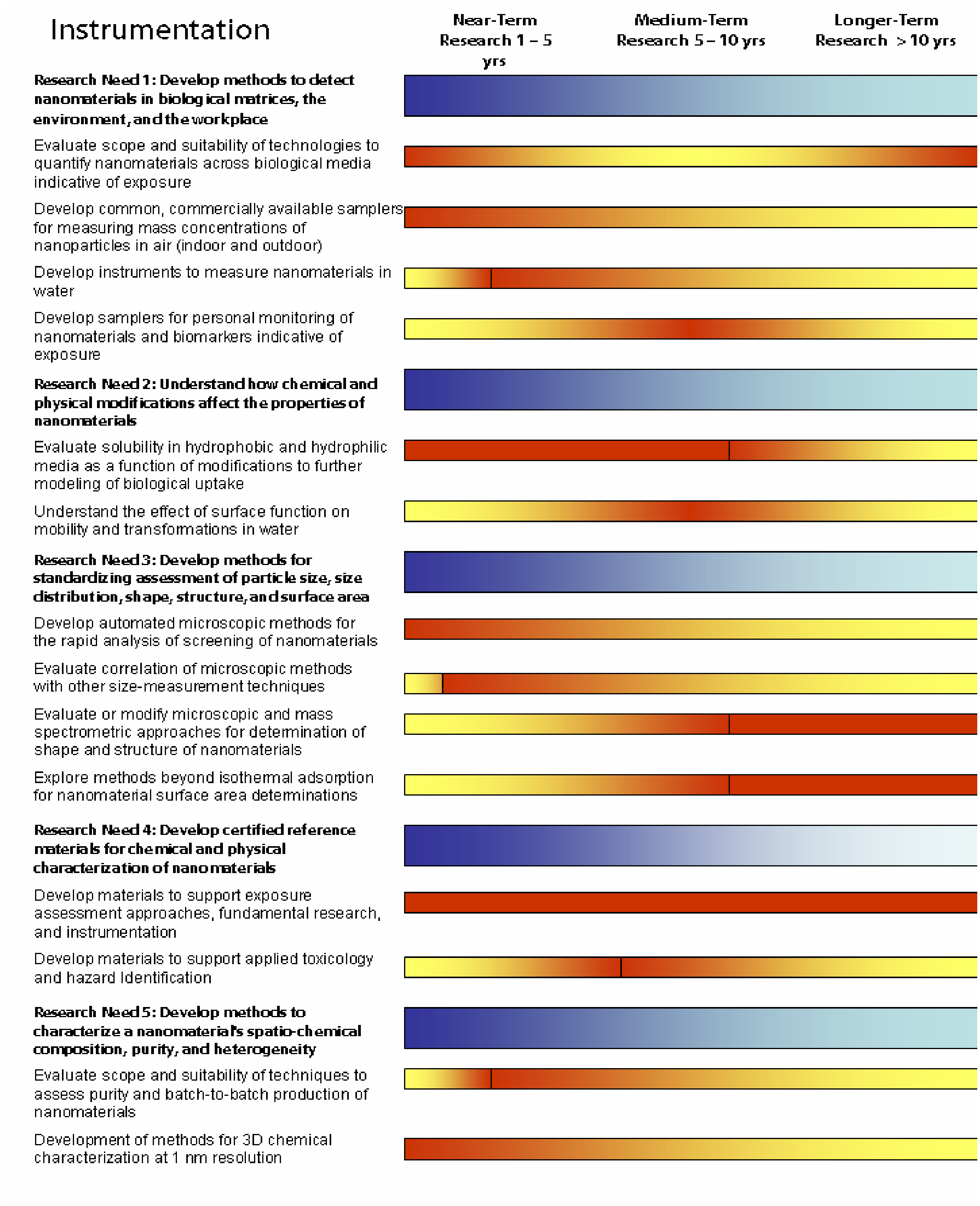

Figure 3. Relative emphasis as a function of time for priority research needs of Instrumentation, Metrology, and Analytical Methods Category

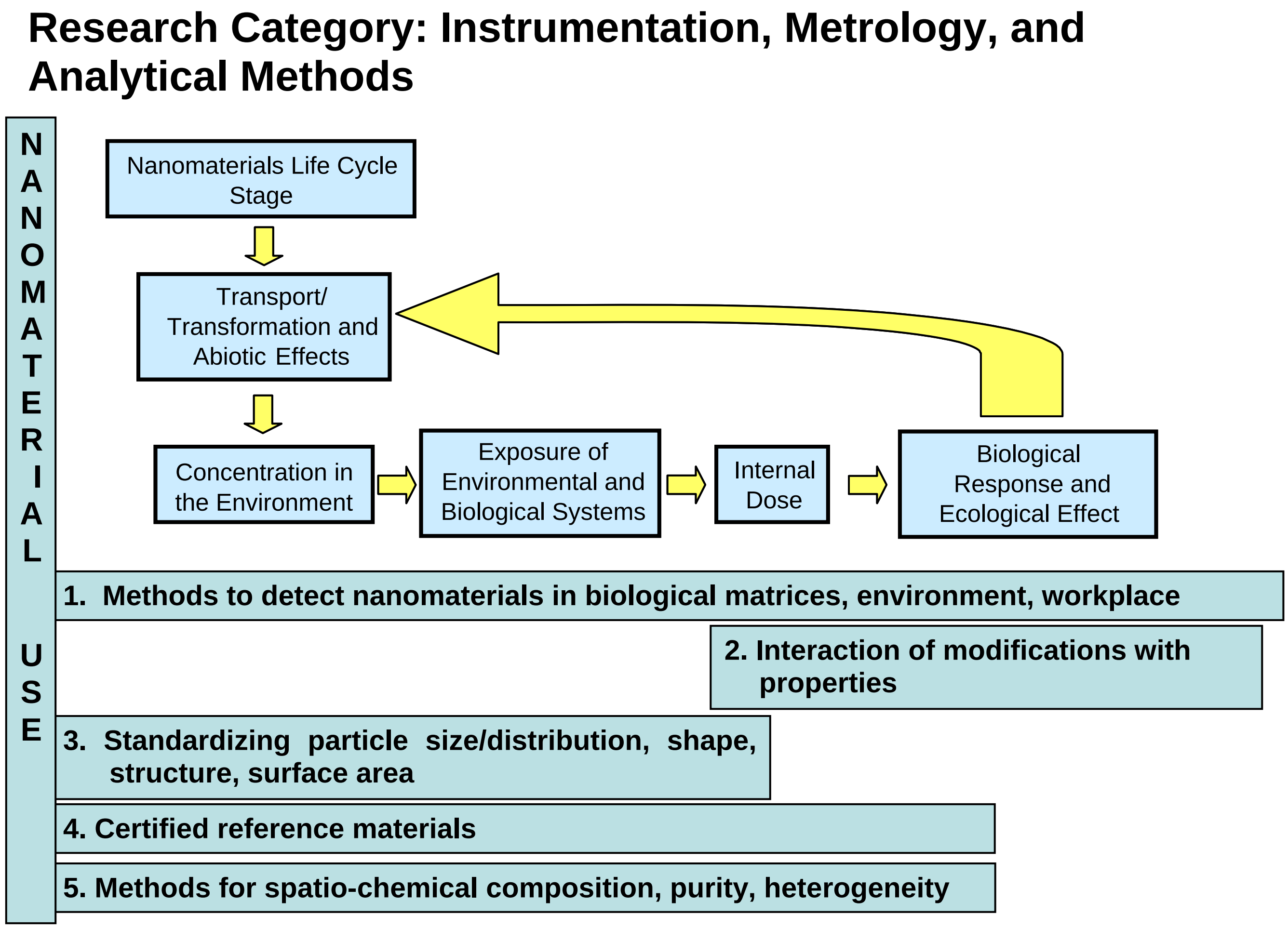

Figure 4. Framework for research on Instrumentation, Metrology, and Analytical Methods Category

Research Category: Nanomaterials and Human Health

Total estimated funding in 2006: $ 24.1M

Total projects: 100

Agencies supporting research in this category: AF, EPA, NIH, NSF, NIOSH, USDA

Prioritized Research Needs[1]	FY06 funding Estimate $K (% of total)	Number of Projects (% of total)
1. Understand absorption and transport through the body	7122 (30 %)	29 (29 %)
2. Develop methods to quantify and characterize exposure to nanomaterials and characterize nanomaterials in biological matrices	2985 (12%)	13 (13 %)
3. Identify or develop appropriate *in vitro* and *in vivo* assays/models to predict *in vivo* human responses to nanomaterials exposure	975 (4 %)	6 (6 %)
4. Understand the relationship between the properties of nanomaterials and how they affect uptake via lungs, skin, digestive tract, assess body burden	2722 (11 %)	11 (11 %)
5. Determine the mechanisms of interaction between nanomaterials and the body at the molecular, cellular and tissular levels	9590 (40 %)	39 (39 %)
Multiple: Projects that capture multiple needs	--	--
Other: Not captured in needs above, but with benefit to the research category	671 (3 %)	2 (2 %)

Background

The five research needs outlined above are critical to addressing the overarching priority to understand generalizable characteristics of nanomaterials in relation to toxicity in biological systems and address critical research steps in the framework. They are essential for the development of predictive models of toxicity and for risk management.

Research on human health often involves complex, interrelated scientific concepts that are investigated most efficiently by a parallel, rather than serial, research paradigm. This parallel structure permits the investigation of single or integrated research questions and the leveraging of progress in related areas. In this analysis, projects may have research components in more than one research need but they are discussed under the research need that describes the primary focus. These broad research needs were considered equally critical to achieving the overarching goal of understanding the potential for and mechanisms of engineered nanomaterials' toxicity in humans and for development of computer models that inform hazard assessment and risk management.

Summary of Analysis by Research Need

Research Need #1: Understand the absorption and transport of nanomaterials throughout the human body

Research in this need focuses on absorption of nanomaterials within the exposure organ, translocation out of the exposure organ, and transport through the body. Research in this need focuses on the uptake of nanomaterials by exposure organs and by cells. There are 29 projects in this need, 16 that directly address this research need and 13 that have a relevant research component.

Several projects examine the physical and chemical characteristics of engineered nanomaterials that govern their absorption through the human routes of exposure, for example, respiratory tract and skin. The grant evaluating absorption and transport through the skin is designed to establish a structure–permeability relationship between nanoparticles and skin, and to develop quantitative methods to assess this relationship. Other projects are examining the transport and deposition properties of nanoparticles and agglomerates in the lung as a function of mobility–equivalent diameter of the nanomaterial.

Research on cellular uptake of nanomaterials draws heavily, but not exclusively, on experimental and in silico biomedical research which designs nanomaterials for improved drug delivery and imaging. Projects in this area are investigating the physical and chemical properties of nanomaterials that enhance or impede transport through the blood and through tissues, cellular uptake and transport through the intracellular compartments and cytoplasm. The role of the protein corona in transport and uptake is also under investigation. Projects in this need will provide information on the interaction of nanoparticles with the cell membrane, identify mechanisms of transport through the body, and the molecular mechanisms for cells to take up nanoparticles. Studies are also testing the intracellular and extracellular forces that stabilize/destabilize micellar nanoparticles, and the properties of nanomaterials that allow them to co-exist benignly with the immune system and the reticulo-endothelial system.

Again, gastrointestinal and intraoccular uptake are not well represented.

Research Need #2: Develop methods to quantify and characterize exposure to nanomaterials and characterize nanomaterials in biological matrices.

Research in this need focuses on methods to quantify and characterize nanomaterials in external and internal microenvironments. There are 13 projects, and 12 directly address this research need.

The ability to characterize nanomaterials *in vivo* is critical to evaluating toxicity in the dose-response paradigm. Additionally, several studies have indicated that, at the nanoscale, it may not be insufficient to report only mass measurement of the materials used in an experiment and that additional physical and chemical parameters will be needed to understand the biological behavior of nanomaterials.

Projects that identify research need 2 as the primary focus of the grant are evaluating multiple methods to characterize nanomaterials. New methods are being developed, such as cell probe force microscopy that measures directly the interaction forces between nanostructures and living cells and intracellular microscopy techniques to localize and quantitate nanomaterials deposition, especially in the nucleus. Lung dosimetry models are being used to understand nanoparticle exposure-deposition relationships.

Methods to characterize nanomaterials in biological systems are used throughout all five research needs to varying degrees. Several projects are evaluating additional metrics of dose, including, surface area, shape, surface charge, and surface reactivity. Additional research noted in this section includes characterization of lipids with CNTs, of nuclear delivery of biomolecular-nanogold complexes, of nanostructured membranes with the intestinal tract, and the pharmacokinetics of nanoemulsions.

Respiratory tract, skin and intravenous injection are the most studied routes of exposure, and gastrointestinal and intraoccular uptake are underrepresented. Methods to characterize and quantify nanomaterials in biological matrices will need further development. Methods to quantify and characterize the exposure before uptake by the body is part of the metrology research program and covered in that section.

Research Need #3: Identify or develop appropriate *in vitro* and *in vivo* assays/models to predict *in vivo* human responses to nanomaterials exposure.

There are 6 projects, and all directly address this research need.

The ability to manipulate easily the surface chemistry of a nanomaterials and the almost infinite number of possible permutations makes rapid, relevant, and accurate assessment of the potential toxicity of nanomaterials an important research need. Additionally, the unique properties that emerge at the nanoscale suggest that the validity of existing test methods should be verified.

Two projects address rapid, high throughput screening directly by employing the well established zebrafish model or rapid screening of the oxidative stress response. Both systems employ a three tiered approach in which a significant response in tier 1 leads to tier 2 testing and, as necessary, tier 3. A third grant is developing a technique to assess cell and genetic alterations in human and animal cells using chromosomal breaks and the molecules of xenobiotic metabolism and DNA repair.

The additional projects are developing tests to measure photophysical properties, dispersity, size dimension, and biolocalization by neutron activation analysis, atomic absorption and radiochemcial analysis to accurately estimate nanoparticle concentration in tissues and biological fluids. Others are developing imaging nanoprobes for PET and MRI that will improve localization in tissues.

The low number of projects in this priority research need suggests that it is an area of research need. However, this assessment does not capture applicable research in other research needs nor many additional research efforts on testing schemes that were not captured by the gap analysis, so a determination of gaps may be misleading.

Research Need #4: Understand the relationship between the properties of nanomaterials and uptake via the respiratory or digestive tracts or through the eyes or skin, and assess body burden

There are 11 projects that have been identified under this priority research need, 7 of which have this research need as a primary focus.

Projects under this research need use animal models to consider skin, lung and oral exposure to nanoparticles and evaluate the standard physical and chemical characteristics of the materials- size, shape, charge, surface area and solubility. The skin projects evaluate skin penetration and the biological response to the nanoparticles that enter the skin. Projects employing inhalation methods examine the dose-response relationship for the lung and the heart and translocation of materials out of the lung. They also investigate the deposition and location of the translocated nanomaterials.

The effects of nanomaterials exposure on disease exacerbation are considered for chronic obstructive pulmonary disease and asthma. The asthma grant employs environmental nanomaterials in air pollution. Data are also derived from biomedical studies on pharmacology and biodistribution, one using oral delivery, of nanoscale drug delivery systems. This application evaluates therapeutic efficacy and not uptake by the GI tract directly.

Measurements of total body burden are not clearly described in any grant, and no ocular assessment is noted.

Research Need #5: Determine the mechanisms of interaction between nanomaterials and the body at the molecular, cellular, and tissular levels

There are 39 projects in this research area, all of which will contribute the accomplishment of this research need.

The relationship of exposure to human health response is mirrored in the relationship of dose to biological response, and this dose-response, or structure-activity, relationship is critical to our understanding of the physical and chemical properties of nanomaterials that support safety and minimize adverse effects. This research need extends and integrates research needs 1, 2 and 3.

Multiple projects within this priority research need systematically assess the *in vitro* biological response at the molecular level by investigating the effect of such parameters as size, functional group density, structure, polyethylene glycol coating and synthesis byproducts, especially heavy metals such as iron, on cellular and organ system function. Critical questions being addressed include interaction of nanomaterials with lipids in the cell membrane, proteins, and DNA, mechanisms for cellular uptake of nanomaterials, disposition of materials once they are in the cell, and cell function, proliferation, and differentiation.

Monitoring of biological pathways that are linked to disease provides an opportunity to identify the physical and chemical properties that may not support safe design and development. Many of these projects include *in vitro* experiments and *in vivo* animal studies. Several projects are investigating whether or not nanomaterials stimulate an immune response, induce cell death through oxidative stress pathways, promote respiratory and cardiovascular disease, or disrupt DNA and cause cancer. Most applications study the effects of acute exposure, but several address chronic exposure. Within this chronic exposure category, a number of biomedical projects are evaluating the biocompatibility and biodegradation of nanostructured implants for soft tissue and bone repair.

Several projects include the development of computational models. These models would use the experimental dose-response data to develop computer models that could predict the potential safety or hazard of new materials.

The projects and projects reported here encompass the multiple aspects of this research need. It is anticipated that, as research progresses, additional projects will be needed to cover completely the landscape of nano-bio-interactions. Additionally, most of the projects employ *in vitro* cellular studies, and there is a need to more fully translate *in vitro* results to animal models and extrapolate data to human exposures.

Projects Classified as "Multiple" or "Other": One project was placed in the "other" research need for this category by the funding agency. This project coordinates research activities on nanoparticles in the workplace.

It should be noted that, because of the integrated nature of biological research, many grants have components related to other research needs. These grants were assigned by their funding agency to the research need that represented the central focus of the research.

Summary of Balance Assessment for Human Health

In 2006, there is solid research activity in all five needs with some weakness observed for gastrointestinal and ocular uptake as well as the validation of *in vitro* and *in vivo* test methods. Much of the research reported in 2006 focuses on medical applications, and while contributing to the overall body of knowledge for human health effects, systematic, targeted study of classes of nanomaterials and the relationship of their physical and chemical properties to biological response would provide integrated data sets for risk assessment and risk management. These efforts should build upon the existing research whose primary focus is human health and safety.

Near term efforts should focus on the research that develops or validates methods to quantify the dose - response, or structure – activity relationship. These efforts should include determination of relevant measurement parameters for each class of nanomaterials in simple exposure matrices and in simple biological matrices, the appropriate parameters for sampling and analysis, and methods for quantification and characterization. Methods to quantify and characterize biological response are also critical to dose – response studies and should be developed in the near term.

Mid term efforts should focus on the application and extension of these methods, as detailed in Figure 5. Missing from the mid term research agenda is the initiation of an informatics structure to collect, curate and annotate research data. This mid term research would support the development of computational models in the long term. In order to advance hazard identification and risk assessment, additional long term research efforts should translate research findings from animal models to humans.

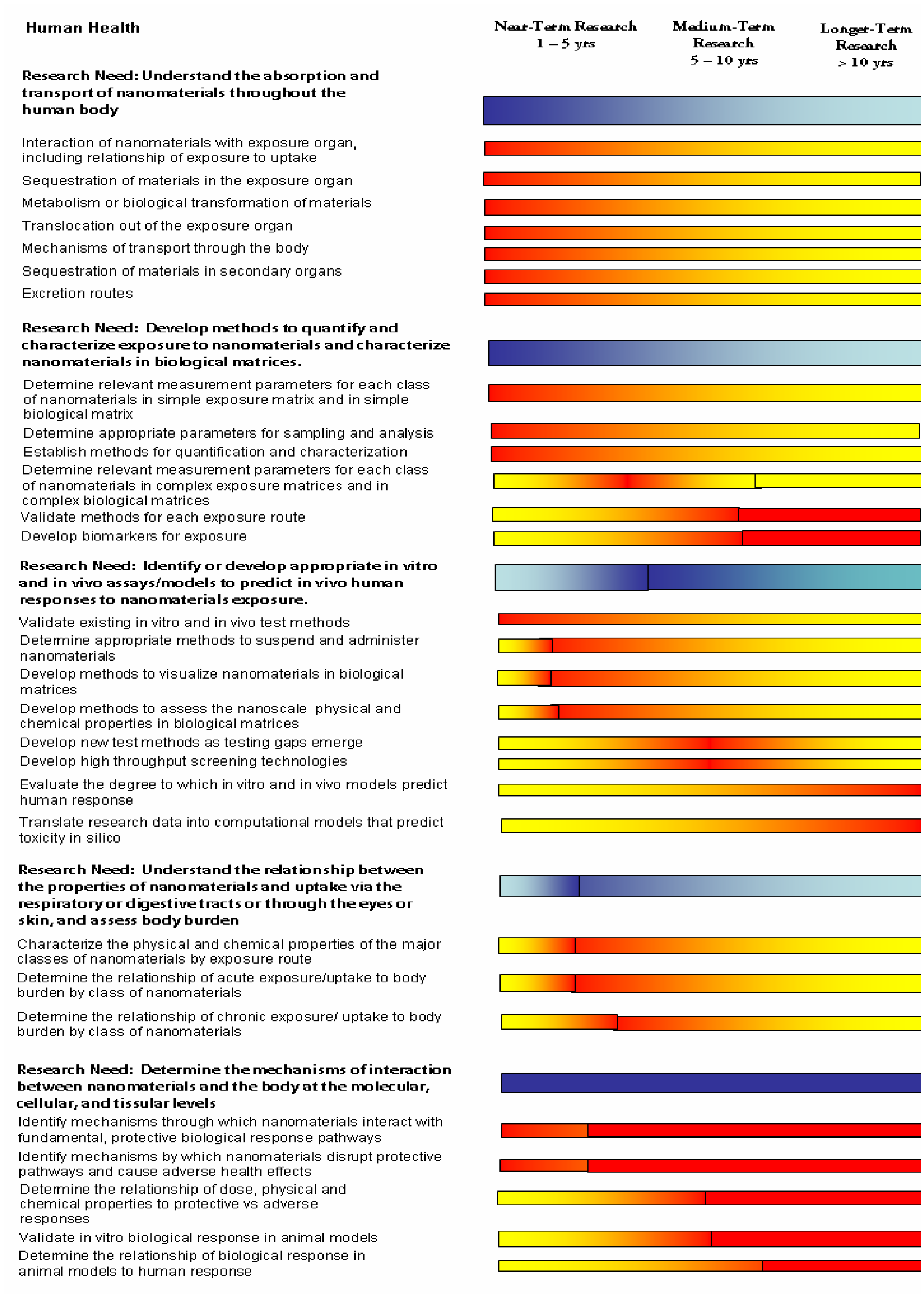

Figure 5. Relative emphasis as a function of time for priority research needs of Nanomaerials and Human Health category

Research Category: Nanomaterials and Human Health

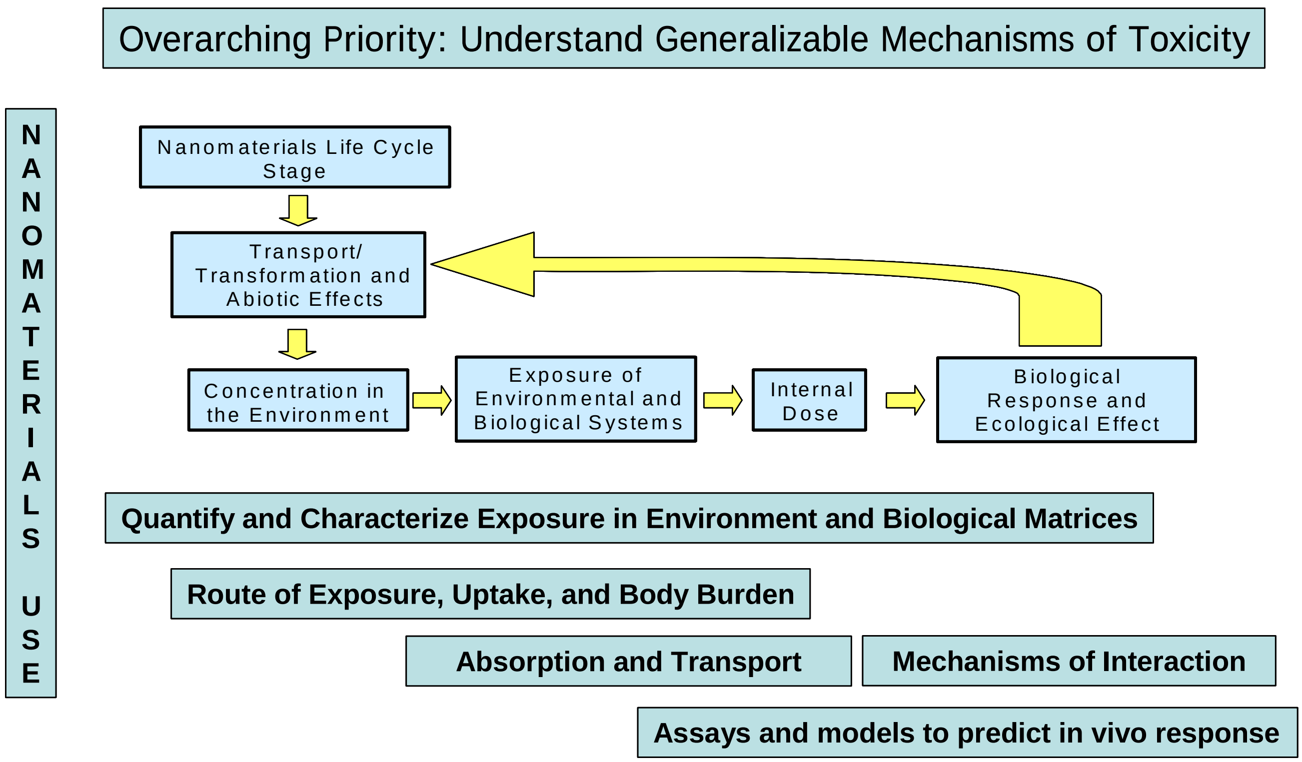

Figure 6. Framework for research supporting Nanomaterials and Human Health category

The dose response relationship provides traditional hazard information on the biological response to an exposure. This relationship can be elaborated as a series of related research steps, each of which provides a discrete set of information that, taken as a whole, provides a comprehensive hazard assessment (Figure 6). Steps within the dose component include measurement and characterization of exposure, route of contact with the materials and internalization of some percentage of the exposure. The response component is comprised of research that includes biotransformation of the material, distribution throughout the system, excretion from the system, and interaction at the cellular, molecular and organ system level. Because biological response is dependent on the genetic make up of the individual, age, health status, and multiple other life factors, susceptible populations are included in the framework to designate these considerations.

Research Category: Nanomaterials and the Environment

Total estimated funding in 2006: $12.7 M

Total projects: 49

Agencies supporting research in this category: AF, EPA, DOE, NSF, USDA

Prioritized Research Needs[1]	FY06 funding Estimate $K (% of total)	Number of Projects (% of total)
1. Understand the effects of engineered nanomaterials in individuals of a species, and applicability of testing schemes to measure effects	1351 (11 %)	5 (10 %)
2. Understand environmental exposures through identification of principle sources of exposure and exposure routes	250 (2%)	1 (2 %)
3. Evaluate abiotic and ecosystem-wide effects	115 (1%)	1 (2%)
4. Determine factors affecting the environmental transport of nanomaterials	4898 (39%)	24 (49%)
5. Understand the transformation of nanomaterials under different environmental conditions	2229 (17%)	8 (16%)
Multiple: Projects that capture multiple needs	--	--
Other: Not captured in needs above, but with benefit to the research category	3885 (30 %)	10 (21 %)

Background

Research to be considered in this category consists of the five EHS needs, in ranked priority order relative to their importance for the evaluation of potential environmental impacts. The first research need comprises research necessary for determining the adverse effects in individuals of both aquatic and terrestrial species and for evaluating the applicability of testing protocols, organisms, and associated testing schemes to determine such effects. Consideration should be given to measuring toxicity, mechanisms such as metabolism, and the development of structure-activity relationships.

The second research need is to identify sources of nanomaterials and their routes to the environment, which should provide insights into which environmental receptors, such as individual species, are exposed. Work in this area also would include research to assess the extent to which nanomaterials bioaccumulate in those receptors, and it would identify relationships between environmental exposure and the absorbed doses in relevant receptors.

The third research need is to determine effects of nanomaterials beyond those in individuals of a species, including those exhibited at the population, community, and ecosystem level, such as alterations to nutrient cycling. This need also includes the study of effects of nanomaterials on other abiotic processes in the environment, such as changes to air quality or photo-oxidative or catalytic effects.

The fourth research need, to determine the factors that affect the transport of nanomaterials in the environment, includes research to understand and predict the transport within and between all environmental media, as well as studies to gain better understanding of the effects of nanomaterials on the transport and partitioning of other environmental chemicals such as metals.

The fifth research need focuses on research to examine transformations of nanomaterials under different environmental conditions, for example, alterations of a material due to changes in groundwater pH or exposure to sunlight.

Research to address all five of the needs in this category should consider not only the parent nanomaterial but also the environmentally altered forms and any by-products caused by reactions, either physical or chemical, of nanomaterials with environmental chemicals or matrices.

Summary of Analysis by Research Need

Research Need #1: Understand the effects of engineered nanomaterials in individuals of a species, and applicability of testing schemes to measure effects

Projects on effects of engineered nanomaterials in individuals of a species and the applicability of testing schemes represent broad coverage of endpoints and species for aquatic receptors. Most of the projects directly address, at least in part, effects in individuals of several species which are included in current test guidelines, including freshwater and marine vertebrates, both benthic and pelagic, and a range of both metallic and carbon-based nanomaterials. Taken together, the projects include a broad range of endpoints from genomic, molecular, and cellular to whole organisms and population-level effects. These projects also include aspects of nanomaterial kinetics, uptake processes, bioavailablity, and food chain transfer. Four manufactured nanomaterial classes (metals, nanoceramics, carbon-based nanoparticles, and organic nanomaterials) were addressed by the five projects (quantum dots were not addressed). Additionally, at least three projects from the Nanomaterials and Human Health category will also contribute to the research needs identified here. Terrestrial effects, test protocol development, dose-response characterization, and testing scheme development are less well represented

Research Need #2: Understand environmental exposures through identification of principle sources of exposure and exposure routes

Research on principle sources of environmental exposures and exposure routes is represented by a single project, and this work appears to be on naturally-occurring nanoparticle effects in geologic systems. This research could be augmented by research in other categories including those appropriate projects under risk management, and health and environmental exposure which provide sources and routes of exposure from the work environment to broader environmental media/compartments. Research will inform which receptors may be of greater concern to examine for effects under research needs #1 and #3.

Research Need #3: Evaluate abiotic and ecosystem-wide effects

Research on effects beyond those in individuals of a species (including abiotic effects) is also represented by a single project. The project addresses natural nanoparticles and their effects on the biogeochemical cycling of metals of concern in the subsurface. Other projects also contribute to an understanding of the effects of nano-scale engineered iron on microbial toxicity, and other higher level effects, in the subsurface. Coverage of broader nanomaterial classes and effects beyond those seen in the subsurface are not provided. Much of the higher-level ecosystem effects work under this research area will be better focused once information from research needs 1, 2, 4 and 5 are obtained.

Research Need #4: Determine factors affecting the environmental transport of nanomaterials

Research on factors affecting the environmental transport of nanomaterials has 23 projects which touch on all four engineered nanomaterial classes (with more emphasis on iron-based particles) and natural nanoparticles, and is funded by five agencies/departments. The transport of nanomaterials in many relevant environmental media are addressed, including soils, the subsurface, surface waters, and wastewater. A significant portion of the research described focuses on the fundamental chemistry and physical properties of nanoparticles which may contribute to the behavior of nanoparticles in the environment (such as formation, stability, media-nanoparticle interactions): such basic information is fundamental to understanding the environmental transport (and transformation) of nanomaterials. However, there is a lack of emphasis in more applied areas related to risk assessment such as determining which physical/chemical processes control the fate and transport of different engineered nanomaterials in environmental media, which in turn would lead to an improved understanding of the key transport processes for commercial nanoparticles. Also, there is a lack of emphasis on the evaluation of traditional existing models and tools to determine their adequacy for predicting nanomaterial transport.

Research Need #5: Understand the transformation of nanomaterials under different environmental conditions

Research on the physical, chemical, and biological transformations of nanomaterials in the various environmental media is represented by ten projects funded by four agencies/departments. The research includes representatives of each manufactured nanoparticle class (including metals, nanoceramics, carbon-based nanoparticles, and organics) and selected naturally-occurring or incidental nanoparticles. A number of important environmental (soil, sediment, air, and water) and biological matrices are addressed, with an emphasis on varied aquatic media. The research includes attention to environmentally-altered forms of nanoparticles, and byproducts of reactions between nanomaterials and environmental chemicals/matrices. A number of transformation processes are examined including coagulation, microbial effects, pH, sorption, and the interactions with specific biomolecules. There is a strong emphasis on fundamental chemical/physical interaction research that will inform transformation processes. In this sense, work described here is similar to that done under Research Need #4, and many studies under these two priorities address topics in both priorities and are mutually supportive. The current state of the science in both priority areas are at an early stage such that the focus on fundamental work is understandable. There is limited work described for biological transformation processes; and there is a need to move toward a focus on key physical, chemical, and biological processes which would be broadly predictive of transformations of manufactured nanomaterials.

Projects Classified as "Other": There are ten projects which are not captured in the five priority research areas. While these projects do not directly answer questions posed by the five priority areas, they are useful in the sense that they lead to fundamental understandings of nanoparticle behavior, and/or will lead to nanotechnology applications that contribute to lessening current environmental contamination resulting from manufacturing/use/disposal of conventional chemicals.

Future Research Needs for the Near, Medium, and Longer Terms

The research gaps in the preceding section have been considered, along with additional information, to determine which gaps should be pursued as future research needs. The highest priority future research needs for this category are related to the first two research needs identified earlier in the NEHI EHS process (see Section 1, Item 1 above). However, four overarching considerations must be taken into account when considering these prioritized future needs: the physical/chemical characterization research that enables identification of nanomaterials in biological and environmental matrices is a fundamental enabler of work under this research area; research should focus on the as-manufactured nanomaterial, and key products of reactions between nanomaterials and the environment following contact with environmental matrices; and work under this research area will be iterative in nature as new nanomaterial classes come closer to commercial production.

Research related to development of test protocols for commercial submissions for Federal consideration/approval, , development of better understandings of dose-response characterizations, and development of tiered testing schemes that incorporate the testing protocols for commercial submissions is needed to better understand the potential adverse effects of nanomaterials to biological receptors prior to their commercialization. This research is considered of highest priority due to the need to better understand potential impacts on receptors prior to their commercialization, due to the limited amount of research conducted in this area to date, due to its achievability in the near term, and due to its high ranking in general across representative Agencies in the NEHI EHS process. Test protocol research can be addressed by a concentrated emphasis on evaluation of existing protocols for their adequacy for nanomaterial testing in the near term, followed by a medium-term effort to develop new test protocols as appropriate. Dose-response characterization work should begin in the near-term, with ADME-related (adsorption, distribution, metabolism, and elimination) work following with a focused effort beginning in the medium term. Work on mode of action should commence with a concerted effort toward the latter part of the near-term, and shift to development of predictive tools including structure-activity relationships in the medium term. Finally, tiered testing scheme development should commence with a heavy emphasis in the latter part of the near-term as adequate test protocols become established.

A second high priority set of research needs for the near term is associated with the second highest priority research need identified in the earlier NEHI EHS process (see Section 1, item 2 above). Research related to principle sources of environmental exposures and exposure routes for commercial nanomaterials will allow identification of appropriate biological and other environmental receptors which could be affected by the release of nanomaterials. Releases from nanomaterial manufacture, and from incorporation of nanomaterials into commercial products should be focused on as soon as feasible in the near term given the likelihood of significant releases from these sources. Life cycle exposures subsequent to manufacture/product incorporation should begin in the latter part of the near-term period as more information becomes available to focus this research. There should be an ability to distinguish deliberate from unintentional releases. Also the amounts entering into, and resulting environmental exposures in, specific media should be identified. Given these categories of exposure information, existing exposure models should be examined for their applicability to nanomaterials, and new exposure models and estimation techniques developed as appropriate. This research area is directly coupled with the first identified above, is considered a high priority amongst NEHI agencies, and is currently represented by very limited amounts of research.

Research on environmental transport and transformation is already represented by a substantial investment in fundamental research, and the two research areas are linked by common areas of investigation. For both of these areas, the emphasis on identification of key physical/chemical properties affecting transport and transformation should continue in the near-term. A heavy emphasis on research on key transport and transformation processes should follow in the beginning of the medium term. Finally, work on models in these two areas must be ongoing as more information becomes available: an initial light emphasis should be placed on such predictive tools in the middle of the near-term, followed by a heavier emphasis in the medium term.

While research on abiotic, and ecosystem-wide effects was ranked as third highest priority in the initial ranking process, it has now moved to fifth priority. This is due to the overarching needs noted in the beginning of this section (in particular the need to understand changes to nanomaterials as they contact environmental matrices) prior to addressing this research area. Further, an evaluation of abiotic and system-wide effects of nanoparticles may have to await additional fundamental research including that from advances in research needs' areas 1 and 2, and 3. Studies on populations of key environmental receptors should begin with a heavy emphasis in the medium term as key receptors are identified by other ongoing research; higher level community effects' research should begin in the longer-term timeframe, and ecosystem/abiotic effects work should start in the latter portion of the long-term timeframe.

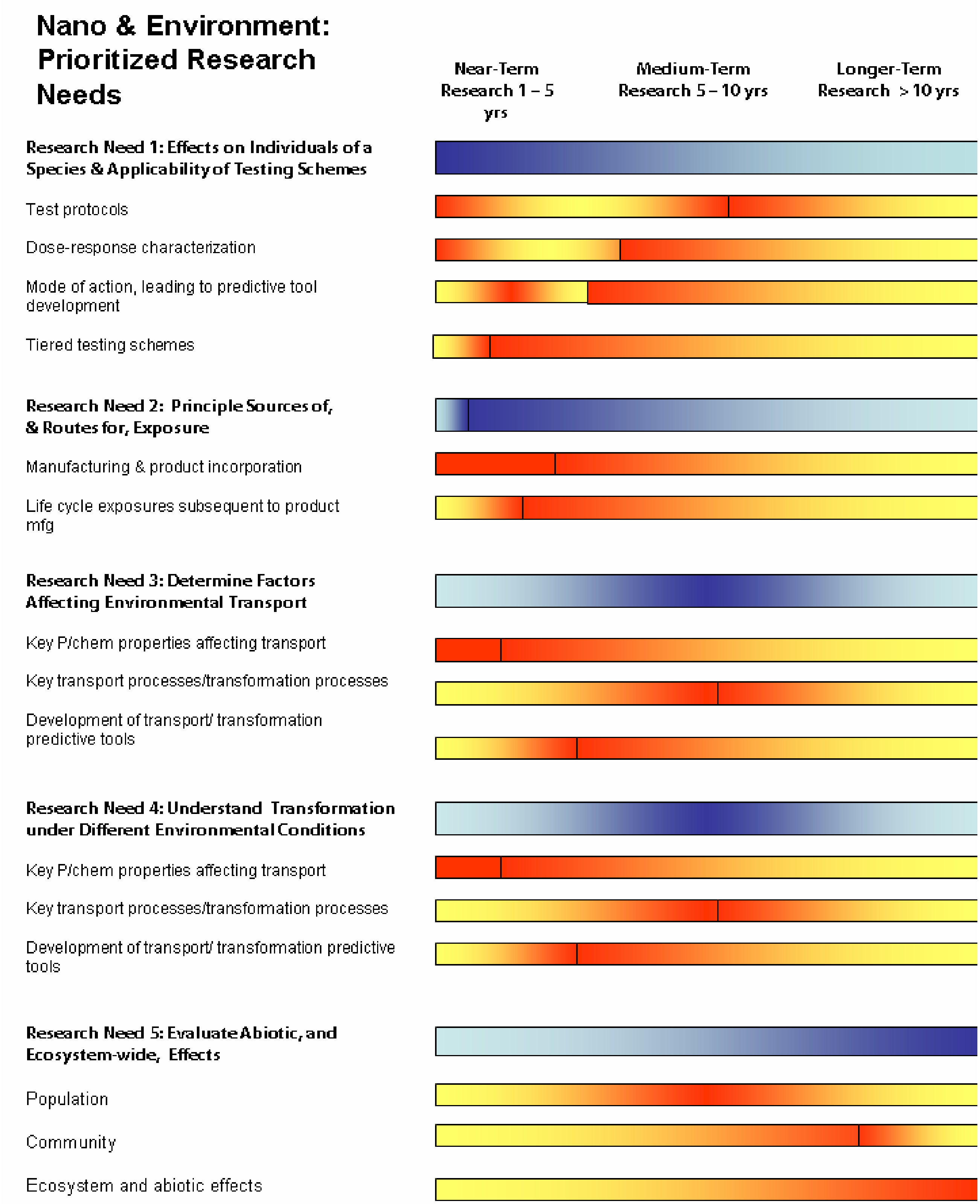

Figure 7. Relative emphasis as a function of time for priority research needs of Nanomaterials and the Environment category.

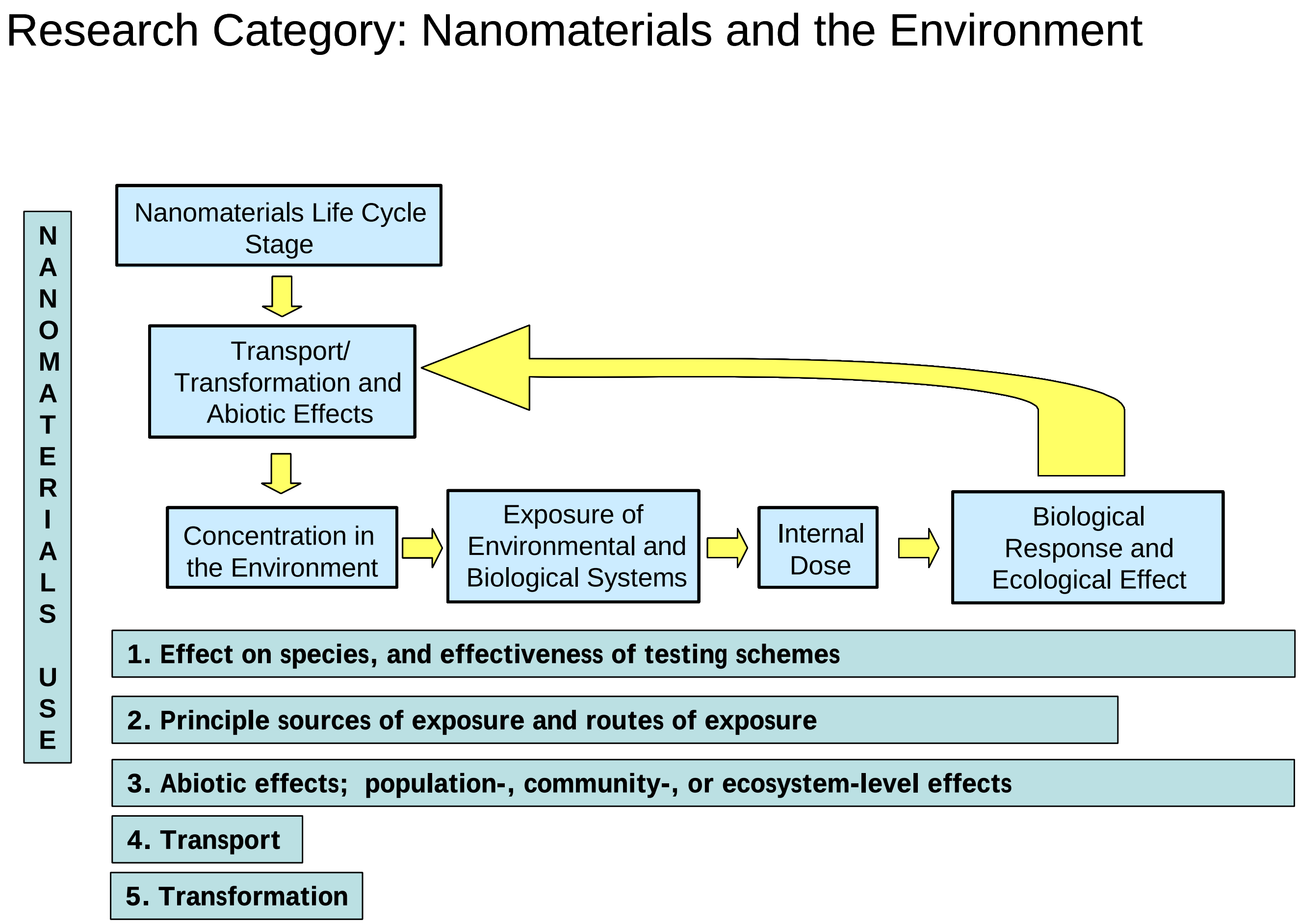

Figure 8. Framework for research supporting the Nanomaterials and the Environment category

Nanomaterials and the Environment research has two different components related to potential adverse effects: those that result in biological responses in individuals (as a result of testing a few relevant ecological receptors of a single species for their responses to a given nanomaterial), and higher level effects that could be manifested at the population, community, or ecosystem levels. These effects are only seen when exposures are sufficient to trigger such effects. Significant exposures can be better identified by examining the various life stages of a nanomaterial (from manufacture of the nanomaterial, to its incorporation into a commercial product, to use by consumers, to disposal). With any of these releases through the life cycle, potential adverse effects can be modified by transformation events, other interactions between nanomaterials and components of environmental matrices, and transport phenomena subsequent to release of the nanomaterial. The five priorities in this research category are arrayed, and overlap in four cases, the sequence of events shown that lead to effects' outcomes.

Research Category: Human and Environmental Exposure Assessment

Total estimated funding in 2006: $1.1 M

Total projects: 5

Agencies supporting research in this category: DHHS/CDC/NIOSH, DOD/AF, NSF

Prioritized Research Needs[1]	FY06 funding Estimate $K (% of total)	Number of Projects (% of total)
1. Characterize exposure among workers	879 (77%)	2 (40%)
2. Identify population groups and environments exposed to engineered nanoscale materials	--	--
3. Characterize exposure to the general population from industrial processes and industrial and consumer products containing nanomaterials	--	--
4. Characterize health of exposed populations and environments	--	--
5. Understand workplace processes and factors that determine exposure to nanomaterials	265 (23%)	3 (60%)
Multiple: (Overarching research need) Evaluate risk management approaches for identifying and addressing risks from nanomaterials	--	--
Other: Not captured in needs above, but with benefit to the research category	--	--

Background

The priority research needs for this category identify work to enable the collection of exposure information. Data collection should group individuals into exposure categories and relate groups potentially exposed to nanomaterials, including workers, patients, consumers, and neighbors of production or utilization plants. Research should consider exposure assessment studies to quantify any general population exposures to nanomaterials resulting from the use of consumer products and to identify cases of unusual injury and patterns of health outcomes suspected of being associated with exposure to nanomaterials. Information on the process, task, and location variables should be evaluated to understand how nanomaterials behave in workplace environments and what factors determine the exposures to nanomaterials in such environments.

The task force identified the following common themes for this category:

1) priorities are intertwined within the same category and between categories;
2) collaborations between several agencies are critical to successfully address research priorities in this category;
3) continuous nature of surveillance research represents additional challenge in identifying time frame for research in this category.

In FY06 the U.S. government invested over $1M into research on Health and Environmental Exposure Assessment. Five projects cover two research needs, Research Need #1 Characterize exposures among workers and Research Need #5 Understand workplace processes and factors that determine exposure to nanomaterials. These projects have relevance to other research categories such as Instrumentation and Metrology, Nanotechnology and the Environment and Risk Management. A project funded by DOD/AF in addition to exposure assessment relevant research looks at evaluating personal protective equipment and developing guidance on handling nanomaterials which are covered by the research category Risk Management Methods. On the other hand, there are projects listed in other research categories that have relevance to this category. Specifically, the project "Particle Surface Area as a Dose Metric" placed in the Nanomaterials and Human Health Research category targets the identification of the proper metrics of exposure. There is also a project funded under the "NSEC: Network for Hierarchical Manufacturing" reported in the Instrumentation, Metrology and Analytical Methods category which has critical relevance to exposure assessment and measurements.

A limited number of projects in this area mirrors to some degree the nascent nature of nanotechnology. Presently, only a limited number and volume of nano-enabled products are manufactured and marketed in the US. Systematic collection of exposure information is hindered by the lack of standardized methods, reference materials, protocols and field-ready and affordable instrumentation for exposure measurements. For example, health surveillance guidelines required to address Research Need #4 have become available in a draft form only recently and are only for occupational settings (http://www.cdc.gov/niosh/review/public/115/). As research priorities in other research categories, especially basic (the development of novel exposure measurement methods) and applied (translating unique measurements into routine field measurements) research in the Instrumentation, Metrology and Analytical Methods category, are addressed, research in the Health and Environment Assessment category can be conducted more effectively.

It is clear that greater efforts are needed to fully address all of the research priorities in this research category. In particular, emphasis should be placed at initiating research needed to address research needs 2, 3 and 4. In the near-term, Research Need #2 Identify population groups and environments exposed to engineered nanoscale materials has the highest priority, since addressing this need will facilitate and optimize research in research needs #'s 3 and 4 by identifying target population groups. Funding levels to address these research priorities are difficult to evaluate given the breadth of the scope of each priority and multiplicity of the agencies that need to be involved with such work. Efforts under the research needs #1 and #5 should be expanded to include exposure characterization and understanding in diverse workplace environments for a wide range of nanomaterials and processes through a complete product life cycle from nanomaterials manufacturing to its incorporation into consumer products to disposal and recycling.

Summary of the Gap Analysis by Research Priority

Research Need #1. Characterize exposures among workers

The purpose of one of the two projects falling under this priority is to develop intramural surveys that will obtain fundamental data on workplace exposures related to nanotechnology. The second project aims at collecting exposure information for workers at facilities manufacturing and using nanoscale and microscale titanium dioxide particles. The study objectives are: 1) to develop a strategy to measure exposure to nanoscale particles and 2) to characterize exposure to nanoscale and microscale TiO_2 for various jobs and tasks at various facilities manufacturing and using TiO_2. The results of the study will be used by NIOSH in setting recommendations to protect workers exposed to nanoscale and microscale TiO_2.

Research Need #5. Understand workplace processes and factors that determine exposure to nanomaterials.

Three projects falling under this priority look at broad characterization and analysis of factors influencing exposures in the workplace and more specifically at the evolution of nanoparticles emitted by production equipment in the workplace environment and its effect on the exposure potential.

The scope of one of the three projects under this priority is to foster the development of partnerships, exposure monitoring instrumentation, operational protocols, and a comprehensive and detailed database of nanoparticles and their properties. These activities are intended to provide the occupational safety and health community with a better understanding of the nature and extent of potential occupational exposures to nanoparticles. A second project aims at measuring the fate of nanoparticles, emitted through a leak in a nanoparticle production process into a workplace environment focusing on changes of the nanoparticle surface area. The third project will identify factors that influence the generation, dispersion, and deposition of nanomaterials in the workplace. The risk of exposure via inhalation or dermal contact will be quantified for benchmark nanomaterials with well defined physical and chemical characteristics.

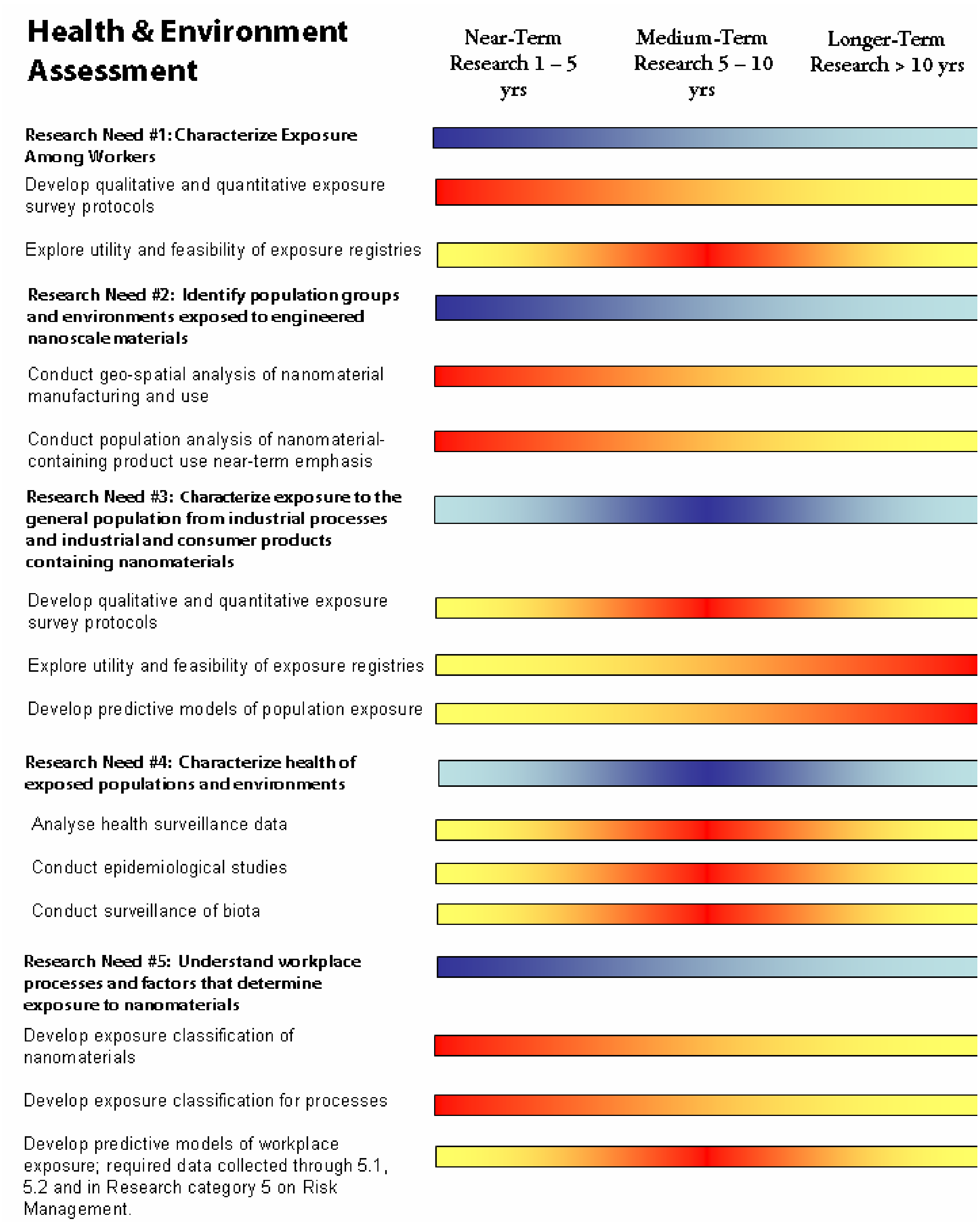

Figure 9. Relative emphasis as a function of time for priority research needs of the Health and Environment Assessment Category

Research in this category aims at characterizing exposures of workers, populations and environments by measuring and modeling exposure levels and by monitoring biological response indicators. Exposures can be assessed at different points in the Risk Assessment framework. Therefore, research needs in this category cross over all elements of the framework shown in Figure 10. Specifically research needs 1, 2 and 3 can be placed under the framework elements from Nanomaterials Life Cycle Stage to Internal Dose, while Research Need 5 fits under the framework elements from Nanomaterials Life Cycle Stage to Exposure of Environmental and Biological Systems. Research Need 4 can be described by the Biological Response and Ecological Effect element of the framework.

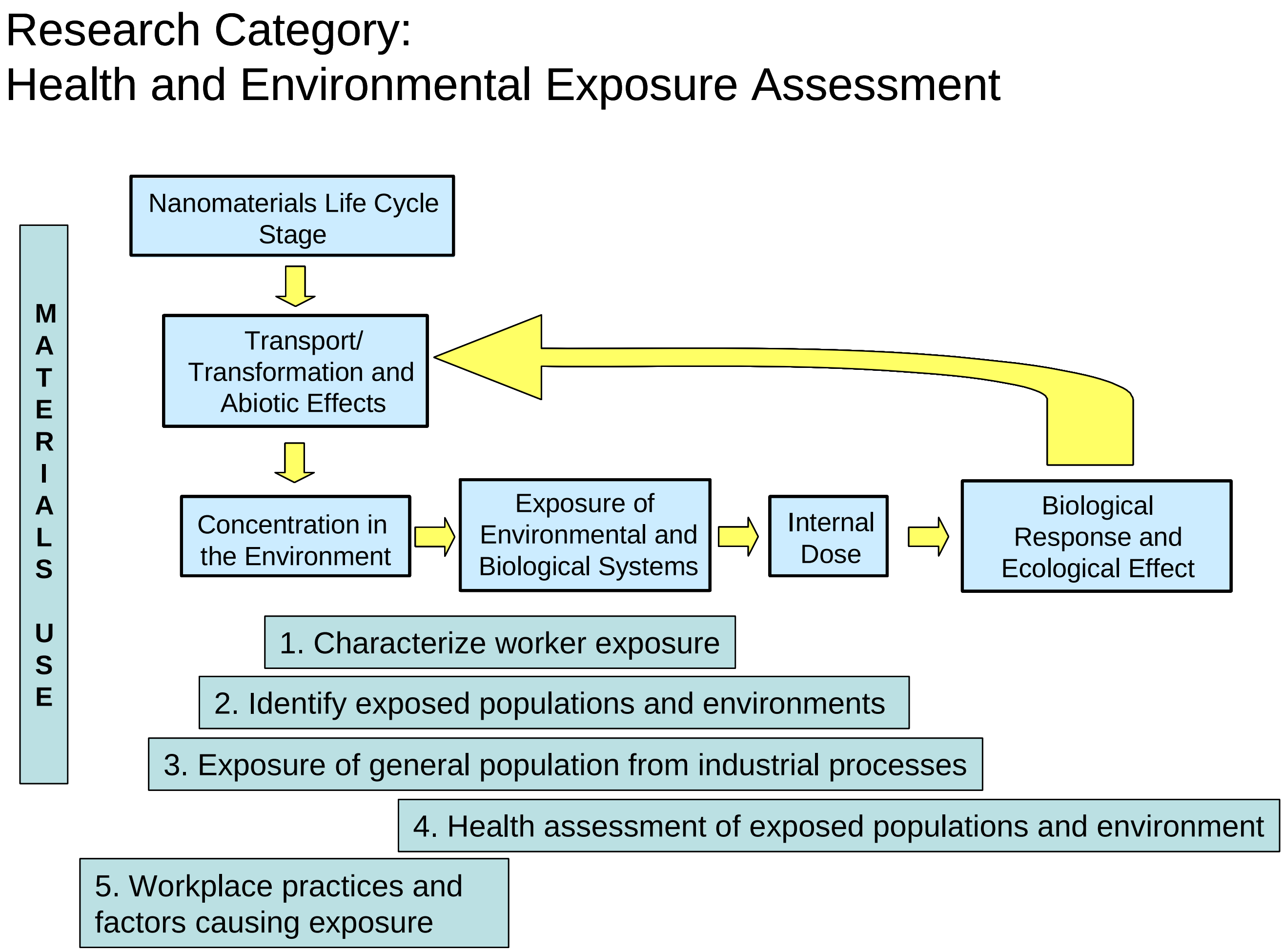

Figure 10. Framework for research supporting Health and Environmental Exposure Assessment

Research Category: Risk Management Methods

Total estimated funding in 2006: $3.3 M

Total projects: 14

Agencies supporting research in this category: AF, EPA, NIOSH, NSF

Prioritized Research Needs[1]	FY06 funding Estimate $K (% of total)	Number of Projects (% of total)
1. Understand and develop best workplace practices, processes, and environmental exposure controls	495 (15%)	4 (29%)
2. Examine product or material life cycle to inform risk reduction decisions	396 (12%)	2 (14%)
3. Develop risk characterization information to determine and classify nanomaterials based on physical or chemical properties	132 (4%*)	1 (7%*)
4. Develop nanomaterial-use and safety-incident trend information to help focus risk management efforts	--	--
5. Develop specific risk communication approaches and materials	231 (7%)	1 (7%)
Multiple: (Overarching research need) Evaluate the appropriateness and effectiveness of current and emerging risk management approaches for identifying those nanomaterials with the greatest potential risks	2046 (62%)	6 (43%)
Other: Not captured in needs above, but with benefit to the research category	--	--

**One project addressed needs 3 and 4 roughly equally*

Background

Research in this category focuses on methods for risk management of nanomaterials including but not limited to research on methods to reduce exposures to potentially hazardous nanomaterials; research to improve procedures for risk and accident avoidance; research to improve work practices, engineering controls, and protective equipment; and research to develop procedures for life cycle assessment.

Approximately two thirds of the funding and nearly half of the projects of this category are directed at the overarching need expressed in the priorities document rather than being separable to one or more of the five specific research priorities. The focus of much of the funding at such a general level may be appropriate for some sectors of nanotechnology ESH risk management research, given the stage of our understanding of the need for new risk management approaches. For example, it may first be necessary to step back and ask general questions regarding whether current risk management approaches are relevant and then parse out individual issues on the basis of that analysis.

Most of the funding identified as relevant to the RMM category was by NIOSH and NSF, which might be interpreted as a lack of funding (or a need for additional funding) by agencies that undertake risk management. However, the apparent lack of funding by regulatory agencies toward risk management methods research could be due to the data call having been focused primarily at grant-related efforts for a topic that may not always be addressed through research. The effectiveness of risk management approaches is likely to be addressed in many cases through agency analysis rather than through funded research. For example, several agencies have expended resources in the evaluation of risk management methods through workshops, task force efforts, white papers, peer reviews, and public meetings. While these more applied methods of evaluation would not be entirely captured as research, they should nonetheless be considered as part of the research need as expressed in the ESH document.

Therefore, when considering gaps for these needs it should be noted that relevant sources of information will be developed through government funding that may not be captured through future data calls or through evaluation of grant funding. Basic and detailed data collection under EPA's stewardship program will yield information relevant to this research need as well. Furthermore, data collection efforts through product development and review through FDA, EPA (e.g., pesticides), and other regulatory efforts are likely to generate information relevant to RMM priority needs. The evaluation of gaps for RMM needs should collect such information and consider its relevance to the specific research needs.

It is difficult to assess the total level of funding with regard to the need for funding. For example, conceptual analysis of existing risk management methods is not necessarily a costly research item. However, Research Need #'s 1, 2, and 3 are of a more distributed nature (for example, workplace controls and life cycle analyses are likely to be specific to a large number of independent contexts and so would need to be developed independently), and so would seem to require more funding than Research Need #'s 4 and 5. Similarly with respect to Research Need #3, developing hazard characterization information necessary for hazard management (for example in transport labeling or spill containment planning) would be substance specific and also involve baseline research into material properties.

Summary of the Gap Analysis by Research Priority

Research Need #1: Understand and develop best workplace practices, processes, and environmental exposure controls.

The projects falling under this need are general in nature with respect to nanomaterials, however, the primary focus is on airborne particles and controls directed at inhalation exposures.

The functionality of specific risk control methods, such as respirator and personal protection equipment, are being considered in the projects that have direct relevance to exposure mitigation. Particulate materials can to some extent be addressed in a general way for respiration, so research and development into these control measures should have wide application to many nanomaterials. As such, the focus of funding on the topics being addressed in this priority has a relatively high likelihood of utility and broad application. One project is also looking at specific characteristics of ultrafine (nanoscale) metallic particles generated in automobile manufacture. This attention to particle characteristics in specific risk management considerations is an important consideration. Broad evaluation of practices and needs is also being addressed, which is a necessary pre-requisite to identification of priorities for additional and more specific evaluations of scenarios and approaches to risk management.

Since this priority is focused on workplace, it is fitting that NIOSH is the only funding agency. While the topics being funded are appropriate, ranging from specific evaluation of respirator function to broad evaluation of practices and needs, it appears that the funding is just beginning to address the potentially wide range of scenarios and methods that could be evaluated with respect to specific novel needs for risk management methods in the workplace. For example, dermal and ingestion exposure routes were not included in FY 06 funding and should be considered. Segregation of analysis to types of particles and to classes of mitigation methods aimed at types of particles has been initiated for automobile manufacture, but should be extended to other particle types and scenarios, based for example on expected hazard or persistence. Because the number of scenarios is large, a necessary pre-requisite to this expansion of evaluation would be consideration of the priorities across potential scenarios.

Research Need #2: Examine product or material life cycle to inform risk reduction decisions.

The funded projects appropriately consider both the general case and specific cases of life cycle analysis (LCA). The EPA funded project is more general in nature but directed at manufacturing technologies rather than particular product types, and the NSF directed at a sector of products (photovoltaic).

Gaps may exist in the particular application of LCA evaluation to product classes that are not covered by the two approaches and projects. A systematic evaluation (such as may occur through the projects funded under the overarching research priority) is needed to evaluate where the most critical of such gaps would exist.

Research Need #3: Develop risk characterization information to determine and classify nanomaterials based on physical or chemical properties

Research Need #4: Develop nanomaterial-use and safety-incident trend information to help focus risk management efforts

Research needs 3 and 4 were addressed roughly equally by one project. The NIOSH "Nanoparticle Information Library" (NIL) seeks to collect, on a voluntarily submitted basis, data on nanomaterial characterization and uses. It will make some information relevant to risk-based classification of nanomaterials (Research Need #3) and to use information (Research Need #4).

Research Need #'s 3 and 4 are not fully addressed by the research funded in FY 06, representing a gap in the research. No projects related to identifying safety-incidents were identified in the funding. Because the data in the NIL project is based on voluntary submissions, it is unlikely to provide comprehensive or consistent coverage of either risk characterization information or trend information on uses. More comprehensive and consistent data across types of materials and industrial sectors is needed so that the information can be used to inform risk management needs.

Research Need #5: Develop specific risk communication approaches and materials. The one project identified under this priority will develop communication products such as web pages, NIOSH numbered documents, technical publications and presentations, to communicate and disseminate research results and recommendations on the health and safety issues involved in nanotechnology. It will also foster development of key stakeholder partnerships in the manufacturing sector to effectively disseminate the products of the project.

This research need was only being addressed by one agency in the FY 06 funding, and that project addresses only workplace related issues. Furthermore, the project addresses specific dissemination of risk communication related materials, rather than the evaluation of risk communication issues and approaches that may be specific to nanotechnology applications. More widespread attention to the need should be initiated, at least in the sense of evaluating whether and what risk communication methods or materials specific to nanomaterials may be warranted. However, the general evaluations of risk management methods being carried out by the bulk of the funding under this category (falling under the overarching need) is likely to address some of this baseline evaluation of what is needed.

Projects Addressing Multiple Research Needs: The majority of the projects under the risk management methods category fall under the overarching need of "Evaluate risk management approaches for identifying and addressing risks from nanomaterials" rather than specific priorities. The 5 projects have broad scopes with regard to evaluation of factors that feed into risk management and so may provide information and perspectives of similar level of coverage to the general considerations of the NNI EHS document. This replication of coverage may provide independent viewpoints that will potentially provide greater assurance of complete consideration of what is important and relevant to identifying and managing risks. The broad evaluation of risk management approaches and needs is also a pre-requisite to prioritized selection of more detailed analysis of specific scenarios under which risk management methods may need evaluation and attention.

The projects seek to provide information and promote collaborations on general questions ranging from ethics and public perception to frameworks for addressing risk evaluation and management to evaluation of regulatory and legislative frameworks and consideration of net benefits of the development of the technology. An important consideration for this level of funding and the general nature of the tasks may be that the projects will overlap and be inefficient or seem contradictory. It is also difficult to ascertain what portions of the funding are directly relevant to the RMM research category, though all projects seemed to have components with high relevance.

It should be noted that issues not typically thought of as pertaining directly to risk management needs, such as ethics and societal considerations, are included in the projects that fall under this category. The relevance of these topics to research priorities is neither clarified nor dismissed in the present analysis, and should be the subject of further evaluation.

Summary of balance issues

The balance of funding in 2006 for risk management methods research is weighted toward more general analyses of approaches rather than specific activities. Furthermore, the specific activities that are represented, such as evaluation of respirator materials in workplace settings, tend to focus on occupational controls and inhalation exposures within the occupational setting. While the focus on occupational inhalation exposures is fitting given that worker populations are likely to be the first affected in product development and production, future funding should also include other scenarios and other exposure pathways. The selection of those scenarios and pathways to include should follow from activities such as life cycle analysis over a broader range of materials than was seen in the 2006 funding, and general evaluations of the existing risk management approaches so that scenarios and pathways are chosen that represent the greatest use of resources to reduce potential risks.

Trend information, and even current information, on uses of nanoscale materials in commerce and consumer products is generally not addressed in 2006 funding, and is generally lacking. Trend and use information is of critical importance to comprehending current and future exposure potential and scenarios in which risk management methods or practice changes may be needed. Trend and use information should be increased in balance in future year funding.

Stemming somewhat from this lack of use and trend information is a similar lack of risk characterization information that could feed into risk management methods. Risk management methods that could use this kind of information would for example include exposure controls or even simpler methods and needs such as Material Safety Data Sheets with regard to changes to inhalation potential, or Department of Transportation hazardous material placards in cases where flammability or reactivity are affected by particle size. The development of this kind of information should receive a higher emphasis in future year funding.

Figure 11 presents relative timing of research needs. The sub-bars under each of the 5 main research needs represent relative timing information for details of research needs that were included in the September 2006 NNI EHS Research Needs Document

Figure 12 presents a conceptual framework for the relationship between risk management methods research, other research activities, and the overall decision context that is supported by these research efforts. Any research to support decisions is at least in principle preceded by a decision need, which then, to the degree necessary would stimulate either the collection of existing data (literature review) or the development of new data that would be applied to a risk assessment. The risk assessment scope would be shaped both by the decision need and to some degree by the available data. The risk assessment would then be considered along with risk management methods to lead to a decision or choice among risk management alternatives, if possible given the certainty of the conclusions with regard to the outcomes of the alternatives. Research could be called for at the decision phase instead of, or in addition to, selection of a risk management alternative. The numbered boxes refer to relative contribution of research needs identified in this document for Risk Management Research.

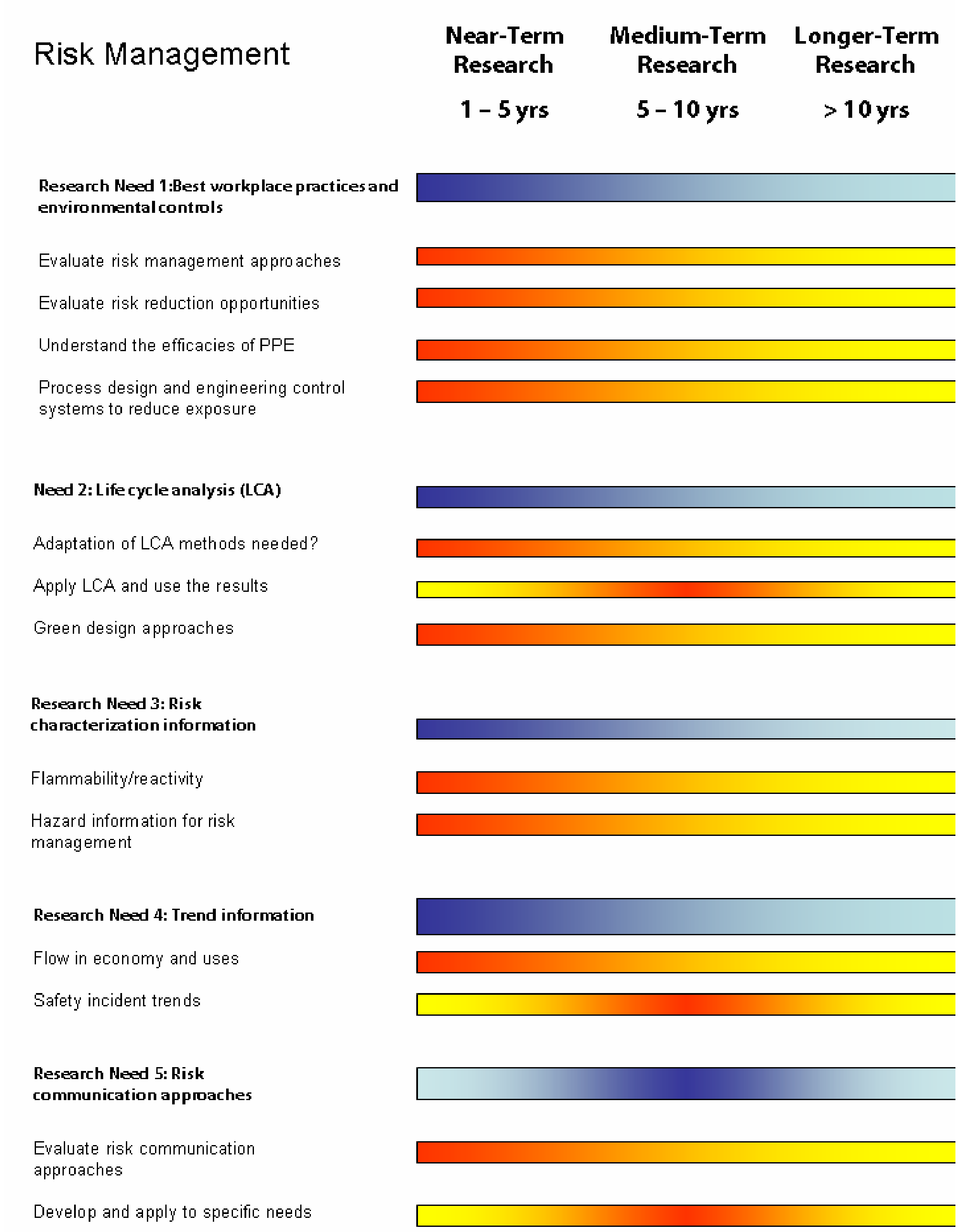

Figure 11. Relative emphasis as a function of time for research on priority research needs for the Risk Management Methods category

Research Category: Risk Management Methods

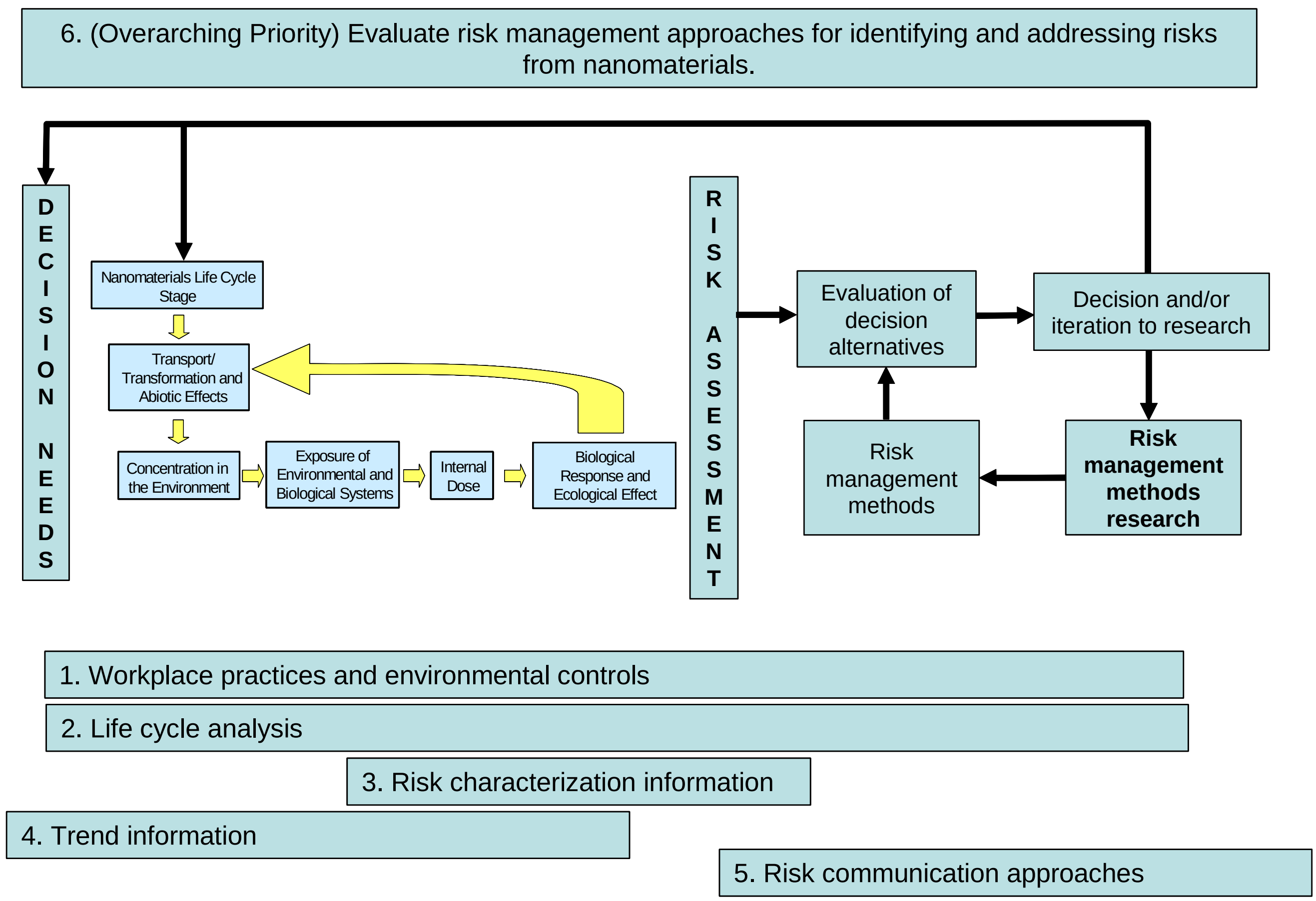

Figure 12. Framework for research supporting Risk Management Methods category

Current balance of research investment.

Between 2005 and 2007, the NNI invested over $120 million on EHS research as defined and reported in the NNI budget supplements. The NNI agencies estimate spending $XX million on EHS research in 2008 and have requested $XX million in the President's Budget for 2009. As noted previously, the annually reported EHS research figures do not capture all of the research that is related to the research needs discussed in this document. This is due to the fact that spending reported in the budget supplement is for research that is primarily focused at understanding potential risks. It does not include research that is aimed primarily at applications or at characterization and measurement of nanomaterials, which has utility beyond EHS risk assessment and risk management. In 2006, the amount reported in the annual budget for EHS research was $38 million. However, the total amount spent on research related to the EHS research needs in 2006 as reported in Section II is $68 million—nearly 80 percent more than the amount reported in the budget. A large fraction of the additional research is that reported under the category of instrumentation, metrology, and analytical methods and to a lesser extent under the category on Nanomaterials and Human Health. The data for EHS spending in 2006 show wide variation in funding level and number of projects among the five research categories. Although the five categories have not been prioritized with respect to each other, there is consensus that instrumentation, metrology, and analytical methods are cross-cutting, supporting research in every other category, and therefore is generally a high priority. Likewise, there are high priority areas of research on health and environmental effects of nanomaterials, as described in Section II. Research on exposure assessment and risk management methods are recognized as critical to risk assessment and risk management. However, some of the research in these areas requires input from other research categories. Therefore, it is appropriate that investments at this time are predominantly in the categories of metrology and health and environmental effects. The balance of spending will evolve in time as research programs mature and efforts that are undertaken sequentially are initiated.

Based on the detailed information available for 2006, it is possible to estimate the spending for the broader range of relevant research, assuming it remains 80 percent greater than the amount reported in the budget. This assumption seems reasonable based on the recognition, especially since 2006, of the importance of instrumentation and metrology for EHS and other aspects of nanotechnology development. Based on this assumption, the estimated spending for the broader range of EHS research would be $105 million in 2007 and an estimated $XXX million in 2008. The request for 2009 would lead to a projected $XXX million for research related to the five categories reported here for 2006. The total calculated estimate for the broad research needed to support risk decision making for 2006 through 2009 is $XXX million. These estimates are approximations; however, they highlight the fact that considerable research is being supported beyond what is captured in the list of projects shown in Appendix A.

The current and future research that is within the scope of the five research categories is diverse in a number of dimensions. This research is highly multidisciplinary, involving researchers from many fields such as chemistry, materials science, biology, engineering, computer science, and medicine. It ranges from basic research to increase fundamental understanding of the properties and behavior of nanomaterials in various environments to applied research, such as development of instrumentation for cost-effective measurement of workplace exposure to nanomaterials. There is research that should continue to be supported in the near term and research that need not or can not be initiated until a future date when additional capabilities or information is available. Finally, the breadth of research that is covered by the 2006 EHS Research Needs document calls for a similarly broad range of activities by many entities—various agencies, industry, and other governments.

III. Framework for addressing needs

Introduction

Addressing the research areas that are identified in this report as needing increased research investment and effort involves multiple agencies that support research and/or use the resulting information. This document has been developed with the participation of all these agencies and represents an overarching assessment of the near term and long-term research needs as presently understood that will support risk assessment and risk management of nanomaterials.

However, it is essential to maintain perspective on the overarching opportunities in nanotechnology-related EHS research that cut across the categories and needs delineated. Continuing basic research to understand fundamental biological responses to nanomaterials remains one such overarching opportunity. For example, modeling and simulation development based on first principles (i.e., more analytical than empirical) will significantly advance nanotechnology EHS research. Similarly, and establishing consensus-based standards, such as a minimum data sets for particular nanomaterials and classes, will broadly facilitate integrative and progressive EHS research. Seizing these broad opportunities in parallel with addressing particular research needs will collectively shorten nanomaterial development timelines and streamline decision making on toxicity and other EHS implications. These opportunities constitute priorities in parallel with identified research gaps, and highlight the need to maintain a broad-based, balanced investment.

Summary and prioritization of gaps or needs to rebalance both within and among categories

Based on this analysis of the 2006 snapshot of Federal funding of EHS research, some of the key gaps in need of new or increased research efforts—particularly in the near-term areas—include the following:

Instrumentation, Metrology, and Analytical Methods (all near term)

- Analytical methods for identifying and measuring the critical parameters related to nanomaterials in biological systems, the environment, and the workplace
- Develop new quantitative nanoscale metrologies and databases of properties
- Develop methods for standardizing assessment of particle size, size distribution, shape, structure, and surface area (rebalance)
- Increase efforts to develop certified reference materials specifically for toxicology and environmental studies (rebalance)

Human Health

- Develop and validate methods to quantify dose-response or structure-activity relationships, including parameters (near-term; links strongly to metrology)
    - Determine measurement parameters relevant for classes of nanomaterial (in priority order based on reasonable expectation of exposure)
    - Develop methods to quantify and characterize biological response
- Translate in vitro test results into in vivo models
- Extrapolate data to human exposures (mid to long-term)

Environment

- Evaluate and modify currently accepted test protocols for assessing effects in individual biological receptors, and improved dose-response characterization.

- Identify principle sources of, and routes for, exposure to environmental receptors based on nanomaterial/commercial product manufacture.
- Identify key physical/chemical properties affecting transport/transformation of nanoparticles.

These results from these near-term needs should assist in follow-on efforts to develop new test protocols for assessing effects in biological receptors, improve understandings of ADME in relevant receptors, and develop predictive tools and robust testing schemes to streamline reviews of commercial nanomaterials. In the areas of exposure, and transport and transformation, again predictive tools and models should result which increases the ability to judge the overall exposures to commercial nanomaterials throughout their life cycles. Finally, work from all of these areas will contribute to evaluating the potential for higher-level ecological effects.

Exposure Assessment

- Identify population groups and environments exposed to engineered nanoscale materials
- Characterize exposure to the general population from industrial processes and industrial and consumer products containing nanomaterials
- Characterize health of exposed populations and environments

Risk Management Methods

- Develop risk characterization information to determine and classify nanomaterials based on physical or chemical properties.
- Develop nanomaterial-use and safety-incident trend information to help focus risk management efforts.
- Expand exposure route-specific risk management methods research and life cycle analysis research on the basis of nanomaterial use scenarios expected to present greatest exposure and potential for health or ecological effect.

The member agencies have examined each of these particular needs carefully, and with respect to each gap, the agencies have agreed within the interagency context to assume the roles identified below to address these gaps in a manner consistent with their specific missions and available resources.

Implementation of strategy for nanotechnology-related EHS research

The framework for implementation outlined below describes the various activities and coordination needed to address these gaps as well as the full spectrum of NNI EHS research. It also provides for participation, interaction, and partnership with non-Federal stakeholders to leverage their efforts and to expedite progress.

- **Support broad base of research to facilitate regulatory decision making and to expand the horizons of nanotechnology-based applications for the environment and health.** The EHS research strategy fundamentally depends on sustaining the broad spectrum of basic research, with support from agencies that fund basic research on the fundamental properties of nanomaterials (including NSF, DOE, NIST, and NIH). The current balance of research funding addresses such basic investigations and supports regulatory decision making. Gaps identified in the research that supports regulatory decision making should not be addressed at the cost of broad-based fundamental research--to do so would ultimately undercut the U.S. nanotechnology initiative as a whole.
- **Coordinate existing and foster expanded agency efforts to address priority research needs and identified gaps.** The NEHI will continue to facilitate coordination and increasing collaboration among the NNI agencies' research programs to address priority research needs both individually and jointly, leverage investment and expertise, and avoid duplication of effort within each research category.

    - A workshop on each research category will be held in 2008-2009 to assess the state of science, current research, and to reassess areas of weakness and gaps. Participants will include representatives from both contributor and user NNI agencies, academia, and industry.
    - Facilitate development of joint programs among NNI member agencies to address research needs of mutual interest.
    - Clarify priorities and areas of focus specific for agencies and collaborations
    - Avoid redundancy and/or marginal research (e.g., research that is decoupled from real-world application)
    - Identify synergistic opportunities
- **Establish regular review process**. The NEHI will conduct periodic progress review and updating of the research needs and priorities, taking into consideration advances from private sector and international entities.
- **Facilitate partnerships with industry.** The NEHI will explore and develop mechanisms with participating agencies for partnering with industry to support priority research that reduces risk uncertainty facing the range of businesses and industry sectors that are commercializing nanomaterials for beneficial and practical applications. One example is the planned NIH NanoHealth Enterprise, an interdisciplinary cross-sector program to integrate critical materials science and biology research and support informatics and training needs for the safe development of nanoscale materials and devices. Organizations like the Foundation for the NIH may provide appropriate authority and structure to facilitate and execute such partnerships.
- **Coordinate efforts internationally.** Participate actively in international efforts, particularly in the OECD Working Party on Manufactured Nanomaterials (WPMN) related to research. In particular, the WPMN efforts to develop internationally agreed EHS research priorities and to share relevant information.
- **Focus on development of consensus-based documentary standards to support oversight.** Participate in and support efforts by national and international standards development organizations to develop nanotechnology-related documentary standards particularly those related to EHS research.
- **Facilitate wide dissemination of research results.** Participate in and support activities aimed at broadly disseminating available information about EHS aspects of nanomaterials. Such activities include those already underway in the OECD WPMN, the ISO Technical Committee on Nanotechnologies (TC 229) Working Group on Health, Safety and Environment, and by the International Council on Nanotechnology (ICON).

Interagency coordination to address EHS research needs

In addition to the investments by individual agencies, Federal spending on nanotechnology-related EHS research also includes coordinated interagency research activities and solicitations. This interagency document will guide programs and investment decisions in the coming years, including investments by the individual agencies and coordination of interagency activities. In fact, the priorities identified in the 2006 EHS Research Needs document and participation of program managers in the development of this document already have influenced agency planning. However, because the agencies have various missions, their individual priorities may differ in scope and extent from those outlined in this report. Annual spending by each agency for nanomaterials EHS research will be determined by not only the priorities described in this document, but also by agency-specific priorities and needs. For this reason, strong interagency coordination is essential.

The NEHI Working Group is perhaps unique among interagency bodies focused on research in giving a lead role in setting priorities to regulatory agencies. Moreover, as users of the research results, the regulatory agencies can benefit from being more than just customers for the research and by helping to coordinate activities and keep attention focused on top priorities.

As stated in the 2007 NNI Strategic Plan, "The NNI consists of the individual and cooperative nanotechnology-related activities of twenty-five Federal agencies with a range of research and regulatory roles and responsibilities. … The NNI as a program does not fund research; however, it informs and influences the Federal budget and planning processes through its member agencies." In the context of this document, both statements hold true for nanotechnology-related EHS research as one component of the overall research and development coordinated through the NNI.

With this understanding and within the roles and responsibilities stated in the charters for the NSET Subcommittee and the NEHI Working Group, member agencies of the committee and working group have agreed among themselves to assume the roles indicated in Table X to move the Federal efforts in nanotechnology-related EHS research forward. There are three roles identified for the agencies for each of the five categories: 1) coordinating agencies, indicated by a ◆ in the table, are those agencies that have agreed to take a leadership role in coordinating and communicating with other NNI member agencies concerning agency needs and the ongoing adaptation of NNI research priorities to new discoveries and new materials; 2) contributing agencies, indicated by a ○ in the table, are those that have funded or are planning to fund or conduct research within their missions that is expected to contribute knowledge, information, or new discoveries to the category; and 3) user agencies, indicated by a ▣ in the table, are those that have expressed a need for research outputs or information to support their agency's missions and responsibilities, whether that be mission agency research needs or regulatory agency needs for information to support their regulatory decision making.

Table X. Roles of Agencies with regard to EHS Research Needs

◆ –Coordinating Agency ○ – Contributor □ – User

Agency \ Research Need	Instrumentation, Metrology, and Analytical Methods	Nanomaterials and Human Health	Nanomaterials and the Environment	Health & Environmental Exposure Assessment	Risk Management Methods
NIH	○□	◆	□	□	
NIST	◆	○	○	○	○
EPA	○□	○□	◆	○□	◆
FDA	□	□	□	□	◆
NIOSH	○□	○□	○	◆	○□
NSF	○*	○*	○*	○*	○*
DOD	□	□	○□	□	○□
DOE	○□	□	□	□	□
USDA	□	○□	○□	□	□
DOT		□	□	□	□
OSHA	□	□		□	□
CPSC	○□	□	□	○	○
USGS	○□		○□	○□	

All coordinating agencies have roles as contributors to and users of the research from the respective categories, with the exception of FDA which is a user as well as a coordinating agency.

* NSF is a contributor according to the mission of the agency covering the upstream, fundamental research on utilization, implications, and risk mitigation of nanotechnology, infrastructure and education.

The NEHI Working Group represents a strong network of individuals across the Federal government. In many instances, agency representatives to the NEHI Working Group are representing intra-agency networks, such as the FDA Nanotechnology Task Force. In the Office of Management and Budget, one person is identified as responsible for coordinating with the budget examiners for all of the NNI agencies to assess EHS and other research government-wide. Not unlike the internet, this highly interconnected "network of networks" is both flexible and robust in its capacity to support the NNI EHS research program. The functional aspects of this network are supported by the National Nanotechnology Coordination Office (NNCO).

The NEHI Working Group network provides a forum for notifying participants of agency-specific research programs and the broad range of activities related to nanomaterials. It also has led to a number of jointly supported activities, including jointly supported EHS research.

The overall NNI EHS research strategy also directly relies on the activities and plans of individual agencies with respect to their respective missions and areas of focus. The table below briefly summarizes many of these activities and highlights

Agency	**Nano EHS Research, Activities, Plans, and Strategic Efforts** (individual and joint)
EPA	▪ *Volunteer Nanoscale Materials Program* launched, January 2008 ▪ *Nanomaterial Research Strategy* (in development) ▪ Joint solicitation with NSF and NIEHS or other multi-agency EHS [title/aim] ▪ Collaboration with NSF and DOE will result in the awarding of an additional $4M to support health impacts research in the first half of 2008 ▪ Research funded: over $22 million (as of FY 2007) of relevant research since NNI inception ($12.2M supporting 35 projects environmental applications and $18.3M supporting 52 projects to study potential health and ecological impacts) ▪ See http://www.epa.gov/oppt/nano/ and http://es.epa.gov/ncer/nano/
FDA	▪ Continue to develop responses to the 2007 FDA Nanotechnology Task Force report. ▪ Continue collaboration with the National Cancer Institute's Nanotechnology Characterization Laboratory ▪ Seek to develop collaborative research relationships through exploration of Public Private Partnerships ▪ Continue efforts aimed toward international harmonization and collaboration through available bilateral cooperation mechanisms and as necessary through multilateral organizations such as the Organization for Economic Cooperation and Development (OECD), CODEX ALIMENTARIUS, the International Council on Harmonization, and other similar organizations. ▪ Continue participation in nanoscale material toxicity research funded through the National Toxicology Program. ▪ INSERT website
NIOSH	▪ Interim guidance on medical screening of workers potentially exposed to manufactured nanomaterials ▪ Nanotechnology Field Teams site visit partnering industrial, academic, military, and research organizations to conduct baseline assessments of occupational exposure to engineered nanomaterials (17 to date). ▪ Updating *Strategic Plan for NIOSH Nanotechnology Research* originally released in 2005 by assessing the state of knowledge in occupational safety and health aspects of nanotechnology and conducting a critical gap analysis of research needs using *Progress Toward Safe Nanotechnology* in Workplace (http://www.cdc.gov/niosh/docs/2007-123/). The updated Strategic Plan will outline NIOSH strategy to lead occupational safety and health community collaboratively in nanotechnology research. ▪ INSERT website

NIH	▪ Through its research project grants and coordinated center programs, NIH supports extensive, fundamental research on nanomaterials and their biologicals interaction that broadly informs and supports EHS research.
	▪ The National Cancer Institute established the Nanotechnology Characterization Laboratory (NCL) in collaboration with NIST and FDA to provide critical infrastructure and nanomaterials characterization services for cancer reseachers. Progress includes:
	    o Continued development of assays and methodologies to characterize nanoparticles' physical attributes, their *in vitro* biological properties, and their *in vivo* compatibility using animal models.
	    o Accelerated transition of basic nanoscale particles and devices into clinical applications.

Agency	**Nano EHS Research, Activities, Plans, and Strategic Efforts** (individual and joint)
	▪ National Institute of Environmental Health Sciences (NIEHS) continues to build our understanding of possible human health effects of nanomaterial exposure through multiple research efforts, including: o Funding of five new extramural grants in 2007 o Initiation of the NanoHealth Enterprise, a partnership of NIH institutes, federal agencies, and public and private partners to support research to address critical research needs for the safe development of nanoscale materials and devices. ▪ The National Toxicology Program (NIEHS) through its Nanotechnology Safety Initiative continues research on: o Non-medical, commercially relevant and available nanoscale materials to which humans are intentionally being exposed, such as cosmetics and sunscreens o Nanoscale materials representing specific classes such as fullerenes (buckyballs) and metal oxides so that information can be extrapolated to other members of those classes o Subsets of nanomaterials to test specific hypotheses about a key physiochemical parameter such as size, composition, shape, or surface chemistry ▪ http://www.becon.nih.gov/nano.htm
NIST	Nanotechnology is a research focus for NIST with a direct emphasis on innovation and traceable measurements to advance not only the development of standards for nanotechnology enabled products and devices, but also the necessary national-scale measurement infrastructure to support the EHS aspects of nanomaterials. Specifically, NIST continues to • Provide a scientific basis to the health and environmental effects of nanotechnology • Enable US industry to safely develop, exploit, commercialize nanotechnologies • Leverage nanotechnology standards development work among other Federal programs • Establish direct collaborations with other Federal agencies • Work with representatives from the risk assessment and regulatory communities represented by not only government, but also academia, industry, and the international community • Work with standard development organizations • Collaborate with the National Cancer Institute's Nanotechnology Characterization Laboratory and the Food and Drug Administration on the development of a battery of characterization tools for preclinical evaluation of nanomaterials and devices intended for cancer therapeutics • Sponsor stakeholder driven nanotechnology workshops and meetings Physical characterization of nanomaterials ▪ Develop standard reference materials ▪ INSERT website
NSF	NSF provides foundational knowledge, education, and infrastructure for EHS in support of nanotechnology and other agency missions. NSF-sponsored research addresses the three sources (natural, incidental, manufactured) of nanostructured materials in different environmental settings (air, water, soil, biosystems, and the work environment), as well as the non-clinical biological implications. The programs are upstream, looking for the utilization, implications and mitigation of the effects of the current and new generations of nanomaterials. These topics are supported through programs in all research directorates. There are several EHS priorities for the societal dimensions of nanotechnology. They are: ▪ New measurement methods and instrumentation for nanoparticle characterization in air, soil

Agency	**Nano EHS Research, Activities, Plans, and Strategic Efforts** (individual and joint)
	and water, for exposure rates and for toxicity of nanomaterials, ▪ Transport phenomena of nanoscale aerosols and colloids, interaction of nanomaterials with cells and living tissues (human, animal and plant); ▪ Physico-chemical-biological processes of nanostructures dispersed in the environment and at the working place; develop models for predicting impact of nanomaterials on health and safety over the entire life cycle ▪ Separation of nanoparticles from fluids, including water filtration ▪ The safety of manufactured nanoparticles ▪ Research on risk governance methods ▪ Development of user facilities, and ▪ Educational programs NSF has established an environmental component of this NNI investment since FY 2001 and now spends about 7% of the nanotechnology budget for this purpose. The NSF estimation for EHS is $28.28 million (7.2% of nanotechnology) in FY 2008, and $30.64 million (7.7% of nanotechnology request) in FY 2009 Request. This includes a new multidisciplinary center in collaboration with EPA to conduct fundamental research on the environmental, health, and safety impacts of nanomaterials. This research will explore the interactions between particles and materials at the nanoscale and the living world with development of innovative methods of investigation and instrumentation. http://www.nsf/nano
US Army ERDC	US Army Engineer research and Development Center (ERDC) is leading the way to understand the unique environmental attributes of engineered nanomaterials used in military applications and potential changes in risk over the life cycle of nano-enabled products. Specifically, ERDC Nanomaterials Risk Research Cluster is focusing on: ▪ Advanced characterization of nanomaterial properties and risks for technology improvement and risk reduction ▪ Risk and decision analysis tools for prioritizing technology needs for product developers ▪ Collaborations with commercial and governmental technology developers to address priority materials ▪ Characterizations of the fate and toxicology of engineered nanomaterials in environmental systems ▪ Recognized leadership and advising role to the Office of the Secretary of Defense, and the North Atlantic Treaty Organization (NATO)
USGS	▪ Research activities of the Contaminant Biology Program and the Toxic Substances Hydrology Program focus on environmental occurrence, fate and effects. ▪ USGS is in the planning phase for additional research on nanoparticles in the environment. ▪ Science on nanoparticles is a component of the recently published USGS Science Strategy, Facing Tomorrow's Challenges—U.S. Geological Survey Science in the Decade 2007–2017.

With the continued growth in EHS research, both within and outside the Federal government, the NNI needs mechanisms that ensure the current level of coordination is sustained. In addition to the existing efforts of the NEHI Working Group and the bottom up development of multi-agency activities and research programs that address agency needs and the research priorities of the NNI, the implementation plans described will help ensure a sustained level of coordination that is currently in place as EHS research continues to grow, both within and outside the Federal government.

Given the early stage of nanomaterials development and their commercialization, as well as the expected increase in information and knowledge about potential risks, the NNI will need to periodically review and update the research priorities. The workshops described above will provide input to such an update, which is anticipated to be necessary every 3-5 years. Furthermore, as part of the legislatively-mandated review of the NNI by the President's Council of Advisors on Science and Technology and the National Academies, it is anticipated that the NNI EHS research strategy will receive independent review and oversight of coordination, progress, implementation, and management in the appropriate context of the overall NNI interagency coordination through the NSET Subcommittee, its working groups, and the NNCO.

V. Appendix—FY2006 EHS Research Projects (NNCO)

This Appendix provides information on one of the steps being used by the NSET Subcommittee to develop a strategy for the federal government to move forward in its approach to funding and conducting nanotechnology EHS research, namely, examining the portfolio of federally funded nanotechnology EHS research. This step is one of the six steps being used to develop a federal government strategy for nanotechnology EHS research: 1) identifying priority research needs in the field of nanotechnology EHS research; 2) choosing the top 25 broad research needs for nanotechnology EHS research; 3) examining the portfolio of federally funded nanotechnology EHS research; 4) identifying weaknesses and/or gaps in the government nanotechnology EHS research; 5) developing a strategy to address the weaknesses and/or gaps in the government portfolio; and finally, 6) periodically reviewing progress toward addressing identified needs and updating the research needs and priorities to take into consideration the introduction of new materials, new research discoveries, and advances made by entities other than U.S. Government-funded bodies.

In carrying out this step, all NNI member agencies funding nanotechnology R&D evaluated their 2006 portfolios in the areas of environmental, health, and safety research R&D for engineered nanoscale materials. To assist with this formative analysis of research programs, the Office of Management and Budget (OMB) issued a one-time call for the agencies to "select from your agency's nanotechnology R&D those FY2006 projects that contribute to the five major categories of EHS R&D identified in EHS Research Need document: (1) Instrumentation, Metrology, and Analytical Methods; (2) nanomaterials and Human Health; (3) Nanomaterials and the Environment; (4) Health and Environmental Exposure Assessment; and (5) Risk Management Methods."

The research reported in response to this call is more extensive than what has been previously reported in the annual NNI supplements to the President's budget. EHS R&D funding reported under the Societal Dimensions Program Component Area (PCA) in the budget supplements is limited to efforts whose primary purpose is to understand and address potential risks to health and to the environment posed by nanotechnology. For the special OMB data call reported herein, agencies were asked to also include those portions of projects reported under other PCAs which are directly relevant to EHS research needs. This captures, for example, the development of instruments for environmental surveillance reported under the Instrumentation, Metrology, and Standards PCA. It also captures an appropriate portion of projects from the National Institutes of Health, which may include research on safety as part of a larger effort to develop health-related nanotechnology reported under other PCAs.

NSET-NEHI representatives worked with agency program staff to verify that each reported project was relevant to one or more of the five major EHS R&D categories. Funding for projects relevant to more than one of the five research needs categories was subdivided whenever each subentry exceeded $50,000, and at the reporting agency's discretion for lesser amounts exceeding 10% of the project total. As the interagency group analyzed the results of the data call, projects were assigned both in terms of the kind of information developed (some information is of greater relevance to supporting risk management than other) and the appropriate sequencing of research (some research should be timed to occur following other research in order to gain the greatest benefit to risk management needs). Projects relevant to more than one category or need were assigned to the need that was primarily being addressed by the research. In a small number of cases, it was not possible to identify a single primary need and these were categorized as addressing "multiple" needs. In some cases, projects were related to the overarching research category, but did not align with any of the top five priority areas identified for a given category. These projects were categorized as addressing "other" needs.

In the use and analysis of these data to identify strength, weaknesses, or gaps with respect to the overarching research needs, the interagency group of experts considered carefully the following limitations of this snapshot of the growing nanotechnology EHS research program. Readers of this document should be equally mindful of these limitations.

- The data represent only research funded in 2006. Many projects are multi-year and therefore actual research associated with projects listed may have taken place in earlier or later years. However, projects begun after 2006 are not captured.
- Projects listed are prospective, that is they are planned research not research results. Basic research projects may diverge from the original proposal, based on initial results or as other information becomes available.
- The list represents only Federally funded research. It does not include any research in these areas that is supported by industry, nonprofit organizations, or other countries.

The tables of nanotechnology EHS projects that follow are grouped by research needs category, research need, funding agency, and type of funding (intramural, extramural, SBIR). They provide the following information for each project:

- Index number – a unique identifier for each project, which may also be used to retrieve award abstracts and additional information on the project from the NNI website www.nano.gov.
- Lead Institution – the institution of the lead principal investigator for the project
- Award ID – Grant, contract, or project number as assigned by the funding agency
- Project – the project title (or a brief description where no title was available)
- Notes – additional information to clarify why the project is relevant to the category and/or particular research need if the title or research topic description was not viewed as adequately descriptive.

Instrumentation, Metrology, and Analytical Methods

Research Need: *Develop methods to detect nanomaterials in biological matrices, the environment, and the workplace*

No. of Projects 36

NIOSH Extramural

Lead Institution	Award ID	Project	Notes
Johns Hopkins University	1R21MH074703-01A1	Power Harvesting In Implanted Neural Probes	This Work Is In The Neural Micro/Nano Systems Area within a biomedical instrumentation laboratory. The development of technologies for recording from neurons or the brain and developing interfaces, at molecular/cellular and at the systems level, are under study. Micro- and nanotechnology are utilized for the fabrication of sensors.
Johns Hopkins University	5R01DK068399-02	Non-viral Liver-targeted Gene Delivery	Project supports the synthesis and characterization of nanomaterials targeted for biological study. Nanomaterials are characterized at the tissue level, the cellular level in the liver, and at the subcellular level by various techniques including electron microscopy.
MONTANA STATE UNIVERSITY (BOZEMAN)	5R21EB005364-02	Targeted MRI with Protein Cage Architectures	
Pinnacle Technology, Inc.	1R43MH076318-01	A TURNKEY, WIRELESS, EEG/EMG/BIOSENSOR MEASUREMENT	In combination with other intracellular measurement techniques, which may involve nanoparticles like quantum dots, this technique will make easier to correlate electrophysiological measurements with intracellular biochemical or genetic pathway measurements. These simultaneous, combined measurements are important and are not currently done.
SANDIA CORP-SANDIA NATIONAL LABORATORIES	5R21EB005365-02	Flourescent Ceramic Nanoprobes	
TDA Research, Inc.	5R21EB005390-02	Cut Nanotube Capsules for MR Imaging	
UNIV OF MASSACHUSETTS MED SCH WORCESTER	3P01DK060564-	Membrane Topography of Cell Signaling Complexes	This program project combines biochemical, structural and imaging approaches to study proteins and effectively combines divergent techniques such as X-ray crystallography, live cell imaging using digital imaging microscopy with laser-based illumination, and powerful deconvolution algorithms to achieve resolution at the nanometer level.
University of Chicago	1R21MH078822-01	Surface Plasmon-Coupled Fluorescence Microscope to Study Ion Channel Dynamics	This work supports nano- to micro scale fluorescence measurements of electric fields in molecules.
UNIVERSITY OF CALIFORNIA IRVINE	5R21MH075059-02	MORPHOGEN GRADIENTS IN MICROFLUIDIC CULTURES	In combination with other intracellular measurement techniques, which may involve nanoparticles like quantum dots, this technique will make easier to correlate electrophysiological measurements with intracellular biochemical or genetic pathway measurements. These simultaneous, combined measurements are important and are not currently done.
University of Florida	2R01DK047858-10A1	A study of model beta-cells in Diabetes Treatment	Project will pave the way for further imaging studies in tissue engineering that may be applicable to the nanoscale.
University of Texas SW Med. Ctr.	5R21EB005394-02	MFe2O4-Loaded Polymer Micelles as Ultra-Sensitive MR Mo*	
WASHINGTON STATE UNIVERSITY	1R01MH071830-01A2	IMPLANTABLE 16-256 CHANNEL DATA SYSTEM FOR SLEEP IN MICE	In combination with other intracellular measurement techniques, which may involve nanoparticles like quantum dots, this technique will make easier to correlate electrophysiological measurements with intracellular biochemical or genetic pathway

measurements. These simultaneous, combined measurements are important and are not currently done.

NIOSH Intramural

Lead Institution	Award ID	Project	Notes
	1Z01HD000261-09	Develop fiber-optic cofocal microscoope with nanoscale depth resolution	The development of methods and instrumentation to image tissues and study biological phenomena with nanoscale resolution are critical elements of this work.

NIST Intramural

Lead Institution	Award ID	Project	Notes
		Quantum Optical Metrology	
		Nanoscale Engineering Sensors	
		Single Photon Sources and Detectors	
		Characterization Methods	
		Surface Metrology	
		Dimensional Metrology	
		Comp. Semic Quantum Nanowires	
		High throughput hyperspectral data analysis using	
		Phase Sensitive Scatterfield Imaging	
		Ultimate fate of nanoparticles	

NSF Extramural

Lead Institution	Award ID	Project	Notes
Boston University	448796	CAREER: Integrated Research and Education in Nano and Microscale Photoacoustic and Photothermal Microscopy	Metrology efforts support development or improvement of methods to detect nanomaterials.
California Institute of Technology		CAREER: Engineering Nucleic Acid Devices (3/15/05 - 2/28/10)	Work is targeted to understanding and developing new principles and the construction of versatile and inexpensive biosensors with nanoscale sensitivity.
Duke University	547273	CAREER: Hybrid Nanomaterials for Multi-Functional Sensors - Synthesis and Characterization of Nanocomposite Thin-Films for Device Applications	Metrology efforts support the development or improvement of methods to detect nanomaterials.
Florida State University	084173	National High Magnetic Field Laboratory (NHMFL); The NHMFL's Fourier Transform-Ion Cyclotron Resonance Mass Spectrometer is unique in the world in analyzing small samples of potentially toxic nanomaterials and their environment	Metrology efforts support development or improvement of methods to detect nanomaterials.
Northwestern University		NSEC: Institute for Nanotechnology (NU)	Efforts aimed to develop state-of-the-art instrumentation for detection of nanoparticles with high accuracy and sensitivity.
Rensselaer Polytechnic Institute	522656	Selective Filling of Nanostructured Packings for Chromatographic Chip Systems	Work in this area is aimed at developing a highly efficient chromatographic chip system able to separate nanoparticles, detect the presence of nanoparticles, and prepare samples by particle size for further chemical and biological characterization.
University of California, Berkeley		NSEC: Center Of Integrated Nanomechanical Systems (COINS)	Projects are targeted to the development and use of two closely related nanosensor systems: (1) a new personal and community-based sensor for the environmental monitoring of nanoparticles, and (2) technology for the chemical/biological sensing of nanoparticles with integrated communication and power for tagging, tracking, and locating applications.
University of Massachusetts Amherst	531171	NSEC: Network for Hierarchical Manufacturing	Metrology efforts support development or improvement of methods to detect nanomaterials.
University of Minnesota-Twin Cities	114372	IGERT: Nanoparticle Science and Engineering	Metrology efforts support development or improvement of methods to detect nanomaterials.
University of	425780	NSEC: Center for Molecular Function at	Work is targeted at developing new instrumentation

Pennsylvania		the Nanoscale	for detection and characteization of nanoparticles in biosystems (such as near-field optical tomography for 3-D structure, multiple modulation scanning probes of molecular function, and combined laser tweezers and polarized fluorescence for single molecule motion.
University South	0528873	SST - Ferroelectric Thin-Film Active Sensor Arrays for Structural Health Monitoring	The advancement of nano investigative techniques are a critical component of this project including a range of microscopy techniques.
Wayne State University	522005	Molecular Simulation of Chemical Warfare Agent Adsorption	Efforts targeted to investigation and design of nanostructured molecular sieves using molecular and atomistic simulation for detection of toxic industrial materials at the nanoscale/molecular level.
Wayne State University	552772	REU Site for Nanoscale Structures and Integrated Biosensors (NSIB)	Metrology efforts support development or improvement of methods to detect nanomaterials.

Research Need: *Understand how chemical and physical modifications affect the properties of nanomaterials*

No. of Projects: *14*

DOE Extramural

Lead Institution	Award ID	Project	Notes
		Single Molecule Fluorescence in Nanoscale Environments	
		Diffraction Studies of Glasses, Liquids, and Nanoclusters	
		Manipulation and Quantitative Interrogation of Nanostructures	
		The Reaction Specificity of Nano Particles in Solutions	
		Nano-Structures Examined with Spin-Polarized Positron Beams	
		Using Plasmon Peaks in Electron Energy-Loss Spectroscopy to Determine the Physical and Mechanical Properties of Nanoscale Materials	
		New Methods and Instrumentation for the Study of Complex Magnetic Materials and Nanostructures Using Soft X-Ray Spectroscopies	

NIOSH Extramural

Lead Institution	Award ID	Project	Notes
ALBANY STATE UNIVERSITY	5P20MD001085-02	Biotechnology Research Infrastructure at ASU - Investigation of aggregation on thin films for gold nanoparticles and nanorods (1P20 MD001085)	Project will use nanotechnology to develop the basic science of nano particle thin films which could lead to the novel nanotechnology based sensors for biomaterials with an affinity for gold (i.e homocysteine, cysteine, etc.) and other functionalized surfaces. Supports efforts to understand and characterize nanoparticle surfaces and modifications to such surfaces.
EMV TECHNOLOGIES, LLC	1R41DK074254-01	Nano-Porous Alumina Membranes for Enhanced Hemodialysis Performance	
NORTHWESTERN UNIVERSITY	5R21DK072450-02	Bladder Tissue Engineering through Nanotechnology	Effects of modifications of materials under study, with an application focus.
University of California Berkeley	3P42ES004705-19S10031	PROJECT 6: USE OF OXIDANTS PRODUCED BY NANOPARTICULATE & GRANULAR ZERO-VALENT	Provides insight into the processes occurring on or near ZVI surfaces. Techniques designed to probe the surface, such as potentiometry, surfaceenhanced Raman spectroscopy and electrochemical quartz microbalance methods under investigation.

NIST Intramural

Lead Institution	Award ID	Project	Notes
		Nano Biotech	
		Theoretical models of chemical properties of nanostructures.	
		Nanocharacterization - NCI	

Research Need: *Develop methods for standardizing assessment of particle size, size distribution, shape, structure, and surface area*

No. of Projects 4

DOE Extramural

Lead Institution	Award ID	Project	Notes
University of Texas		A Fundamental Study of Transport Within a Single Nanoscopic Channel	Quantification of mass transport through single-nanopore models having well-defined structures is important and an essential foundation for many technologically significant processes including size-based separations. Such work supports the development of methods for the determination of particle size.

NIOSH Extramural

Lead Institution	Award ID	Project	Notes
NEW YORK UNIVERSITY SCHOOL OF MEDICINE	1R01OH008807-01	Monitoring and Characterizing Airborne Carbon Nanotube Particles	

NIST Extramural

Lead Institution	Award ID	Project	Notes
		Nanoparticle risk impact and assessment program	

NSF Extramural

Lead Institution	Award ID	Project	Notes
University of Arkansas Little Rock	526977	IMR: Developement of an Analyzer for Size and Charge Characterization of Nanoparticles in Research and Training	

Research Need: *Research which meets multiple priority needs via activities on characterization and the development of tools or infrastructure to support measurements*

No. of Projects: *2*

NSF Extramural

Lead Institution	Award ID	Project	Notes
Cornell University	335765	National Nanotechnology Infrastructure Network (NNIN)	
University of Idaho	447689	EPSCoR: Idaho Research Infrastructure Improvement	Work that is targeted to development and use of nanosensors in aqueous environmental settings.

Research Need: *Develop certified reference materials for chemical and physical characterization of nanomaterials*

No. of Projects: *6*

NIH Extramural

Lead Institution	Award ID	Project	Notes
GEORGIA INSTITUTE OF TECHNOLOGY	1R01DK073991-01A1	Cryopreservation of tissue engineered substitutes	This project focuses on the development of tissue engineered substitutes with an emphasis on understanding the effects of cryopreservation on cells and on biomaterials. Such work is critical for the groundwork on the development of reference materials that would be cell- or bio-based, for example bio-based materials that may be implanted with nanomaterials.

NIH SBIR

Lead Institution	Award ID	Project	Notes
LNKCHEMSOLUTIONS	5R43ES013367-02	SUBMICRON PARTICLES AND FIBERS FOR TOXICOLOGICAL STUDIES	

NIST Intramural

Lead Institution	Award ID	Project	Notes
		Nanotube Processing	
		SPM Reference Specimens	
		R&D for Carbon Nanotube Reference Materials	
		R&D for Nanoparticle (non-carbon nanotube) Reference Materials	

Research Need: *Develop methods to characterize a nanomaterial's spatio-chemical composition, purity, and heterogeneity*

No. of Projects: *15*

DOE Extramural

Lead Institution	Award ID	Project	Notes
		Directed Energy Interactions with Surfaces	
		Three-Dimensional Imgaging of Nanoscale Materials by Using Coherent X-rays	
		High Resolution Lenseless 3D Imaging of Nanostructures with Coherent X-Rays	
		Atomic Scale Chemical Imaging in 3 Dimensions	
		Studies of Nanoscale Structure and Structural Defects of Advanced Materials	
		Microscopy Investigations of Nanostructured Materials	
		Electron Diffraction Determination of Nanoscale Structures	
		Quantitative Electron Nano-Crystallography and Nano-Spectroscopy	
		Chemical Analysis of Nanodomains	

NIOSH Extramural

Lead Institution	Award ID	Project	Notes
MINIATURE TOOL AND DIE	1R43DK074237-01	Thin-walled Micromolding	Measuring flow in nano-volumes and furthering the evaluation of the physical properties of materials at this scale supports metrology needs and the development of methods to characterize a material's composition, purity, or heterogeneity.

NIST Intramural

Lead Institution	Award ID	Project	Notes
		Nanostrucutre Fabrication and Metrology	
		Chemical Imaging of 3D nano structures	

NSF Extramural

Lead Institution	Award ID	Project	Notes
Colorado State University	310717	Engineering Research Center for Extreme Ultraviolet Science and Technology	Goal is to make EUV light, now mostly limited to a handful of large national facilities, available routinely in a broad variety of laboratory settings, for applications such as high-resolution imaging, spectroscopy, elemental- and bio-microscopy, and nano-fabrication.

Lead Institution	Award ID	Project	Notes
SUNY at Stony Brook	449268	CAREER: Multi-Scale and Multi-Disciplinary Aspects of Indentation	Work is targeted to obtaining small samples from the surface of nanostructured materials or nanostructured particles in order to characterize them and obtain spatial distribution of the nanomaterial properties.
University of California - Merced	619398	Acquisition of a Powder X-ray Diffractometer for Environmental and Materials Research at UC Merced	

Research Need: *Research within the category but not captured in the five priority needs*

No. of *1*

NSF Extramural

Lead Institution	Award ID	Project	Notes
Virginia Polytechnic Institute and State University	610213	SGER: MEMS-Based Preconcentrators with Nano-Structured Adsorbents for Micro Gas Chromatography	Work is targeted to using nanostructured thin films for improving the performance of sorbents in gas chromatography for improving gas analysis, with applications in homeland security, monitoring food freshness, industrial process control, biomedical diagnostics, and surveying environment quality. This is an application of nanomaterials for improving measurements in environmental and occupational safety.

Nanomaterials and Human Health

Research Need: *Overarching Research Priority: Understand generalizable characteristics of nanomaterials in relation to toxicity in biological systems.*

No. of Projects: 2

NIH Extramural

Lead Institution	Award ID	Project	Notes
WASHINGTON UNIVERSITY	5U01HL080729-03	Integrated Nanosystems for Diagnosis and Therapy	The EHS component is identified as the animal core in this center will perform a systematic review of the chain lengths and branching, as well as composition of polymer-based structures, including biodistribution and excretion

NIOSH Intramural

Lead Institution	Award ID	Project	Notes
NIOSH Nanotechnology Safety and Health		Coordination	

Research Need: *Understand the absorption and transport of nanomaterials throughout the human body*

No. of Projects: 13

NIH Extramural

Lead Institution	Award ID	Project	Notes
		Physicochemical characterisation and formulation of fullerene C60 and titanium dioxide	
Nanomedex, Inc	2R44GM072142-02	NanoMedex Propofol Microemulsions: Preclinical Studies to FDA IND Application	The goal of this grant is to make a nanoparticle-based emulsion of the propofol, a widely used anesthetic. The EHS-relevant component of this research is to determine the pharmacokinetic effects and biocompatibility properties of this emulsion using in vivo model systems.
North Carolina State University	5R01CA098194-04	Multifunctional Nanoparticles for Intracellular Delivery	
SUNY at Stony Brook	5R44GM063283-04	Bioabsorbable Membranes for Prevention of Adhesions	The goal of this grant is to develop anti-adhesion nanostructured products that reduce the formation of internal adhesions after surgery. The EHS-relevant component of this research is to assay for biocompatibility of these nanostructured products using *in vitro* methods.
University Of Florida	5R01GM063679-04	Local Anesthetic Cardiotoxicity: Nanotechnology Therapy	

NIOSH

Lead Institution	Award ID	Project	Notes
NIOSH		Generation & Characterization of Nanoparticles	

NIOSH Extramural

Lead Institution	Award ID	Project	Notes
OHIO STATE UNIVERSITY	1R01OH009141-01	Role of Surface Chemistry in the Toxicological Properties of Manufactured Nanoparticles	

NIOSH Intramural

Lead Institution	Award ID	Project	Notes
		Nanoparticles: Lung Dosimetry and Risk Assessment	
		Particle Surface Area as a Dose Metric	

NSF Extramural

Lead Institution	Award ID	Project	Notes
Old Dominion University Research Foundation	507036	NIRT: Design of Biocompatible Nanoparticles for Probing Living Cellular Functions and Their Potential Environmental Impacts	
Clemson University	630823	SGER: Aquatic Nanotoxicology of Nanomaterials and Their Biomolecular Derivatives	
Ohio State University	425626	NSEC: Center for Affordable Nanoengineering	The overarching goal of this center is to design and fabricate polymer-based, 3D nanofluidic circuits for manipulating the shape, orientation and transport behavior of individual biomolecules in well-defined nanoscale flow fields. The EHS focus of this work lies in designing and assessing transport and biocompatibility of various nanostructures in the test system. This will include development of polymer-based low-cost nanoengineering technology that can be used to produce nano-fluidic devices and multifunctional polymer-nanoparticle-biomolecule nanostructures for the next generation medical diagnostic and therapeutic applications. Biocompatibility issues will be addressed in parallel with the development of new nano-fluidic designs and devices. It fits in Nano-Health, Priority 6 (with relevance to understanding general processes and applications)
University of Florida	609311	NER: Novel Cell Culture Stylus for the Rapid Assessment of Functional Nano-Bio Interfaces	

Research Need: *Develop methods to quantify and characterize exposure to nanomaterials and characterize nanomaterials in biological matrices*

No. of Projects: 29

AFOSR Extramural

Lead Institution	Award ID	Project	Notes
		Multidisciplinary University Research Initiative (MURI): Effect of nanoscale materials on biological systems: Relationship between physicochemical properties and toxicological properties	

EPA Extramural

Lead Institution	Award ID	Project	Notes
North Carolina State University	R833328	Impact of physicochemical properties on skin absorption of manufactured nanomaterials	

NIH Extramural

Lead Institution	Award ID	Project	Notes
Brown University	5P42ES013660-030002	Genotoxic Potential of Mixed Dust Exposures	This grant uses ambient nanoparticles.
Case Western Reserve University	5R21CA112436-02	Design of Targeting Enhancement for Drug Delivery	The objective of the proposal is to apply a combined theoretical and experimental approach to gain fundamental understanding of the physical principles of targeting by complex polymer nanoparticles. The EHS-relevant component of this research will supply an experimental practitioner with specific recommendations concerning the grafting density, PEG chain length, architecture, nanoparticle size and density of functional groups that ensure effective targeting of nanoparticles.
Emory University	5U54CA119338-02	Emory-Ga Tech Nanotechnology Center for Personalized and Predictive Oncology	The EHS component derives from research that integratse nanotechnology with cancer biomolecular signatures and will provide data on the interaction of nanomaterials with cells.
Massachusetts General Hospital	5R01DK064850-04	*In vivo* imaging of diabetogenic cytotoxic T-lymphocytes	The goal of this project is to use iron oxide nanoparticles for enhanced MR imaging. The EHS-relevant component of this research is the mechanistic understanding of cell uptake of nanoparticles.
Massachusetts Institute of Technology	5U54CA119349-02	The MIT-Harvard Center of Cancer Nanotechnology Excellence	This grant has a Toxicity Core and a Mouse Models Core that will provide *in vivo* information about nanomaterials behavior in model systems.
Northeastern University	5R01CA119617-02	Nanotherapeutic Strategy for Multidrug Resistant Tumors	In the proposed study, the strategy to overcome multi-drug resistance in chemotherapy relies on a multifunctional approach to optimize delivery of pro-apoptotic drugs to the tumor mass, using tumor-targeted biodegradable polymer-based engineered nanocarriers for encapsulation of the drugs. The EHS-relevant component of the study will develop, characterize, and optimize long-circulating, biodegradable polymeric nanocarriers and evaluate the uptake, distribution, and intracellular concentrations of carried drugs.
Northwestern University	5R33DK066990-03	Nanoparticle, Raman-based Fiber-optic Glucose Sensor	This grant will provide data on the implantation of noble metal nanoparticles in the skin.
Northwestern University	5U54CA119341-02	Nanomaterials for Cancer Diagnostics and Therapeutics	The EHS component involves the use of nanomaterials in living systems and the evaluation of the biocompatibility and biodistribution of materials in the bosy and within cells.
Oregon Health and Science University	5R01NS034608-10	CNS Gene Delivery and Imaging in Brain Tumor Therapy; Using viral-sized nanoparticles as a model for virus particle uptake	The goal of this project is to use iron oxide nanoparticles for enhanced MR imaging. The EHS-relevant component of this research is the mechanistic understanding of influx and uptake of nanoparticles to the brain.
Rice University	1R21CA118778-01	NIR Absorbing Nanoparticles For Cancer Therapy	The EHS component of the grant will evaluate biodistribution, biocompatibility and tumor ablation efficacy of these NIR-absorbing nanoparticles.
Stanford University	1U54CA119367-01	Stanford Center of Cancer Nanotechnology Excellence	The goal of this project is to employ nanoparticles for imaging. The EHS-relevant component is the mechanistic understanding of nanoparticle uptake and cell interaction.
Synergene Therapeutics, Inc.	1R41CA121453-01	A Tumor-Specific Nanoimmunocomplex Markedly Improves MR Imaging	The EHS copmponent will better characterize nano-immuno-liposomes in animal models, determine optimized dose, optimal time to imaging, and perform toxicity studies in mice
University of California San Diego	5U54CA119335-02	Center of Nanotechnology for Treatment, Understanding, and Monitoring of Cancer	The goal is the development, of a multi-functional "smart mothership" platform that will: (1) evade the reticuloendothelial system and immune system, while attaching specifically to the tumor and its vasculature; (2) assemble a multi-functional complex at the tumor site; (3) deliver payloads of both nanosensors and therapeutics that are activated *in situ.* The EHS-

			relevant component project focuses on the production of tumor-targeted, non-toxic nanoparticles
University of Michigan Ann Arbor	5R01CA119409-02	DNA-Linked Dendrimer Nanoparticle Systems for Cancer Diagnostics	The goal of this project is to employ dendrimer modules linked by oligonucleotides for targeted delivery of chemotherapeutic agents and for imaging. The EHS-relevant component is the mechanistic understanding of nanoparticle uptake and cell interaction.
University of Nebraska Medical Center	5R01NS050660-02	Bioengineering of the blood-brain barrier permeability; development, characterization, and use of nanogel carriers through the BBB	The goal of this project is to use Nanogel for targeted drug delivery across the blood/brain barrier. The EHS-relevant component of this research is the mechanistic understanding of brain uptake of nanoparticles.
University of North Carolina Chapel Hill L	5U54CA119343-02	Carolina Center of Cancer Nanotechnology Excellence	This project will bring together nano-particle engineering with the understanding/treatment of cancer for the delivery of therapeutic, detection and imaging agents for the diagnosis and treatment of cancer. The EHS-relevant component of the project is the fabrication of "smart" functional particles for studies and evaluations. This will allow the fabrication of nano-biomaterials to accelerate translational understanding, detection and treatment of cancer.
University of Texas MD Anderson	5R01CA119387-02	Near-Infrared Fluorescence Nanoparticles for Targeted ….	The goal of this project is to develop novel nanoparticles for molecular optical imaging applications for human cancers. The EHS-relevant component of the project will establish the effect of particle characteristics on the pharmacokinetics, biodistribution, clearance, extravasation, and intratumoral distribution of the nanoparticles.
University of Texas MD Anderson	5R01DK067683-04	Imaging Tumor Blood Vessels in Bone Metastases from Breast Cancer	The goal of this project is to use nanoshells for enhanced MR imaging. The EHS-relevant component of this research is the mechanistic understanding of cell uptake of nanoparticles.
University of Utah	5R01CA097465-03	Polymer Chelate Conjugates for Diagnostic Cancer Imaging	The goal of this project is to employ gadolinium nanoparticles for targeted delivery of chemotherapeutic agents and for imaging. The EHS-relevant component is the mechanistic understanding of nanoparticle biodistribution and clearance.
University of Utah	5R01CA101850-04	Engineered Intelligent Micelle for Tumor PH Targeting	The primary purpose of this research is to engineer functional polymeric micelles which target solid tumors in acidic extracellular fluid and utilize acidic endosome to treat sensitive and multidrug resistant tumors. The EHS-relevant component is to design biodegradable polymers sensitive to tumor acidity and to engineer polymeric micelles with or without targeting moiety that can truly recognize tumor pile or endosomal pH for triggered release, while keeping a minimal release rate during circulation.
University of Washington	5R21CA114143-02	Nanoparticles for Efficient Delivery to Solid Tumors	The goal of this research is to harness forces generated by actin polymerization to propel nanoparticles within the interstitial space by energy-mediated, cell-to-cell transfer, thus resulting in more efficient nanoparticle penetration. The EHS-relevant component of this research will demonstrate modifications that produce efficient delivery systems.
University of Washington	5R21NS052030-02	Nanoparticles for siRNA delivery to mammalian neurons; designing nanoparticles that will move through the CNS	The EHS component will characterise the interaction of nanoparticles with neurons.
Washington University	5U54CA119342-02	The Siteman Center of Cancer Nanotechnology Excellence	The goal of this project is to employ nanoparticles for targeted delivery of chemotherapeutic agents and for imaging. The EHS-relevant component is the mechanistic understanding of nanoparticle uptake and cell interaction.

NIOSH Intramural

Lead Institution	Award ID	Project	Notes
	1Z01DK043400-07	Early Detection of Renal Injury	The goal of this project is to use gadolinium nanoparticles for imaging. The EHS-relevant component of this research is the mechanistic understanding of nanoparticle uptake, distribution, and clearance.

NSF Extramural

Lead Institution	Award ID	Project	Notes
North Carolina State University	602906	Materials World Network: Designer Nanodiamonds for Detoxification	
University of Minnesota-Twin Cities	553682	SGER: Nanostructured Interfaces for Targeted Drug Delivery	NSF project #184 has 50K in funding that is aimed at understanding and designing nanostructured interfaces for drug delivery targeting that specifically binds to infection or inflammation sites in human body. This engineered formulations of fractalkine-targeted stealth liposomes, their transport properties and binding capabilities will be evaluated *in vitro*.
University of Minnesota-Twin Cities	646507	Lung Deposition of Highly Agglomerated Nanoparticles	

Research Need: *Identify or develop appropriate in vitro and in vivo assays/models to predict in vivo human responses to nanomaterials exposure*

No. of Projects: 39

AFOSR Extramural

Lead Institution	Award ID	Project	Notes
ONAMI		Safer Nanomanufacturing	
University of California, Riverside	CA-R*-NEU-7524-H	Identifying Critical P-C characteristics of NP that elicit toxic effects	The goal of this grant is to determine the relationship between the toxicity and physicochemical characteristics of nanoparticles. The EHS-relevant component of this research is to develop methodologies to characterize nanoparticles and test nanomaterials for toxicity using *in vitro* and *in vivo* techniques.

AFOSR Intramural

Lead Institution	Award ID	Project	Notes
		Biological Interaction of Nanomaterials	

EPA Extramural

Lead Institution	Award ID	Project	Notes
University of Utah	R833336	Effects of ingested nanoparticles on gene regulation in the colon	

NIH Extramural

Lead Institution	Award ID	Project	Notes
		Tumorigenicity of Photoactive Nanoscale Titanium Dioxide in Tg.AC Transgenic Mice	Research performed by the National Toxicology Program will provide improved understanding of biological mechanisms and interactions of engineered nanomaterials. The research will also enhance scientific knowledge of how such materials are transported withing and between biological components. This research is EHS-relevant.
Barnes-Jewish Hospital	3R01AR032788-19S1	Mechanisms of Orthopedic Implant Osteolysis	This grant studies the mechanism of orthopedic implant osteolysis and other forms of inflammation-induced bone loss to understand the mechanisms of interaction between nanomaterials and the body at the molecular, cellular and tissue levels.

BRIGHAM AND WOMEN'S HOSPITAL	5R01DK065939-03	Novel Lentiviral Packaging Systems	A portion of this grant will examine the interaction of Nanomaterials with viral perticles.
CASE WESTERN RESERVE UNIVERSITY	1R21NS053798-	Stimulus-responsive, Mechanically-dynamic Nanocomposite for Cortical Electrodes; Developing polymer and investingating the tissue response	The EHS component will test the the chronic astrocytic and tissue response to a polymer nanocomposite.
CASE WESTERN RESERVE UNIVERSITY	5R21CA112436-02	Design of Targeting Enhancement for Drug Delivery	The grant tests nanomaterials in *in vitro* binding study and cell uptake study
LYNNTECH, INC.	1R43DE017505-01	New Nanoparticles for Antimicrobial Therapy of Dental Plaque Related Diseases	The goal of this project is to develop a new antimicrobial photodynamic therapy based on nanomaterials for the treatment of oral diseases. The EHS-relevant component is to conduct cytotoxicity assays of the fullerene photosensitizers.
MASSACHUSETTS GENERAL HOSPITAL	5U01HL080731-03	Translational Program of Excellence in Nanotechnology	The goal of this project is to develop nanotechnology application for better diagnosis and treatment of heart, lung, blood and sleep disorders using noninvasive imaging and sensing, targeted therapies, tissue repair and regeneration and drug delivery. The EHS-relevant component is to develop multidimensional cell screens to rapidly and sensitively test biosafety of novel materials.
NANO INTERFACE TECHNOLOGY, INC	5R43AR051249-02	Nano-Apatite Coating of the Porous Surface of Implants	The EHS component will test the biocompatibilty and toxicity of unagglomerated nanoparticles of the carbonated hydroxyapatite as well as coating of Ti-alloy with nanoparticles of carbonated hydroxyapatite that are used in implanted devices .
NANOMECH, LLC	5R43DE015730-02	Nanocoatings for Biomedical Implants	The goal of this project is to develop a nanoparticle coating of hydroxyapatite on titanium dental implants. The EHS-relevant component is to test biocompatibility of the coated dental implants. That is, the performance of the coated dental implants in terms of biocompatibility and effects on osteoblast adhesion, will be tested in cell cultures and compared with that of porous-graded cp-Ti samples without HAp coating.
NEW YORK UNIVERSITY SCHOOL OF MEDICINE	1R01ES015495-01	LONG TERM CARDIOVASCULAR EFFECTS OF INHALED NANOPARTICLES	
NEW YORK UNIVERSITY SCHOOL OF MEDICINE	1R01ES015495-01	Inhalation Toxicity of Fullerene C60	As the title indicates, this research is geared towards understanding interactions between engineered nanomaterials and various biological components, both at molecular and cellular levels. This research is EHS-relevant.
NORTHWESTERN UNIVERSITY	5P50NS054287-02	Center of Excellence in Translational Human Stem Cell Research; investigating the effects of nanogels on hESC and then using those for regeneration	The EHS component utilizes bioactive peptide amphiphiles that can self-assemble into nanofiber scaffolds which will be used for cell culture and delivery. Project 2 (Kessler) will use nanofiber scaffolds in his spinal cord injury model to seed stem cells as a treatment. Core B (Stupp) will manufacture the nanofiber matrices using photopolymerizable peptide amphiphiles (IKVAV, YIGSR, RGD or EIKLLIS sequences from laminin and fibronectin).
NORTHWESTERN UNIVERSITY	5R01DE015920-02	Nanotechnology Strategies for Growth of Bones and Teeth	The goal of this project is to develop peptide nanostructures for bone mineralization. The EHS-relevant component is to test overall biocompatibility and biodegradation of peptide nanostructures. That is, scaffold biodegradation, inflammatory zone, and the vascular invasion level will be evaluated by Masson's trichrome stains (MTS) and H&E stains using light and confocal microscopy
ROSWELL PARK CANCER INSTITUTE CORP	5R01CA104479-02	Imaging Nanocomposites Targeting Tumor Microvasculature	This project will provide provide information on functionalised nanogold.
RUSH UNIVERSITY MEDICAL CENTER	5R01AR039310-15	Systemic Implications of Total Joint Replacement	This grant investigates metallic degradation products of total joint replacement to understand the

			mechanisms of interaction between nanomaterials and the body at the molecular, cellular and tissue levels.
SCRIPPS RESEARCH INSTITUTE	5R01CA112075-03	Using Viral Nanoparticles to Target Cancer	The EHS component investigaes the behavios of viral nanoparticles *in vivo*.
SEPULVEDA RESEARCH CORPORATION	1U01AG028583-01	Curcumin and Curcumin derivatives for Alzheimer's	A portion of this grant will evaluate the efficacy, bioavailability and toxicity of a curcumin lipid nanoparticles *in vivo*.
UNIVERSITY OF ALABAMA AT BIRMINGHAM	5R01DE013952-06	Nanotechnology in Osseointegration of TMJ Implants	*In vivo* biocompatibility testing of nanostructured diamond and calcium phosphate ceramics will be carried out using standardized model systems,including injection of particulate debris, plus soft and hard tissue evaluations of particulates and implants. The *in vivo* part will be carried out in collaboration with an oral and maxillofacial clinician/surgeon at UAB, who actively participates in the area of TMJ surgical reconstruction.
UNIVERSITY OF CALIF-LAWRENC BERKELEY LAB	5R01DE015633-04	Complex Nanocomposites for Bone Regeneration	The goal of this project is to develop hydroxyapatite crystal structures for bone mineralization. The EHS-relevant component is to test new composite materials *in vitro* in cell cultures and *in vivo* in an animal model.The behavior of the developed new composite material will be tested *in vitro* in cell cultures.
UNIVERSITY OF CALIFORNIA SAN FRANCISCO	5R01CA107268-04	Pharmacology of Targeted Therapy to Brain Tumors	The goal of this grant is to develop non-viral gene nanoparticle carriers to target brain tumors. The EHS-relevant component of this research is to characterize the factors that optimize the ability of nanolipoparticles to target brain tumors and enhance the therapeutic efficacy of nanolipoparticles using in vitro and *in vivo* techniques.
UNIVERSITY OF CINCINNATI	1R21DE017703-01	Designing ECM-Inspired Peptide Biomaterials for Regenerative Medicine	The goal of this project is to engineer new biomaterials formulated from self- assembling peptides or peptidomimetics to produce synthetic extracellular matrices useful for tissue repair or regeneration. The EHS-relevant component is to understand the humoral and cellular immunologic response to the multimerizing peptides.
University of Illinois at Chicago	5R01AG024026-03	Micellar VIP Nanoparticles for Rheumatoid Arthritis	The grant will test the ability of a disease-related molecule to self-associate with 17nm phosopholipid particles and will examine biocompatibility and biodegradability. The EHS research will explore how proteins interact with nanovesiclea.
University of Illinois at Chicago	5R01DE016533-03	Biomimetic Scaffold for Bone-Repair	To assess the immune response to the new peptide amphiphiles single-branched RODS nanofiber gels were transplanted intraperitoneally in isogeneic C57BL/6 strain mice. After 30 days *in vivo*, the gels were removed for histochemical analysis the branched RGDS nanofiber scaffolds appear to produce only mild, non-specific inflammatory reactions and do not incite specific immune responses. Although peptides are often immunogenic, the biocompatibility of these materials is likely related to their low molecular weight.
University of Michigan Ann Arbor	1R01EB005028-01A2	The Interaction of Polycationic Organic Polymers with Biological Membranes	The goal of this research is to understand the basic mechanisms for delivery of nano-scale materials in biological systems. The EHS-relevant component of this research will be the elucidation of interactions between nano-scale materials (some engineered, some not) and cellular components within biological systems.
University of Michigan Ann Arbor	5R21EB003793-03	RECONFIGURABLE NANOENGINEERED EXTRACELLULAR MATRICES	There is some engineered nano and cell proliferation data that will be generated through this research; however, the bulk of the research goals are aimed at unerstanding nanoscale biological materials which may have limited use for understanding interactions between engineered nanomaterials and biological

Lead Institution	Award ID	Project	Notes
			components of EHS relevance.
University of Minnesota-Twin Cities	1R21CA121832-01	Multifunctional nanoparticles for targeted DNA vaccine delivery	The goal of this grant is to develop a platform DNA vaccine delivery technology based on rationally designed polymer-based nanostructures that will have a significant impact on gene-based immunotherapy for treating cancer and infectious diseases. The EHS-relevant component of this research is to synthesize biodegradable multifunctional polymer nanoparticles and evaluate their efficacy and efficiency using *in vivo* and *in vitro* techniques.
UNIVERSITY OF MONTANA	1R01ES015497-01	NANOPARTICLE DISRUPTION OF CELL FUNCTION	As the title indicates, this research is geared towards understanding interactions between engineered nanomaterials and various biological components. This research is EHS-relevant.
UNIVERSITY OF WASHINGTON	5R01CA119408-02	Nanotechnology Platform for Pediatric Brain Cancer Image	The goal of this grant is to develop tumor targeting nanoparticle agents to improve the diagnosis and treatment of brain cancer in children. The EHS-relevant component of this research is to develop multifunctional nanoparticle agents that target brain tumors and characterize the factors that optimize the therapeutic efficacy and delivery of these nanoparticles to brain tumors using *in vitro* and *in vivo* techniques.
Virginia Polytechnic Institute and State University	5R01AG022617-04	Nanoparticles as Promoters of Cell Longevity	

NIOSH Intramural

Lead Institution	Award ID	Project	Notes
		Nanotechnology Characterization Laboratory	Research performed at this laboratory will provide improved understanding of biological mechanisms and interactions of engineered nanomaterials. The research will also enhance scientific knowledge of how such materials are transported withing and between biological components. This research is EHS-relevant.
	1Z01ES050046-28	MECHANISMS OF CHEMICALLY INDUCED PHOTOSENSITIVITY	As the title indicates, this research is geared towards understanding interactions between engineered nanomaterials and various biological components, both at molecular, cellular and tissue levels. This research is EHS-relevant.

NIOSH Extramural

Lead Institution	Award ID	Project	Notes
UNIVERSITY OF PITTSBURGH	1R01OH008282-01A1	Lung Oxidative Stress/Inflammation by Carbon Nanotubes	

NIOSH Intramural

Lead Institution	Award ID	Project	Notes
		Pulmonary Toxicity of Carbon Nanotube Particles	
		Systematic Microvascular Dysfunction Effects of Ultrafine versus Fine particles	The goal of this grant is to identify cardiovascular effects in rats after inhalation of fine TiO_2 particles and nanoparticles. The EHS-relevant component of this research is to measure markers of pulmonary inflammation and systemic microvascular dysfunction in rats after exposure to nanoparticles.

NSF Extramural

Lead Institution	Award ID	Project	Notes
University of Massachusetts Amherst	609107	NIRT: Controlling Interfacial Activity of Nanoparticles: Robust Routes to Nanoparticle-based Capsules, Membranes, and Electronic Materials	NSF project #197 has 600K in funding that is targeted to using nanoparticles and their selfassembling for development of release systems used in therapeutic drug treatments, and of nanostructured

membranes for water purification and filtration.

Research Need: *Understand the relationship between the properties of nanomaterials and uptake via the respiratory or digestive tracts or through the eyes or skin, and assess body burden*

No. of Projects 6

EPA Extramural

Lead Institution	Award ID	Project	Notes
Oregon State University,	RD-833320	A rapid *in vivo* system for determining toxicity of manufactured nanomaterials	

NIH Extramural

Lead Institution	Award ID	Project	Notes
UNIVERSITY OF CALIFORNIA LOS ANGELES	1R01ES015498-01	DEVELOPMENT OF METHODS AND MODELS FOR NANOPARTICLE TOXICITY SCREENING: APPLICATIO	The goal of this project is to develop novel cytotoxic nucleotide drugs embedded in a nanoscale polymer carriers that help stabilize, protect and target the drug. The EHS relevant component of this research is to determine whether the polymer-nucleotide complexes can increase the cytotoxic effects of the non-encapsulated nucleotide analogues.
UNIVERSITY OF CALIFORNIA SAN FRANCISCO	5R01CA119414-02	Detecting Cancer Early with Targeted Nano-Probes for Va*	The goal of this grant is to develop hybrid gold-nanoparticle-based molecular imaging and therapeutic agents for diagnosis and treatment of prostate cancer. The EHS relevant component of this research includes characterization and study of photophysical properties, size, dispersity, biolocalization, pharmacokinetics and *in vivo* profiles of stabilized gold nanoparticles.
UNIVERSITY OF MISSOURI-COLUMBIA	5R01CA119412-02	Hybrid Nanoparticles in Imaging and Therapy of Prostate*	The goal and EHS relevance of this research is to develop and implement techniques to detect and characterize genetic damage that may result from a variety of chemicals and materials in the environment, including carbon nanotubes.)
UNIVERSITY OF NEBRASKA MEDICAL CENTER	5R01CA102791-04	Polymer-Nucleotide Complexes with Cytotoxic Activity	The goal of this project is to develop targeted nano-probes for molecular imaging to enable non-invasive early detection of cancer. The EHS relevant component of this research involves the pharmacokinetic testing of nano-probes (linking peptide targets to a variety of nanostructures) in mouse models to identify the best candidate nanoprobes for clinical evaluation.

USDA(CSREES) Extramural

Lead Institution	Award ID	Project	Notes
University of California, Riverside	CA-R*-NEU-7524-H	ROLE OF CHROMOSOME ALTERATIONS IN ENVIRONMENTAL CARCINOGENESIS	

Research Need: *Understand the mechanisms of interaction between nanomaterials and the body at the molecular, cellular, and tissular levels*

No. of Projects 11

NIH Extramural

Lead Institution	Award ID	Project	Notes
		E2156_NCTR: Skin Penetration, Phototoxicity, and Photocarcinogenesis of Nanoscale Oxides of Titanium and Zinc	
		Toxicokinetics of Quantum dots in rats	
BAYLOR COLLEGE OF MEDICINE	3U10HD037242-08S1	Pharmokinetics of therapeutic antibody-targeted gold nanoparticles	
THERAPYX, INC	1R43DK075190-01	Treatment of Type 2 Diabetes with Oral Administration of Nanoencapsulated	This work seeks to optimize a system to deliver glucagon-like peptide 1 (GLP-1) (which lowers

		GLP-1	plasma glucose) into diabetes patients through non-invasive orally administered GLP-1-encapsulated nanoparticles.
UNIVERSITY OF CALIFORNIA LOS ANGELES	1R01ES015498-01	Toxicokinetic studies of fullerene C60	
UNIVERSITY OF TEXAS EL PASO	5S11ES013339-02	UTEP-UNM HSC ARCH PROGRAM ON BORDER ASTHMA	This work seeks to develop data relating ultrafine (less than 100 nanometer) air particulate contamination with asthma causation. Baseline information on the characteristics of ultrafine particles will be developed, including specific focus on occurrence of carbon nanotubes in kitchens and in vitro data on inflammatory measures following carbon nanotube exposure.
WAYNE STATE UNIVERSITY	5U10HD037261-07	Apply nanotechnology to targeted drug delivery across blood brain barrier	

NIOSH Intramural

Lead Institution	Award ID	Project	Notes
		Dermal Effects of Nanoparticles	
		Pulmonary Deposition and Translocation of Nanomaterials	
		Role of CNT's in Cardiovascular Inflammation & COPD Related Diseases	

NSF Extramural

Lead Institution	Award ID	Project	Notes
University of Florida	540920	Biochemical, Molecular and Cellular Responses of Zebrafish Exposed to Metallic Nanoparticles	

Nanomaterials and the Environment

Research Need: *Understand the effects of engineered nanomaterials in individuals of a species and the applicability of testing schemes to measure effects*

No. of Projects 5

EPA Extramural

Lead Institution	Award ID	Project	Notes
Arizona State University - University of Delaware,	R8333327	Methodology development for manufactured nanomaterial bioaccumulation test	The bioconcentration, bioaccumulation, and biomagnification of manufactured nanomaterials will be evaluated in a simulated food chain and aquatic organisms, consisting of algae, daphnia, and zebrafish.
Carnegie Mellon University , Chapman University , Rice University	R833326	The effect of surface coatings on the environmental and microbial fate of nanoiron and Fe-oxide nanoparticles	The study objectives are to determine the effect of common NP surface coatings on nanoiron and nanoiron-oxide reactivity, mobility, fate, and effect on soil bacteria.
NYU School of Medicine, Department of Environmental Medicine,	RD833317	Aquatic toxicity of waste stream nanoparticles	Investigation of particle-type dependent difference in the developmental toxicity of manufactured nanoparticles in aquatic species; work will involve 1) measuring toxicity of several types of nanoparticles in an estuarine fish species; and 2) identifying whether early life stages are particularly susceptible to carbon nanoparticle vs. nanotubes.

Research Need: *Understand environmental exposures through identification of principle sources of exposure and exposure routes*

No. of Projects: 1

NSF Extramural

Lead Institution	Award ID	Project	Notes
University of Notre Dame	221966	Environmental Molecular Science	This study should provide some basis for the

		Institute: Actinides and Heavy Metals in the Environment - The Formation, Stability, and Impact of Nano- and in the Environment	understanding of nanoparticle behavior and routes to the environment.

Research Need: *Evaluate abiotic and ecosystem-wide effects*

No. of Projects:1

NSF Extramural

Lead Institution	Award ID	Project	Notes
Washington University	608749	NER: Nanoscale Size Effects on the Biogeochemical Reactivity of Iron Oxides in Active Environmental Nanosystems	Work will provide information on the effect of naturally-occuring nanoparticles on the biogeochemical cycling of metals of concern in the subsurface.

NSF Extramural

Lead Institution	Award ID	Project	Notes
University of Florida	540920	Biochemical, Molecular and Cellular Responses of Zebrafish Exposed to Metallic Nanoparticles	One of the main objectives is to compare toxicity of metals to zebrafish in the dissolved and nanoparticle state as well as the nanoparticles of different sizes and shape. *In vitro* work will also be done.

USDA (CSREES) Extramural

Lead Institution	Award ID	Project	Notes
Clemson University	SC-1700288	Cellular and materials-based studies of marine invertebrates to advance biomineralization, antifouling and nanotechnology fields	Cellular and/or whole organism responses to nanomaterials (including coverage of molluscs, daphnia, and fat head minnows) will be examined for toxicity, larval settlement and attachment processes, and apoptosis.

Research Need: *Determine factors affecting the environmental transport of nanomaterials*

No. of Projects: 22

AFOSR SBIR

Lead Institution	Award ID	Project	Notes
NanoComposix, Inc	FA8651-06-C-0136	Measure the transport of modified nanoparticles through soil	nanoComposix will investigate the fate, transport, and compartimentalization of nanoparticles in the environment. The transport and toxicology of commercially availabe powered aluminum and tantalum nanoparticles will be compared to precisely engineered nanoparticles produced in-house at nanoComposix.

DOE Extramural

Lead Institution	Award ID	Project	Notes
University of California at Berkeley,		How Do Interfacial Phenomena Control Nanoparticle Structure?	Work will provide information on the stability and transformation processes which may help inform our
University of California at Davis		How Do Interfacial Phenomena Control Nanoparticle Structure?	
Virginia Polytechnic Institute,		Frontiers in Biogeochemistry and Nanomineralogy: Studies in Quorum Sensing and Nanosulfide Dissolution Rates	Work will provide information on the stability and transformation processes which may help inform our understanding of environmental transport.

EPA Extramural

Lead Institution	Award ID	Project	Notes
Arizona State University - Main Campus	R833322	Biological fate and electron microscopy detection of nanoparticles during wastewater treatment	

University of Tennessee - Knoxville	R833333	Ecotoxicology of underivatized fullerenes (C60) in fish	Work will provide information on the stability and transformation processes which may help inform our understanding of environmental transport.
WASHINGTON STATE UNIVERSITY	R833321	Carbon nanotubes: environmental dispersion states, transport, fate, and bioavailability	

NIH Extramural

Lead Institution	Award ID	Project	Notes
ONMATERIALS, LLC	1R43ES014114-01A1	SUB-MICROMETER ZERO VALENT METAL FOR IN-SITU REMEDIATION OF CONTAMINATED AQUIFERS	

NSF Extramural

Lead Institution	Award ID	Project	Notes
Carnegie-Mellon University	521721	Development of a Copolymer-Based System for Targeted Delivery of Nanoparticulate Iron to Environmental Non-Aqueous Phase Liquids	Work will include transport of iron nanoparticles in the subsurface
Howard University	506951	NIRT: Metal Ion Complexation by Dendritic Nanoscale Ligands: Fundamental Investigations and Applications to Water Purification	Work examines dendrimer binding of metals.
Rensselaer Polytechnic Institute	610537	SGER: Particle Incorporation of PAH in Aquatic Environments: Implications to Fate and Transport	
Rutgers University New Brunswick	636820	SGER: Metallic Nanocatalysts for Rapid Transformation of Polychlorinated Dibenzo-p-Dioxins	
University of Illinois at Urbana-Champaign	120978	Center of Advanced Materials for Purification of Water with Systems	Research to be conducted on water processing and the Angstrom to nanometer scale interactions between aqueous solutions and solid substrates for separation/transformation of compounds in water.
University of Illinois at Urbana-Champaign	349282	CAREER: Carbonaceous Particles of Tarry Origin	Characterization of the physical and chemical properties of carbonaceous particles generated in the combustion of solid fuels
University of Michigan Ann Arbor	553764	Carbon Nanoparticles in Combustion: A Multiscale Perspective	
Washington University	546219	CAREER: Interfacial Reactions Affecting Heavy Metal Fate and Transport: An Integrated Research and Education Plan	
Yale University	646247	Aggregation and Deposition Behavior of Carbon Nanotubes in Aquatic Environmrnts	

USDA (CSREES) Extramural

Lead Institution	Award ID	Project	Notes
North Carolina State University	NC09323	CONFERENCE SYMPOSIUM: ENVIRONMENTAL MINERALOGY AND TOXIC METALS	
UNIV OF CALIFORNIA	CALR-2006-02656	REACTIVITY, AGGREGATION AND TRANSPORT OF NANOCRYSTALLINE SESQUIOXIDES IN THE SOIL SYSTEM	
UNIVERSITY OF DELAWARE	DEL00622	COLLOID INTERFACIAL REACTIONS IN OPEN MICROCHANNEL REPRESENTING UNSATURATED SOIL CAPILLARIES	Work will provide information on the stability and transformation processes which may help inform our understanding of environmental transport.
UNIVERSITY OF MISSOURI	MO-NRSL0728	ELUCIDATING INTERACTIONS AND TRANSFORMATIONS OF POLLUTANTS AND ORGANIC MATTER IN SOIL	Transformation processes and nanopore effects on organic compound sorption and retention to mineral surfaces.

WASHINGTON STATE UNIVERSITY	WNP00385	SORPTION AND AVAILABILITY OF METALS AND RADIONUCLIDES IN SOILS	

Research Need: *Understand the transformation of nanomaterials under different environmental conditions*

No. of Projects: 9

DOE Extramural

Lead Institution	Award ID	Project	Notes
Waychunas, Lawrence Berkeley National Laboratory,		Experimental, Theoretical, and Model-Based Studies of Crystallographically Controlled Self-Assembly During Nanocrystal Growth	Use of zinc nanosulfides to determine the nanocrystal growth in water and other media to evaluate morphological transformation changes.

NSF Extramural

Lead Institution	Award ID	Project	Notes
Duke University	653659	Collaborative Research: Fullerene Aggregation in Aquatic Systems	
MINORITY POSTDOC RSRCH FLW-NEW	610373	Environmental Biogeochemistry and Nanoscience: Applications to Toxic Metal Transport in the Environment	
Ohio State University	518042	The formation rates and structure of nanodroplets	
Rice University	647452	NSEC: Center for Biological and Environmental Nanotechnology (Rice U.)	Project encompases a wide range of nanoparticle research including interaction of nanoparticles with biomolecules, polymer flow, and contaminant sorption
University of Central Florida	448491	CAREER: Gas-Phase Catalytic Processes on Metal Nanoclusters(4/1/05 - 3/31/10)	Transformation of nanoparticles due to catalytic processes
University of Delaware	544246	Investigating the Surface Structure and Reactivity of Bulk and Nanosized Manganese Oxides	
Vanderbilt University	547024	CAREER: An Integrated Research and Education Program in Long-Term Durability of Nano-Structured Cement-Based Materials during Environmental Weathering	

USDA (CSREES) Extramural

Lead Institution	Award ID	Project	Notes
WASHINGTON STATE UNIVERSITY	WNP00581	THE CHEMICAL AND PHYSICAL NATURE OF PARTICULATE MATTER AFFECTING AIR, WATER, AND SOIL QUALITY	Work examines nanoparticles from agricultural emissions to air, water, and soil

Research Need: *Other*

No. of Projects 11

NSF Extramural

Lead Institution	Award ID	Project	Notes
mention to RMM to evaluate; HH request from Mike; go to environmental	447610	EPSCoR: Delaware Research Infrastructure Improvement Program EPSCoR	Project has an environmental nanotechnology component linked to educational goals.
methods and materials development: HH request from Mike go to environmental	447675	EPSCoR: Alabama Research Infrastructure Improvement	A reseach center will harness the benefits of nanoparticle infusion for the manufacture of bulk nanostructures materials with superior mechanical, chemical, optical, electrical, and thermal properties.
New Jersey Institute of Technology	506722	NIRT: Environmentally Benign Deagglomeration and Mixing of Nanoparticles	

Northwestern University	403581	Reactive Membrane Technology for Water Treatment	
Rensselaer Polytechnic Institute	608978	NIRT: Actively Reconfigurable Nanostructured Surfaces for the Improved Separation of Biological Macromolecules	
University of Alabama Tuscaloosa	608896	NIRT: Active Nanoparticles in Nanostructured Materials Enabling Advances in Renewable Energy and Environmental Remediation	
University of Cincinnati	448117	CAREER: Hydroxyl Radical and Sulfate Radical-Based Advanced Oxidation Nanotechnologies for the Destruction of Biological Toxins in Water 7/1/05-6/30/10)	
University of Michigan Ann Arbor	537626	Nanoscale Mineralogy and Geochemistry of Arsenian Pyrite in Ore Deposits	
University of New Mexico	447691	EPSCoR: New Mexico Research Program	Applications' work for water sensing and purification
University of South Florida	408933	Magnetocaloric Effect in Nanoparticle Assemblies for Refrigeration Applications	
Worcester Polytechnic Institute	448758	CAREER: On the Prevention of Selenium and Arsenic Release into the Atmosphere (2/15/05-1/31/09)	

Health and Environmental Exposure Assessment

Research Need: *Characterize exposures among workers*

No. of Projects: 2

NIOSH Intramural

Lead Institution	Award ID	Project	Notes
NIOSH/DART		Nanotechnology Research coordination	The purpose of this project is to develop intramural surveys that will obtain fundamental data on workplace exposures related to nanotechnology.
NIOSH/DSHEFS		Titanium Dioxide (TiO2) Nanoparticle Exposure Study	

Research Need: *Understand workplace processes and factors that determine exposure to nanomaterials*

No. of Projects: 3

AFosr Extramural

Lead Institution	Award ID	Project	Notes
		Small Business Innovation Research (SBIR): The impact of nanomaterials on occupational safety and health	This project aims at identify factors that influence the generation, dispersion, and deposition of nanomaterials in the workplace.

NIOSH Intramural

Lead Institution	Award ID	Project	Notes
NIOSH/DRDS		Nanoparticles in the Workplace	The purpose of this project is to foster the development of partnerships, exposure monitoring instrumentation, operational protocols, and a comprehensive and detailed database of nanoparticles and their properties aimed at providing the occupational safety and health community with a better understanding of the nature and extent of potential occupational exposures to nanoparticles.

NSF Extramural

Lead Institution	Award ID	Project	Notes
University of Minnesota-Twin Cities		Experimental and numerical simulation of the fate of airborne nanoparticles from a	

Lead Institution	Award ID	Project	Notes
		leak in a manufacturing process to assess worker exposure	

Risk Management Methods

Research Need: *Overarching need: Evaluate risk management approaches for identifying and addressing risks from nanomaterials*

No. of Projects: 5

Air Force SBIR

Lead Institution	Award ID	Project	Notes
Luna Innovations	F071-033-1470	WINGS™--Web-Interfaced Nanotechnology ESH Guidance System for Force Health Protection	

NSF Extramural

Lead Institution	Award ID	Project	Notes
Northeastern University	425826	NSEC: Center for High Rate nanomanufacturing	Research funded at the center includes risk management issues such as green design and net benefits analysis are incorporated in nanomanufacturing process evaluation and policy analysis.
Northeastern University	609078	NIRT: Nanotechnology in the Public Interest: Regulatory Challenges, Capacity, & Policy Recommendations	Research funded through the NIRT award includes development of public engagement approaches, regulatory and risk management policy evaluation, and education relevant to risk management policy development.
University of Minnesota-Twin Cities	608791	NIRT: Evaluating Oversight Models for Active Nanostructures and Nanosystems: Learning from Past Technologies in a Societal Context	Research funded through this NIRT award evaluates risk management oversight approaches as they apply to nanoscale materials.
University of Wisconsin-Madison	425880	NSEC: Center for Templated Synthesis and Assembly at the Nanoscale	Research funded at the center includes development of public engagement approaches and regulatory and risk management policy evaluation.

Research Need: *Understand and develop best workplace practices, processes, and environmental exposure controls*

No. of Projects: 4

NIOSH Extramural

Lead Institution	Award ID	Project	Notes
UNIVERSITY OF IOWA	1R01OH008806	Assessment methods for Nanoparticles in the Workplace	

NIOSH Intramural

Lead Institution	Award ID	Project	Notes
NIOSH/DART		Automobile Ultrafine Intervention	
NIOSH/NPPTL		Development and evaluation of nanofiber-based Filter Media	
NIOSH/NPPTL		Penetration of Nanoparticles through Respirator Filter Media	

Research Need: *Examine product or material life cycle to inform risk reduction decisions*

No. of Projects: 2

EPA Extramural

Lead Institution	Award ID	Project	Notes
Columbia University	R833334	Comparative life cycle analysis of nano- and bulk materials in photovoltaic energy	

generation

NSF Extramural

Lead Institution	Award ID	Project	Notes
University of Illinois at Chicago	646336	The Life Cycle of Nanomanufacturing Technologies	

Research Need: *Develop risk characterization information to determine and classify nanomaterials based on physical or chemical properties, and develop nanomaterial-use and safety-incident trend information to help focus risk management efforts*

No. of Projects: 1

NIOSH Intramural

Lead Institution	Award ID	Project	Notes
NIOSH/SRL		Developing a Web-Based nano-Information Library	

Research Need: *Develop specific risk communication approaches and materials*

No. of Projects: 1

NIOSH Intramural

Lead Institution	Award ID	Project	Notes
NIOSH/EID		Nanotechnology Information Dissemination	

Research Need: *Overarching need : Evaluate risk management approaches for identifying and addressing risks from nanomaterials,* and *develop specific risk communication approaches and materials, and develop specific risk communication approaches and materials*

No. of Projects: 1

NSF Extramural

Lead Institution	Award ID	Project	Notes
University of California-Santa Barbara	531184	NSEC: Center for Nanotechnology in Society at University of California, Santa Barbara	Research funded at this center examines societal impacts, and develop cross discipline collaborative approaches including societal aspects, and risk perception concerning nanotechnology.

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