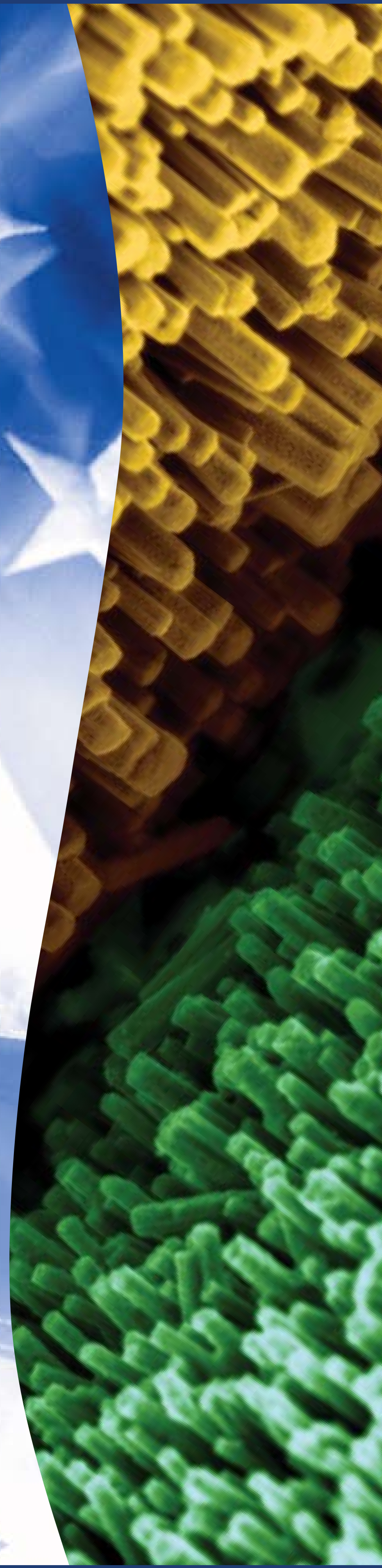
★ ★ ★ ★ ★ ★ ★

THE NATIONAL NANOTECHNOLOGY INITIATIVE:

Second Assessment and Recommendations of the National Nanotechnology Advisory Panel



About the President's Council of Advisors on Science and Technology

President Bush established the President's Council of Advisors on Science and Technology (PCAST) by Executive Order 13226 in September 2001. Under this Executive Order, PCAST "shall advise the President ... on matters involving science and technology policy," and "shall assist the National Science and Technology Council (NSTC) in securing private sector involvement in its activities." The NSTC is a Cabinet-level council that coordinates interagency research and development activities and science and technology policy-making processes across Federal departments and agencies.

PCAST enables the President to receive advice from the private sector, including the academic community, on important issues relevant to technology, scientific research, mathematics and science education, and other issues of national concern. The PCAST-NSTC link provides a mechanism to facilitate the public-private exchange of ideas that inform Federal science and technology policy-making processes.

As a private sector advisory committee, PCAST recommendations do not constitute Administration policy but rather provide advice to the Administration in the science and technology arena.

PCAST follows a tradition of Presidential advisory panels on science and technology dating back to Presidents Truman and Eisenhower. The Council's 35 members, appointed by the President, are drawn from industry, education, and research institutions, and other nongovernmental organizations. In addition, the Director of the Office of Science and Technology Policy serves as PCAST's Co-Chair.

About the National Nanotechnology Advisory Panel

The National Nanotechnology Advisory Panel (NNAP) was created by the United States Congress in the 21st Century Nanotechnology Research and Development Act (P.L. 108-153), signed by President Bush on December 3, 2003. The Act required the President to establish or designate an NNAP to review the Federal nanotechnology research and development program. On July 23, 2004, President Bush formally designated the PCAST to act as the NNAP.

About this Report

The Act that created the NNAP calls for this advisory body to conduct a review of the NNI and report its findings to the President. The Act calls upon the NNAP to assess the trends and developments in nanotechnology, and the strategic direction of the NNI, particularly as it relates to maintaining U.S. leadership in nanotechnology research. The Act also requires comment on NNI program activities, management, coordination, implementation, and whether the program is adequately addressing societal, ethical, legal, environmental, and workforce issues. The Act calls for the NNAP to report on its assessments and to make recommendations for ways to improve the program at least every two years. The Director of the Office of Science and Technology Policy is to transmit a copy of the NNAP report to Congress. This is the second report of the NNAP under the Act.

Front cover: Scanning electron microscopy (SEM) image showing piezoelectric zinc oxide nanowires grown around two conductive microfibers. One fiber is coated with metal (top left) and one is not (bottom right). The two sets of nanowires meet teeth-to-teeth, allowing the metal-coated microfibers to scrub those not coated with metal to produce electricity via a coupled piezoelectric-semiconducting process. This approach can be applied to harvesting electrical energy from mechanical energy produced by body movement, light wind, vibration, and sound, with potential for powering small biomedical devices, nanoelectronics, nanosensors, and even personal electronics. Courtesy of Zhong Lin Wang, Georgia Institute of Technology (see Qin, Wang, and Wang 2008 for more information). Cover design by Nicolle Rager Fuller of Sayo-Art.

The National Nanotechnology Initiative:

Second Assessment and Recommendations of the National Nanotechnology Advisory Panel

Report of the
President's Council of Advisors on Science and Technology

April 2008

EXECUTIVE OFFICE OF THE PRESIDENT
PRESIDENT'S COUNCIL OF ADVISORS ON SCIENCE AND TECHNOLOGY
WASHINGTON, D.C. 20502

April 7, 2008

President George W. Bush
The White House
Washington, D.C. 20502

Dear Mr. President:

We are pleased to send you the report, *The National Nanotechnology Initiative: Second Assessment and Recommendations of the National Nanotechnology Advisory Panel*, prepared by your Council of Advisors on Science and Technology (PCAST) in the advisory role you formally designated for it in July 2004 by Executive Order.

The National Nanotechnology Initiative (NNI) remains a model program with world-class infrastructure at our universities and national labs and strong management and interagency coordination. In short, our review shows that the NNI continues to:

- Provide effective coordination across agencies, with industry, and with other nations;
- Facilitate expanding technology transfer efforts and build connections across the unparalleled innovation ecosystem in the U.S.; and
- Prioritize environmental, health, and safety research that facilitates appropriate risk analysis and risk management in step with technological innovation.

To strengthen the NNI and bolster implementation, our recommendations include:

- Expand communication and outreach efforts, particularly with respect to real and perceived benefits and risks associated with nanotechnology;
- Develop and implement standards critical for nanomaterial identification, characterization, and risk assessment; and
- Coordinate strategically-guided nanotechnology environmental, health, and safety research across agencies, sectors, and countries and include balanced assessment of risks and benefits in the context of specific, real-world applications.

The full PCAST discussed and approved this report at its public meeting on January 8, 2008. We continue to anticipate broad and significant societal benefits from nanotechnology and will continue to monitor on your behalf the progress of Federal programs to this end.

John H. Marburger, III
Co-Chair

E. Floyd Kvamme
Co-Chair

President's Council of Advisors on Science and Technology

Chairs

John H. Marburger, III
Co-Chair and Director
Office of Science and Technology Policy

E. Floyd Kvamme
Co-Chair and Partner
Kleiner Perkins Caufield & Byers

Members

F. Duane Ackerman
Former Chairman and CEO
BellSouth Corporation

Paul M. Anderson
Chairman and CEO
Duke Energy

Charles J. Arntzen
Regents' Professor and
Florence Ely Nelson Presidential Chair
The Biodesign Institute
Arizona State University

Norman R. Augustine
Former Chairman and CEO
Lockheed Martin Corporation

Carol Bartz
Executive Chairman of the Board
Autodesk, Inc.

M. Kathleen Behrens
Managing Director
Robertson Stephens & Co.

Erich Bloch
Director
The Washington Advisory Group

Robert A. Brown
President
Boston University

G. Wayne Clough
President
Georgia Institute of Technology

Michael S. Dell
Chairman of the Board
Dell Inc.

Nance K. Dicciani
President and CEO
Honeywell Specialty Materials

Raul J. Fernandez
CEO
ObjectVideo

Marye Anne Fox
Chancellor
University of California, San Diego

Martha Gilliland
Senior Fellow
Council for Aid to Education

Ralph Gomory
President
Alfred P. Sloan Foundation

Bernadine Healy
Health Editor and Columnist
U.S. News and World Report

Robert J. Herbold
Former Executive Vice President
Microsoft Corporation

Richard H. Herman
Chancellor
University of Illinois at Urbana-Champaign

Martin J. Jischke
President Emeritus
Purdue University

Fred Kavli
Founder and Chairman
Kavli Foundation

Bobbie Kilberg
President
Northern Virginia Technology Council

Walter E. Massey
President
Morehouse College

E. Kenneth Nwabueze
CEO
SageMetrics

Steven G. Papermaster
Chairman
Powershift Ventures

Luis M. Proenza
President
University of Akron

Daniel A. Reed
Director of Scalable and Multicore Computing Strategy
Microsoft Corporation

George Scalise
President
Semiconductor Industry Association

Stratton D. Sclavos
Chairman of the Board, President, and CEO
VeriSign

John Brooks Slaughter
President and CEO
The National Action Council for Minorities in Engineering

Joseph M. Tucci
Chairman, President, and CEO
EMC Corporation

Charles M. Vest
President
National Academy of Engineering

Robert E. Witt
President
University of Alabama

Tadataka Yamada
President, Global Health Program
Bill and Melinda Gates Foundation

Executive Director

Scott J. Steele

OSTP Staff Liaison

Travis M. Earles

Table of Contents

Executive Summary

The 21st Century Nanotechnology Research and Development Act of 2003 (Public Law 108-153) calls for a National Nanotechnology Advisory Panel (NNAP) to periodically review the Federal nanotechnology research and development (R&D) program known as the National Nanotechnology Initiative (NNI). The President's Council of Advisors on Science and Technology (PCAST) is designated by Executive Order to serve as the NNAP. This report is the second NNAP review of the NNI, updating the first assessment published in 2005.

Including the NNI budget request for fiscal year (FY) 2009 of $1.5 billion, the total NNI investment since its inception in 2001 is nearly $10 billion. The total annual global investment in nanotechnology is an estimated $13.9 billion, divided roughly equally among the United States, Europe, and Asia. Industry analysis suggests that private investment has been outpacing that of government since about 2006. The activities, balance, and management of the NNI among the 25 participating U.S. agencies and the efforts to coordinate with stakeholders from outside the Federal Government, including industry and other governments, are the subject of this report.

The first report answered four questions: How are we doing? Is the money well spent and the program well managed? Are we addressing societal concerns and potential risks? How can we do better? That report was generally positive in its conclusions but provided recommendations for improving or strengthening efforts in the following areas: technology transfer; environmental, health, and safety (EHS) research and its coordination; education and workforce preparation; and societal dimensions.

Since the first report, increasing attention has been focused on the potential risks of nanotechnology, especially the possible harm to human health and the environment from nanomaterials. In this second assessment, the NNAP paid special attention to the NNI efforts in these areas.

During its review, the NNAP obtained input from various sources. It convened a number of expert panels and consulted its nanotechnology Technical Advisory Group (nTAG) and the President's Council on Bioethics. NNI member agencies and the National Nanotechnology Coordination Office (NNCO) also provided valuable information.

The NNAP finds that the United States remains a leader in nanotechnology based on various metrics, including R&D expenditures and outputs such as publications, citations, and patents. However, taken as a region, the European Union has more publications, and China's output is increasing. There are many examples of NNI-funded research results that are moving into commercial applications. However, measures of technology transfer and the commercial impact of nanotechnology as a whole are not readily available, in part because of the difficulty in defining what is, and is not, a "nanotechnology-based product."

The NNAP commends and encourages the ongoing NNI investment in infrastructure and instrumentation. Leading-edge nanoscale research often requires advanced equipment and facilities. The NNI investment in over 81 centers and user facilities across the country that provide broad access to costly instrumentation, state-of-the-art facilities, and technical expertise has been enormously important and successful. These facilities, which have been funded by many different agencies in order to address a variety of missions, support a diverse range of academic, industry, and government research. In addition, the NNI investment has been used to leverage additional support by universities, State governments, and the private sector.

Advances in nanotechnology are embodied in a growing number of applications and products in various industries. Many early applications have been more evolutionary than revolutionary. However, research funded by the NNI today has the potential for innovations that are paradigm shifting, for example in energy and medicine.

As with any emerging technology, there is potential for unintended consequences or uses that may prove harmful to health or the environment or that may have other societal implications. The NNAP notes that existing regulations apply to nanotechnology-based products, and those who make or sell such products have responsibilities regarding workplace and product safety. As in 2005, the NNAP believes that the greatest risk of exposure to nanomaterials at present is to workers who manufacture or handle such materials. However, environmental, health, and safety risks in a wide range of settings must be identified and the necessary research performed so that real risks can be appropriately addressed.

The NNAP views the approach for addressing EHS research under the NNI as sound. The recent reports by the interagency Nanotechnology Environmental and Health Implications (NEHI) Working Group are good steps by the NNI to prioritize needed EHS research and to coordinate EHS activity across the Federal Government. The NNAP feels that calls for a separate agency or office devoted to nanotechnology EHS research or to set aside a fixed percentage of the budget for EHS research are misguided and may have the unintended consequence of reducing research on beneficial applications and on risk.

In addition to EHS implications, the NNAP considered ethical and other societal aspects of nanotechnology. **In consultation with the President's Council on Bioethics, the panel concluded that at present, nanotechnology does not raise ethical concerns that are unique to the field.** Rather, concerns over implications for privacy and for equality of access to benefits are similar to concerns over technological advances in general. This finding does not diminish the importance of continued dialogue and research on the societal aspects of nanotechnology.

Overall, the members of the NNAP feel that the NNI continues to be a highly successful model for an interagency program; it is well organized and well managed. The structure of the interagency Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the National Science and Technology Council effectively coordinates the breadth of nanotechnology activities across the Federal Government. The NSET working groups target functional areas in which additional focus is required. The NNCO provides important support that is a key to the success of the program. The Strategic Plan updated in 2007 clearly communicates the goals and priorities for the initiative and includes actions for achieving progress. With the separation in the updated plan of EHS research from that on other societal dimensions, the NNAP finds the Program Component Areas (PCAs) that are defined for purposes of tracking programs and investments serve the NNI well.

The NNAP has a number of recommendations for strengthening the NNI, which are grouped into six areas.

1. **Infrastructure, management, and coordination.** The NNAP feels that the substantial infrastructure of multidisciplinary centers, user facilities, along with instrumentation, equipment, and technical expertise, is vital to continued U.S. competitiveness in nanotechnology and should be maintained. Whereas the NNAP finds the coordination and management among the NNI participating agencies to be generally strong, intra-agency coordination should be improved, especially in large, segmented agencies. The NNI member agencies should continue to support international coordination through effective international forums, such as the Organisation for Economic Co-operation and Development (OECD). Such efforts will aid in the development of information related to health and safety, as well as addressing economic barriers and impacts. Implementing and monitoring this recommendation should lead to more effective use of agency resources.
2. **Standards development.** Nanotechnology standards are necessary for activities ranging from research and development to commerce and regulation. Federal agencies should continue to engage in national and international standards development activities. The NNI should maintain a strong U.S. representation in international forums and seek to avoid duplicative standards development work. Where appropriate, NIST and other NNI agencies should develop reference materials, test methods, and other standards that provide broad support for industry production of safe nanotechnology-based products.
3. **Technology transfer and commercialization.** The NNI should continue to fund world-class research to promote technology transfer. Strong research programs produce top-notch nanoscale scientists, engineers,

and entrepreneurs, who graduate with knowledge, skills, and innovative ideas. Such programs also have the potential to attract more U.S. students to related fields. NNI-funded centers should be structured to spur partnering with industry, which enhances technology transfer. The NNI should seek means to assess more accurately nanotechnology-related innovation and commercialization of NNI research results. These efforts should be coordinated with those of the OECD to assess economic impact of nanotechnology internationally.

4. **Environmental, health, and safety implications.** The NNAP feels that the NNI has made considerable progress since its last review in the level and coordination of EHS research for nanomaterials. Such efforts should be continued and should be coordinated with those taking place in industry and with programs funded by other governments to avoid gaps and unnecessary duplication of work. Moreover, EHS research should be coordinated with, not segregated from, applications research to promote risk and benefit being considered together. This is particularly important when development and risk assessment research are taking place in parallel, as they are for nanotechnology today. The NNI should take steps to make widely available nonproprietary information about the properties of nanomaterials and methods for risk/benefit analysis.

5. **Societal and ethical implications.** Research on the societal and ethical aspects of nanotechnology should be integrated with technical R&D and take place in the context of broader societal and ethical scholarship. The NNAP feels that this approach will broaden the range of perspectives and increase exchange of views on topics that affect society at large.

6. **Communication and outreach.** The NNAP is concerned that public opinion is susceptible to hype and exaggerated statements—both positive and negative. The NNI should be a trusted source of information about nanotechnology that is accessible to a range of stakeholders, including the public. The NNI should expand outreach and communication activities by the NNCO and the Nanotechnology Public Engagement and Communications Working Group and by coordinating existing agency communication efforts. To enhance effectiveness, the information should be developed with broad input and through processes that incorporate two-way communication with the intended audiences.

This review complements an assessment by the National Research Council (NRC) of the National Academies. The NNAP agrees with many of the NRC recommendations. However, the NNAP questions the recommendation for a formal, independent advisory panel. The panel feels that the current arrangement—whereby the NRC panels of technical experts, the high-level science and technology management leaders of PCAST, and the nanotechnology experts on the nTAG each provide distinct and useful input to the NNI review process—provides a broader perspective than would a single group consisting of a smaller number of advisors.

I. Introduction

Nanotechnology

Nanotechnology involves the understanding, control, and use of matter at dimensions of roughly 1 to 100 nanometers, where unique characteristics enable novel applications. A nanometer is one-billionth of a meter; a strand of human hair is about 100,000 nanometers in diameter. At the nanoscale, the physical, chemical, and biological properties of materials often differ in fundamental and valuable ways from the properties of individual atoms and molecules or from the properties of bulk matter.

Nanotechnology has emerged in the last decades of the 20th century with the development of new enabling technologies for imaging, manipulating, and simulating matter at the atomic scale. The frontier of nanotechnology research and development (R&D) encompasses a broad range of science and engineering activities directed toward understanding and creating improved materials, devices, and systems that exploit the properties of matter that emerge at the nanoscale. The results promise benefits that will shift paradigms in biomedicine (e.g., imaging, diagnosis, treatment, and prevention); energy (e.g., conversion and storage); electronics (e.g., computing and displays); manufacturing; environmental remediation; and many other categories of products and applications.

With such a broad range of applications, nanotechnology R&D is taking place in academic, government, and industry laboratories across the country and around the world. Often, nanotechnology research is at the intersection of traditional disciplines, including chemistry, biology, materials science, and computer science. As cutting-edge research proceeds, early commercial uses are coming to market, typically in the form of improvements to existing products and processes such as coatings and composite materials.

The National Nanotechnology Initiative (NNI)

The NNI was established in FY 2001 to coordinate the diverse nanotechnology activities across the Federal Government and to leverage expertise and investments among Federal agencies and with precompetitive and noncompetitive activities by industry and by other governments. The initiative continues to be an R&D priority of the Administration.

Today, the NNI comprises 25 Federal agencies, 13 of which have designated R&D budgets for nanotechnology. Collectively, the nanotechnology R&D budget amounts to a requested $1.5 billion in FY 2009, bringing the total Federal investment in nanotechnology research and development since the NNI was established in 2001 to nearly $10 billion.

Operational interagency coordination of the NNI occurs through the National Science and Technology Council (NSTC), Committee on Technology, Subcommittee on Nanoscale Science, Engineering, and Technology (NSET), which is composed of representatives from all Federal agencies participating in the NNI. The NSET Subcommittee has established four working groups to address distinct programmatic aspects of the NNI:

- Global Issues in Nanotechnology (GIN) Working Group supports U.S. Government activities in international forums related to nanotechnology.
- Nanotechnology Environmental and Health Implications (NEHI) Working Group addresses Federal nanotechnology-related environmental, health, and safety (EHS) research; develops coordinated EHS research strategy; and facilitates interagency activities related to EHS aspects of nanotechnology.
- Nanomanufacturing, Industry Liaison, and Innovation (NILI) Working Group coordinates industry collaboration and supports commercialization, manufacturing, and technology transfer.

- Nanotechnology Public Engagement and Communications (NPEC) Working Group coordinates relevant communications and outreach efforts across agencies and internationally, including those related to ethical and societal issues.

The National Nanotechnology Coordination Office (NNCO) provides dedicated technical and administrative support to the NSET Subcommittee, the four working groups, and the NNI agencies with respect to NNI activities, coordination, and communication with the public.

The NNI is subject by law to regular, extensive oversight. In its role as the National Nanotechnology Advisory Panel (described below), the President's Council of Advisors on Science and Technology (PCAST) reviews the NNI on a biennial basis through reports such as this one. The National Academies also conducts an external assessment of particular aspects of the NNI on a triennial basis. In addition to these statutory reviews, the Government Accountability Office is currently evaluating NNI coordination and reporting of nanotechnology-related EHS research.

National Nanotechnology Advisory Panel (NNAP)

The 21st Century Nanotechnology Research and Development Act of 2003 (108th Congress 2003, Public Law 108-153) calls for the President to establish or designate a National Nanotechnology Advisory Panel (NNAP). In 2004, by Executive Order the President designated the duties of the NNAP to PCAST. The NNAP is responsible for assessing:

- trends and developments in nanotechnology science and engineering
- implementation progress
- any need for programmatic revisions
- the balance among the components of the NNI, including funding levels for the NNI program component areas
- how the NNI is helping to maintain U.S. leadership in nanotechnology
- management, coordination, implementation, and program activities
- how the NNI is addressing societal, ethical, legal, environmental, and workforce concerns.

In May 2005, PCAST released the report of its first biennial review of the NNI in its capacity as the National Nanotechnology Advisory Panel (PCAST 2005). The report addressed four questions: (1) Where do we stand? (2) Is this money well spent and the program well managed? (3) Are we addressing societal concerns and potential risks? (4) How can we do better?

The panel's principal findings at the time were as follows:

- The United States is the acknowledged leader in nanotechnology research and development. Federal research investment accounts for roughly one-quarter of the current government investment by all nations. It also leverages larger investments from the private sector and State and local governments. The United States hosts the most nanotechnology-based start-up companies and produces by far the most patents and publications in nanotechnology. However, growing public and private investment around the world is raising competitive pressure on U.S. leadership.
- U.S. Federal Government investment in nanotechnology is robust and well spent. The NNI Strategic Plan provides an appropriate guide to program development, and the interagency NSET Subcommittee, with the support of the NNCO, effectively coordinates program implementation and management and facilitates interaction with industry and the public at large. Continued robust funding is important in order to realize long-term benefits.
- The NNI is working to identify, prioritize, and practically address environmental and health effects of nanotechnology as well as other societal and ethical implications of nanotechnology.

Based on its first assessment, the NNAP noted some specific areas for further attention and made the following recommendations to strengthen the NNI:

- **Technology transfer –** The NNI should expand efforts to dialogue with U.S. industry, increase Federal-State coordination, and improve knowledge management of and access to NNI assets (e.g., user facilities and instrumentation).
- **Environmental and health implications –** The NNI should continue its efforts to understand the possible toxicological effects of nanotechnology, particularly in workplace settings where nanomaterials are manufactured or used and where exposure is most likely to occur. Where evidence of harmful human or environmental health effects exist, pertinent Federal agencies should apply appropriate regulatory mechanisms. Strong interagency collaboration as well as international coordination on these issues is essential.
- **Societal implications –** The NNI should support research aimed at understanding societal (including ethical, economic, and legal) implications of nanotechnology and should actively work to inform the public about nanotechnology.
- **Education/workforce preparation –** The NNI should establish relationships with the Departments of Education (DOEd) and Labor (DOL) to develop education and training systems to improve the Nation's technical proficiency in areas related to nanotechnology.

NNAP review of the NNI is complemented by that of the National Research Council (NRC) of the National Academies. In December 2006, the NRC released its first triennial review of the NNI, largely in parallel to the initial NNAP review, but including specific one-time studies on the technical feasibility of molecular manufacturing and the responsible development of nanotechnology (NRC 2006). Appendix D presents a summary of the key findings from that report.

The NNAP offers the following specific comments on the NRC recommendations:

- The members of the NNAP believe the Federal Government does play a unique role in support of nanotechnology research and development that balances short- and long-term goals in support of basic and applied research and that cultivates and maintains a "robust supporting infrastructure."
- The NNAP concurs that it is premature to rigorously assess the levels of risk posed by engineered nanomaterials. Adequate tools are being developed but are not yet in place; therefore, expanded nanotechnology EHS research, broad-based protocol development, and particularly standardization are necessary.
- The NNAP questions the need for a formal, independent advisory panel with "specific operational expertise in nanoscale science and engineering; management of research centers, facilities, and partnerships; and interdisciplinary collaboration." Functionally, the latter two of these areas are not unique or specific to nanotechnology. The current arrangement, whereby the NRC panel of technical experts, the high-level science and technology management expertise of PCAST, and the nanotechnology experts on the ad hoc Nanotechnology Technical Advisory Group (nTAG) each provide input to the NNI review process, provides a broader perspective than would a single group consisting of a smaller number of advisors. Under the Federal Advisory Committee Act (FACA) guidelines, the number of such panels is closely managed and should only be established when they are essential to attaining clear Federal priorities. In addition, the NRC and NNAP will continue to provide regular oversight, assembling for the task an appropriately broad range of technical advisors having specific expertise related to nanotechnology.
- Assessing and projecting economic impacts of nanotechnology investment are indeed challenging. The NNAP welcomes a study on the feasibility of developing metrics to better quantify the economic return on government investment in nanotechnology.
- The NNAP supports the idea of increasing coordination through the NNI focused on education, training, and workforce preparation in conjunction with DOEd and DOL participants.

This report represents the second biennial review of the National Nanotechnology Initiative by PCAST in its capacity as the NNAP. NNAP members brought to their review of the NNI a considerable range of expertise, including significant experience managing large-scale, multidisciplinary research, development, and commercialization endeavors. The NNAP also solicited assessments and recommendations broadly from representatives of industry and the academic community (from both science and humanities disciplines), through the nTAG, as well as from members of the NSET Subcommittee and other agency representatives. Together, these representatives addressed the wide range of nanotechnology research, development, education, technology transfer, commercialization, environmental, health, and safety issues, as well as societal and ethical concerns related to the NNI. The NNAP also convened a public meeting on June 25, 2007, to discuss the same issues.[1] Collectively, these sources supplemented the broad and deep expertise of NNAP members with detailed and current expertise, feedback, and perspectives in a range of relevant technical and societal areas.

This report updates the assessment of and recommendations for the NNI issued by the NNAP in May 2005, noting specifically relative progress and status in nanotechnology research and development; applications and fostering commercialization; and implications for the environment, health, safety, and ethics issues, including public perception and the importance of sound communication.

[1] See http://www.ostp.gov/pdf/agenda6_07.pdf for meeting agenda and presentations.

II. Progress and Status: Leading Changes Since 2005

Principal Findings

- *Investment in research, development, and commercialization continues to increase in the United States and around the world.*
- *Scientific research is demonstrating greater potential from nanotechnology for both evolutionary and revolutionary changes. More nanotechnology-based products are coming to market.*
- *The world-class research and development infrastructure of the NNI continues to grow and strengthen, enabling broader participation in leading-edge research and multidisciplinary collaborations, and accelerating technology innovation towards functional applications.*
- *Progress is evident in many areas of opportunity, as identified by the Nanotechnology Technical Advisory Group (nTAG) and in response to specific recommendations from the NNAP in 2005.*
- *NNI investment is broadly leveraged. NNI leadership has catalyzed increased investment in the private sector and around the world. The NNAP commends the NNI agencies for their leadership in international forums, such as the Organisation for Economic Co-operation and Development (OECD) and the International Organization for Standardization (ISO).*

Growing Investment

U.S. investment in nanotechnology research and development continues to grow. Overall Federal funding for nanotechnology-related research and development has grown from a request of $982 million for FY 2005[2] to a request of $1.53 billion for FY 2009—a growth of over 50%—and has tripled from the initial NNI funding in 2001 (see Figure II-1) (NSTC/NSET, FY 2009 Budget, 2008). The growth rate has slowed somewhat over the past few years.

Funding is distributed across the NNI-designated Program Component Areas (PCAs) (see list of PCAs in Appendix B) by all 13 agencies that have designated nanotechnology R&D budgets; this reflects the importance to the NNI agency missions of simultaneous advances in all of the PCAs (see Figure II-2 and Appendix C, which set out the FY 2009 agency appropriation requests by PCA).

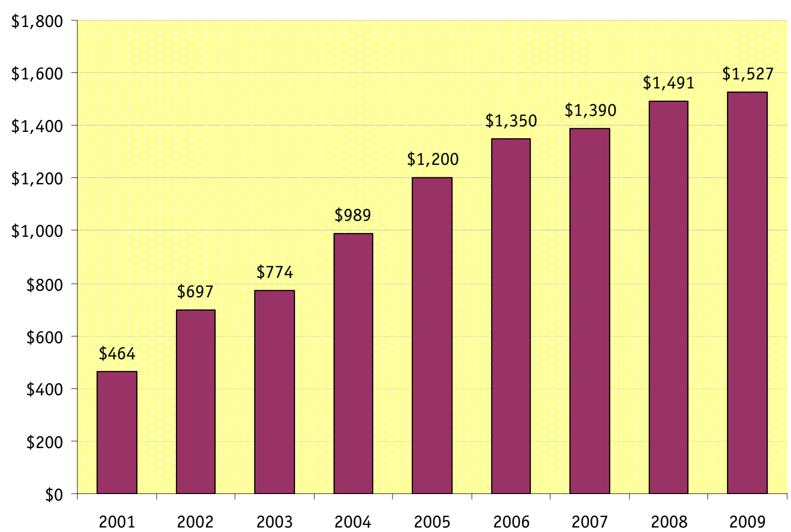


Figure II-1. Collective agency funding (in millions of dollars) reported since inception of the NNI (the 2008 figure is estimated; the 2009 figure is requested.

[2] Note that actual spending in 2005 was $1.2 billion, well over the amount requested, due to a combination of programmatic changes and Congressional additions, or earmarks, during the appropriation process.

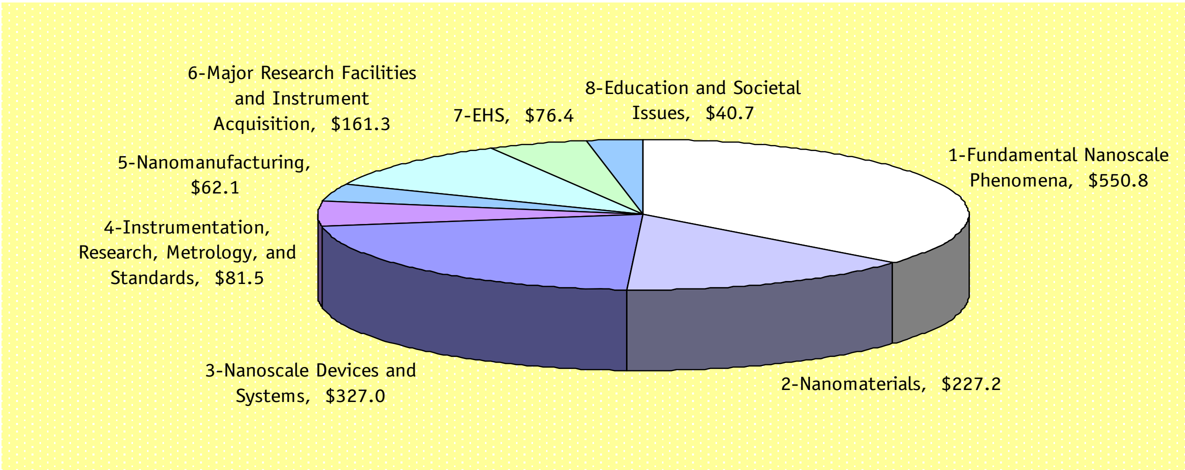


Figure II-2. NNI funding (in millions of dollars) by Program Component Area (PCA) (planned for FY 2009).

International private sector funding (both corporate and venture capital) has also increased since 2005, from an estimated $5 billion to over $7 billion in 2007. Total public and private sector support for nanotechnology R&D continues to grow around the globe, topping an estimated $13.9 billion worldwide as of 2007 (Lux Research 2007), divided roughly equally among the United States, Europe, and Asia.

The continued growth in total R&D investment worldwide reflects the widely recognized potential for broad-based benefits from nanotechnology, in both the near and the long term. In the collective memory of NNAP and nTAG members regarding the technology industry, this is the first time that U.S. investment has been so closely matched by European and Asian investment. This requires a more focused look at the competitiveness of the U.S. program.

Evolutionary changes introduced by nanotechnology are already impacting the market in a variety of materials and consumer products, including textiles, food packaging, home improvement tools and materials, sporting goods, reformulated drugs, and automobile parts. Ongoing research and development advances promise forthcoming revolutionary changes in energy capture and storage, molecular electronics, environmental sensing and remediation, and personalized medicine.

The research infrastructure created by the NNI to date remains the essential framework for fundamental nanotechnology research and innovation in the United States—and a central distinction of U.S. leadership in this field. Since 2005, the NNI infrastructure has continued to expand: the National Institutes of Health (NIH) established 21 new research centers focused on cancer nanotechnology and nanomedicine development, including the National Cancer Institute's Nanotechnology Characterization Laboratory; all five Nanoscale Science Research Centers (NSRCs) at Department of Energy (DOE) national laboratories have come on line, significantly boosting available research user facilities; the National Institute of Standards and Technology (NIST) opened the Center for Nanoscale Science and Technology in conjunction with its state-of-the-art Advanced Measurement Laboratory; and the National Science Foundation (NSF) set up two Centers for Nanotechnology and Society as well as the Network for Informal Science Education at the Nanoscale and the National Nanomanufacturing Network (see Figure II-3).

In all, the NNI leads the world in supporting over 81 centers, networks, and user facilities for pursuit of nanotechnology R&D, education, and discourse (NSTC/NSET 2007). This research capacity supports a broad base of scientific communities and facilitates extensive interdisciplinary research and development, which is essential for maintaining a competitive position in both fundamental science and emerging applications of nanotechnology. This unmatched array of user facilities should help U.S. industry stay ahead in the competition for leadership in nanotechnology commercialization.

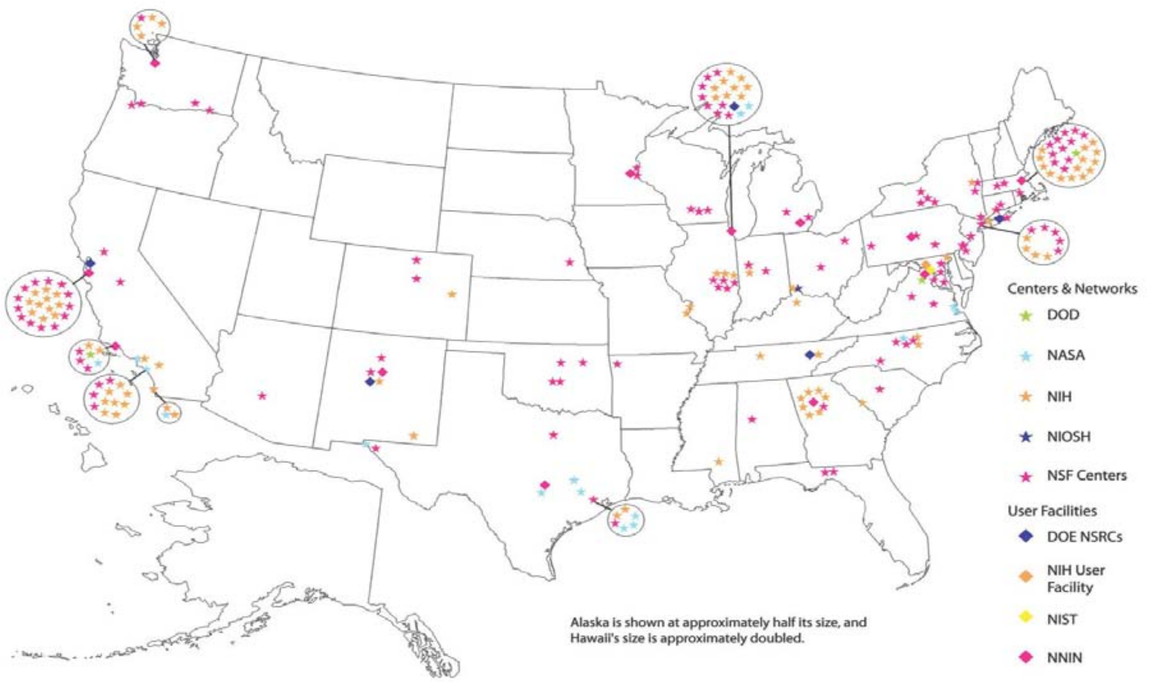


Figure II-3. NNI centers, networks, and user facilities.

Measuring Progress

Identifying meaningful metrics and securing relevant data with respect to advancements in the broad range of research, development, and commercialization outcomes related specifically to nanotechnology remains challenging. By and large, this is not unique to nanotechnology. Entire academic careers are spent studying how best to measure and account for scientific progress. When it comes to nanotechnology, however, such endeavors encounter numerous complicating factors. The fact that nanoscale research is integral to forefront research in many disciplines—including physics, chemistry, materials science, engineering, medicine, and biology—makes it difficult to separate and quantify research results directly attributable to nanotechnology. Assessing commercial impact is equally difficult. There is not a "nanotechnology industry," but rather, nanotechnology is developed and applied in almost every industry sector, making it infeasible to quantify the number of nanotechnology products or workers. Such inconsistency across discipline and product boundaries confounds comparisons based on funding, production, and commercialization and highlights the need for standardization of terminology, not just for assessment purposes, but to facilitate knowledge sharing and collaboration.

Nonetheless, appropriate metrics are essential for evaluating both internal progress and the competitiveness of the United States in terms of research support and output, infrastructure development, innovation progress, and ultimately, economic and societal benefit. Commonly used measures include bibliometrics such as publications, patents, and citations; knowledge mapping; counts of research centers, networks, user facilities, principal investigators, new trainees, start-ups, new products, initial public offerings, and acquisitions; and amounts of funding support from public and private sectors (corporate R&D as well as venture capital).

In the course of this review, the NNAP considered numerous efforts to collect and analyze such data on research output and commercialization efforts underway in the United States and around the world. While available data and viable metrics are limited, the panel found bibliometric analyses (numbers of publications and citations) and patent counts to be the most salient metrics for purposes of its assessment of the NNI progress and the relative position of the United States with respect to the rest of the world.

Publications and Citations

Nanotechnology publication and citation data provide some measure of research output in terms of both quantity and quality. On a country-by-country basis, the United States continues to exceed all others by these measures of nanotechnology publications (Figures II-4 and II-5)[3]. The United States also leads in the percentage of number of cited publications (Figure II-6), as another measure of quality. The 27 nations of the European Union, when considered as a whole, exceed the United States in total publications (Figure II-4). And China and Taiwan have seen a significant increase in their percentage of publications since 2004 (Figure II-6), demonstrating the heightened focus on nanotechnology research and development in those countries. However, thus far, their increase in percentage of publications has not been accompanied by a concomitant increase in cited publications (Figure II-7).

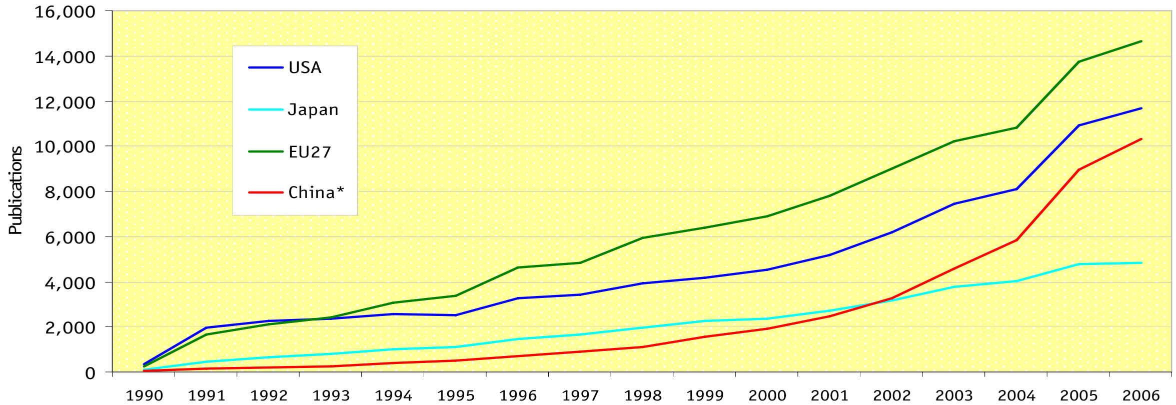


Figure II-4. Nanotechnology publications in the *Science Citation Index* (SCI) (*China includes Taiwan) (Shelton 2007).

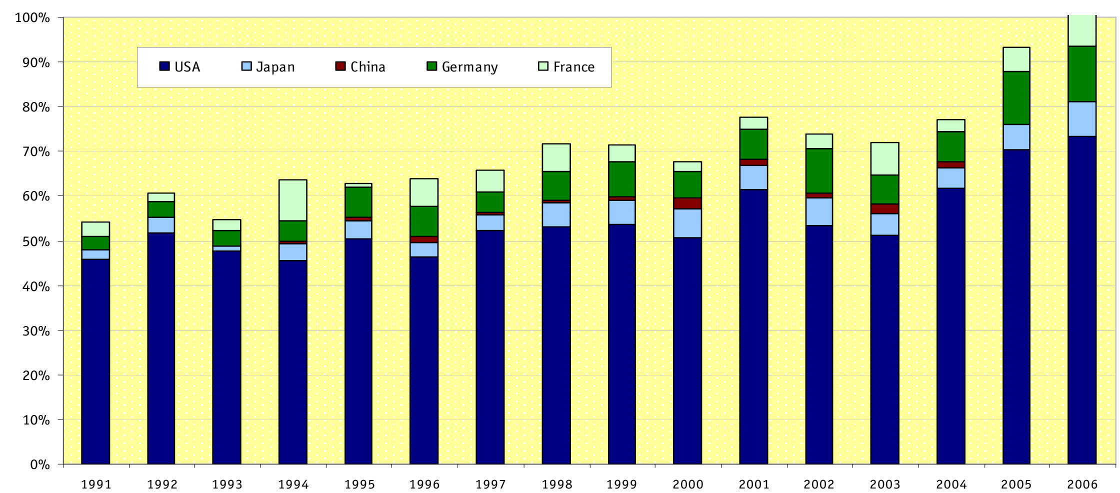


Figure II-5. Percent contribution by country to nanotechnology publications (by title-abstract search) in *Science*, *Nature*, and *Proceedings of the National Academies of Science* (top 3 journals based on citation index by other nanotechnology papers and patents) (Chen and Roco 2008; Hu et al. 2007).

[3] Data for Figure II-4 based on text search of the *Science Citation Index* as of 2006 for nano* excluding terms of scale alone (e.g., nanosecond, nanoliter, nanogram, nanomolar, nanonewton) and including relevant terms without the nano prefix (e.g., quantum dot, quantum well, molecular device, molecular wire, fullerene, spintronic, molecular electronic or dendrimer).

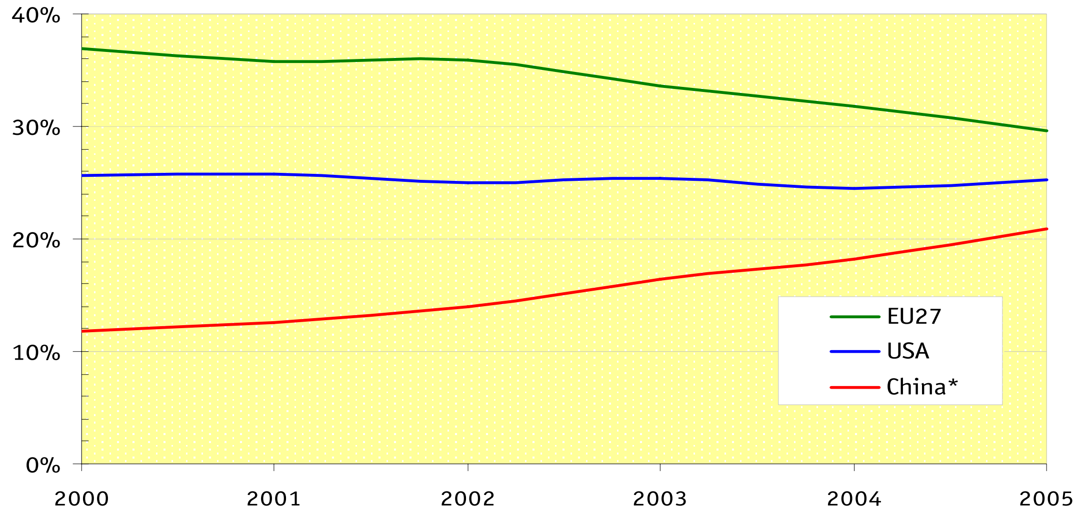


Figure II-6. Fraction of number of nanotechnology publications in *Science Citation Index* over time (*China includes Taiwan) (Lewison 2007).

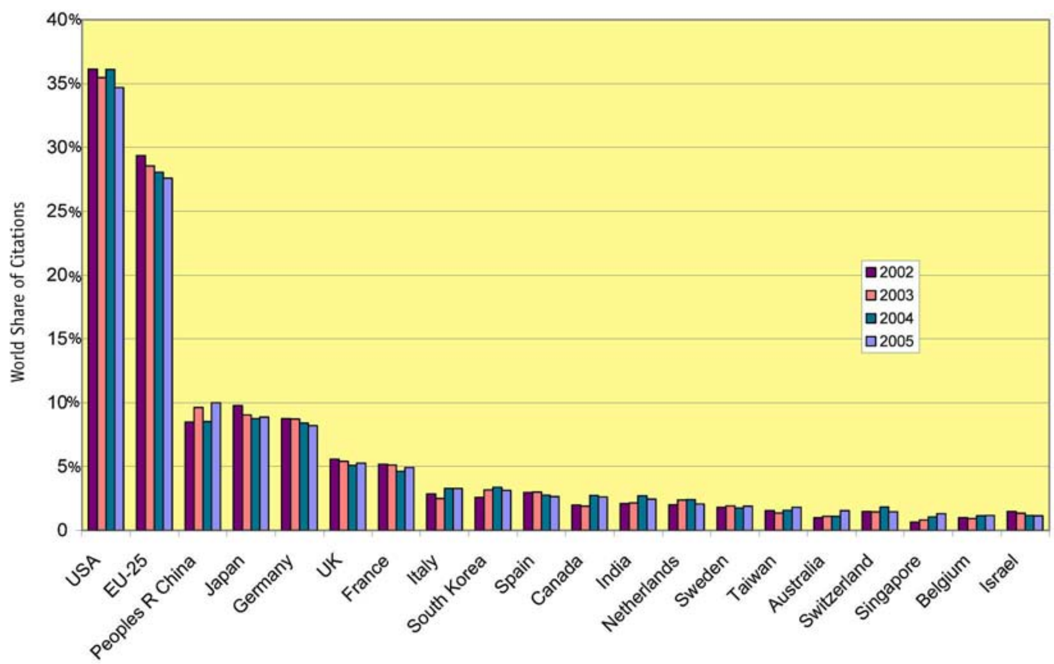


Figure II-7. Citations by country (Leydesdorff and Wagner 2006).

Ideas and Inventions

According to one recent publication, the numbers of nanotechnology-related patents published in the United States Patent and Trademark Office (USPTO) and the European Patent Office (EPO) continued to increase nearly exponentially from 1980 to 2004 (Figure II-8). (The numbers of nanotechnology-related patents published in the Japan Patent Office (JPO) during the same period are uneven.) Additionally, when country of patent assignment data is available, the United States has a dominant number of nanotechnology-related patents and number of patent citations in the USPTO and EPO databases.

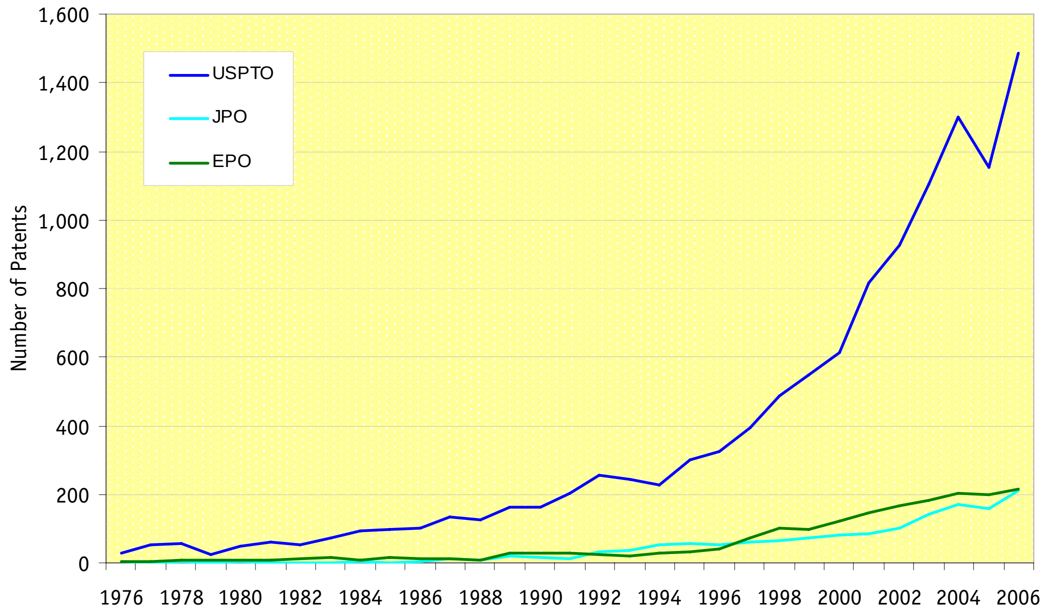


Figure II-8. Number of nanotechnology patents by title/abstract search worldwide (Li et al. 2007).

An independent analysis by the USPTO confirms that United States-origin inventors and assignees have the most nanotechnology-related patent publications globally. Additionally, the United States-origin inventors and assignees hold the most nanotechnology-related inventions with patent publications in 3 or more countries, demonstrating a more aggressive pursuit of international patent protection (Figure II-9). This is an indication of the impact of United States-origin nanotechnology-related patents. Given the interest in the global market and the perception of potential commercial value, the United States is producing more widely marketable ideas. The next most active countries pursuing nanotechnology-related patents globally are Japan, Germany, Korea, and France, in descending order.

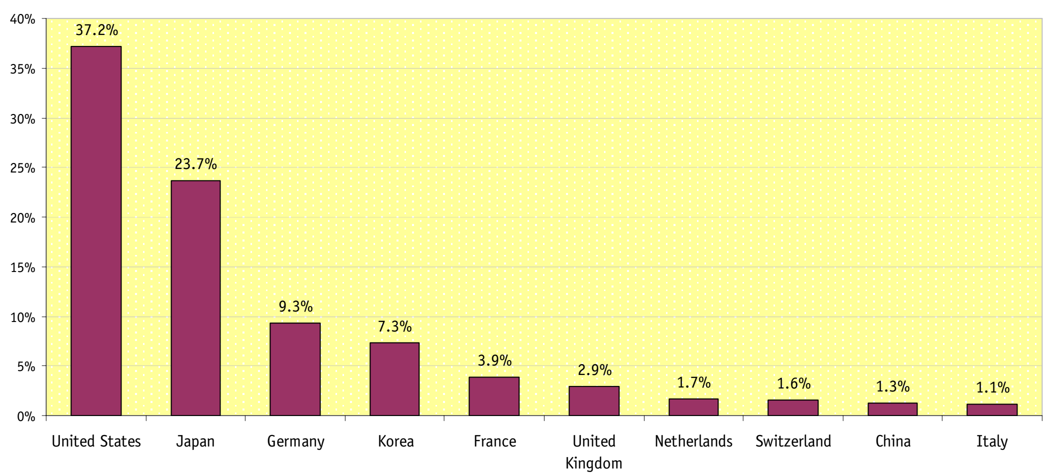


Figure II-9. Nanotechnology-related patents published on the same invention in three or more countries, by country of assignee (1985-2005) (Kisliuk 2008).

Managing Resources and Engaging Stakeholders

NNI agencies continue to broaden access to the knowledge base of basic research and instrumentation available at Government-supported laboratories. DOE has significantly expanded scientific user facility availability for nanoscale research and collaboration with its NSRCs, which are co-located with national laboratories at Argonne, Berkeley, Brookhaven, Oak Ridge, and Sandia/Los Alamos (see http://www.science.doe.gov/nano/). NSF continues to support the National Nanotechnology Infrastructure Network (NNIN; http://www.nnin.org/) launched in 2004, an integrated group of university lab user facilities designed to serve the research community in both academia and industry. These centers constitute a crucial part of the NNI backbone and are playing an important role in early development and in facilitating commercial innovation, particularly by small businesses but also by large corporations. U.S. competitiveness should greatly benefit from the availability of these facilities.

Industry Collaboration

Successful advancement of nanotechnology from discovery through application depends on effective and specific government and industry communication, coordination, and collaboration. Enabled by the breadth and depth of its facilities infrastructure, the NNI has continued working with various industry groups (e.g., semiconductor, chemicals, and forest products) to facilitate nanotechnology development, largely through the NILI Working Group. The Nanoelectronics Research Initiative (NRI; http://nri.src.org/) is one example of a promising joint industry-government program that is focused on realizing next-generation information processing technologies beyond CMOS (the complementary-symmetry metal-oxide-semiconductor structure used almost universally in today's integrated circuits) through collaborative activities with industry centers and joint training programs based in U.S. universities.

Global Coordination

The United States has been closely involved in the establishment and leadership of the OECD working parties on nanotechnology (WPN) and manufactured nanomaterials (WPMN). The United States is taking a leadership role in coordinating nanotechnology-related environmental, health, and safety efforts in the WPMN, which is chaired by a representative from the EPA. The WPMN is leading efforts to share EHS information and coordinate the collaborative development of information that is needed by governments and industries worldwide.

The development of effective standards is fundamental for large-scale growth of nanotechnology commercialization as well as for better understanding, communication, and oversight. Representatives from the NSET Subcommittee and NNI member agencies are participating in standardization activities domestically and abroad through the ISO. The ISO technical committee on nanotechnologies is working to develop standards for terminology and nomenclature; instrumentation and metrology; and health, environment, and safety. ISO standards often are adopted widely. The NNAP endorses the NNI's continued participation and leadership in these activities.

Update of the NNI Strategic Plan

As this report was being finalized, the NNI issued its legislatively mandated update to its strategic plan, first issued in 2004. The NNI Strategic Plan provides the framework for the U.S. Government to realize the fundamental goals and priorities of the NNI: driving cutting edge research, maintaining the strong research infrastructure and interdisciplinary training, facilitating technology transfer, and addressing EHS issues directly.

The revised NNI Strategic Plan of December 2007 retains the program component areas for strategic investment, although for functional consistency and clarity it formally divides the earlier Societal Dimensions PCA into two separate PCAs: Environment, Health and Safety; and Education and Societal Dimensions (which covers education, ethics, legal issues, and economics). The revised strategic plan (2007) also features a set of illustrative high-impact research opportunities representative of applications where nanotechnology may enable progress that significantly impacts our economy and society. The changes in the strategic plan reflect progress in the science and in the NNI's management and coordination of its broad interagency effort and its impact on academic and industrial research, development, and innovation.

The NNAP recommends that the legislation regarding NNI oversight be changed such that the NNAP review occurs on a triennial basis (as does the NRC review), and that it be due after the triennial update to the NNI Strategic Plan to enable the Panel to more fully evaluate the revised plan in its future reports.

III. Applications: Fostering Present Commercialization and Emerging Innovation

Principal Findings

- *The growing impact of nanotechnology development remains broadly distributed in terms of industry coverage and product composition.*
- *The extent to which a product or process is enabled by nanotechnology or composed of nanomaterials varies substantially, complicating standards development, market evaluation, and regulatory assessment.*
- *Although many initial applications have been evolutionary in nature, nanotechnology innovations nonetheless are promising paradigm-shifting applications in the near future.*
- *The NNI plays a central role in overcoming the barriers in the process of nanotechnology innovation and commercialization, through basic and application-targeted research support, critical infrastructure development, and education and training.*

Context of Commercialization

Nanotechnology encompasses a vast range of engineered materials and devices with an increasingly broad scope of applications and differing degrees of risk and benefit. The extent to which a product, process, or application is enabled by nanotechnology or composed of nanomaterials may vary substantially, complicating categorization, standards development, market evaluation, and regulatory assessment. For example, many commercial applications utilize nanomaterials as raw materials in the manufacturing process, but the final commercial product no longer contains nanomaterial that can be recognized as such, as is the case with many solar cell technologies and composite materials.

Furthermore, what constitutes nanotechnology—beyond scale—defies consensus, and most attempts to define an industry or to catalog such products have resulted in unwarranted inclusions or exclusions that obscure the main issues surrounding nanotechnology development and implementation. For example, there are claims that a new, ostensibly "nanotechnology"-based product reaches the market every day; such claims create the impression that nanotechnology development is a runaway train. This can obscure the reality that the great majority of current commercial nanotechnology applications involve a core set of materials: carbon nanostructures, silver or gold nanoparticles and nanowires, nanoscale metal oxides, and a few other compounds. (The OECD has put forward some fourteen materials that collectively account for most nanotechnology-based applications to date.) The Federal Government continues to fund and conduct extensive research on these and other nanomaterials and specific applications in support of responsible development and thorough assessment from a complete risk/benefit perspective.

The challenges to developing, manufacturing, and marketing nanotechnology-enabled products and processes are by and large not unique. A business or investor looks for advantages over existing products and a path to reproducible, reliable, and cost-effective manufacture. And, as with any product, the responsibility for the safety of workers and consumers lies with the manufacturer.

Firm assessments of current economic impact and projections of future economic impact of U.S. investment in nanotechnology are difficult to obtain. Various estimated market assessments typically include nanotechnology-enabled products often well downstream from nanotechnological innovation. Those market projections based on well-defined categories of fundamental nanomaterials and devices, and specific classes of products enabled by them, allow for some reasonable estimates—if they are properly qualified. This is not inappropriate, given the fundamental nature of nanotechnology and the sheer breadth of current and potential effects on everyday materials, products, and processes.

The current impact of nanotechnology on commercial activities may be evaluated via the number and extent of company efforts (both "pure play" and "integrators"), number of new start-ups, and amount of corporate R&D investment and venture capital (VC), where such data or estimates are available. Table III-1 summarizes by state such data on new nanotechnology-based companies.[4]

Table III-1. New nanotechnology-based firms and venture capital investment (1995-2006) by state.[5]

State	New nano firms	#New nano firms with VC	Sum of VC to nano firms (in million $)
Alabama	2	0	0
Arizona	5	1	40
Arkansas	2	0	0
California	42	13	447
Colorado	6	1	32
Connecticut	2	0	0
Delaware	1	0	0
Florida	7	1	4
Georgia	2	2	41
Illinois	9	6	54
Iowa	1	1	2
Kansas	2	0	0
Kentucky	1	0	0
Maryland	3	1	11
Massachusetts	25	7	244
Michigan	12	2	27
Minnesota	7	2	5
Missouri	3	1	20
New Jersey	7	2	50
New Mexico	10	2	46
New York	13	2	37
North Carolina	5	2	8
Ohio	5	1	16
Oklahoma	3	0	0
Pennsylvania	12	4	97
Rhode Island	2	0	0
Tennessee	8	0	0
Texas	17	4	91
Utah	1	0	0
Virginia	7	0	0
Washington	2	2	10
Wisconsin	4	3	38
Wyoming	2	0	0
Total	**230**	**60**	**1324**

The NNI is expanding efforts to assess national and international nanotechnology-related innovation and commercialization activities. Through its member agencies and NNCO-supported activities, the NNI has

[4] "Nanotechnology-based companies" is defined as firms established primarily in the period 1990–2005 to develop or apply nanotechnological processes, materials, tools, and devices, as identified from compiled and validated lists of new nanotechnology-based firms available in various nanotechnology-based firm directories.

[5] Source of VC data: *PricewaterhouseCoopers/National Venture Capital Association MoneyTree™ Report*, based on data from Thomson Financial. Computed September 2007 by Jue Wang, Program in Research and Innovation Systems Analysis, Center for Nanotechnology in Society (CNS-ASU) at the Georgia Institute of Technology Technology Policy and Assessment Center.

supported a number of activities aimed at collecting and analyzing data on innovation (e.g., patenting trends and industry surveys and data collection). While this NNAP panel commends these efforts, the members recommend closer involvement in these issues from the Department of Commerce (DOC) and continued U.S. participation in the OECD to obtain better data on an international level.

Case Studies

Input from a number of nTAG representatives indicated their consensus that nanotechnology development has not yet produced the commercial revolution that was anticipated, and that many of the early applications evident today are only evolutionary improvements over existing materials and products. At the same time, they noted that nanotechnology research and development has advanced faster than expected in many areas, including drug delivery devices and semiconductor electronics.

The NNI has existed since 2001. Many nanotechnology-based applications are now coming to market, in part as a result of NNI investments to date, and many remarkable innovations are emerging as well. The cases that follow provide examples of how the NNI supports present commercialization and emerging innovation in four sample categories: consumer products, biomedicine, energy, and electronics. An additional case highlights carbon nanotubes as the preeminent example of a nanomaterial platform technology with cross-cutting applications.

Consumer Products

Nanoscale metal oxides in sunscreen: balancing risks and benefits of a specific application in the broader context of human health. Sunscreens are perhaps one of the better-known examples of consumer products purposefully using nanoscale materials. Titanium dioxide, a highly inert metal oxide used in multiple products for its light-modifying qualities, is a key ingredient in many sunscreens. In this application, the compound is "micronized" into microscale and/or nanoscale particles (Figure III-1). Doing so provides two particular benefits: (1) the sunscreen becomes transparent instead of white and adheres better when it is applied, and (2) the sunscreen can absorb harmful UVA rays more effectively than conventional sunscreens.

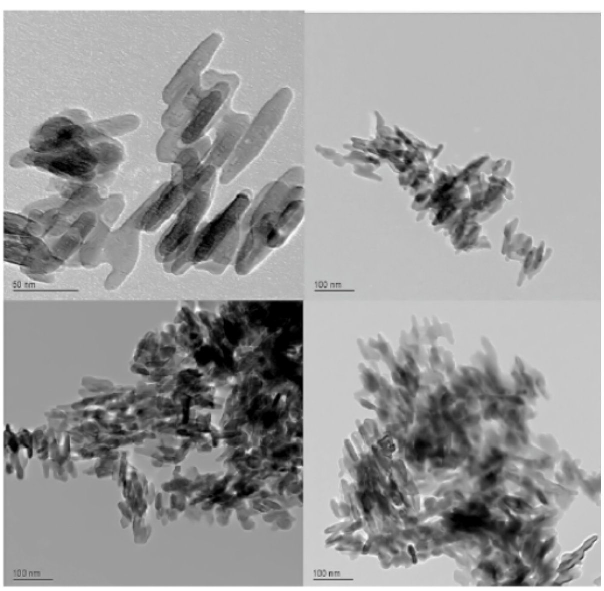


Figure III-1. Nanoscale rutile titanium dioxide. (Image credit: National Toxicology Program.)

A substantial body of research on biological responses to nanoscale titanium dioxide and other metal oxides has already been published. Researchers continue to investigate whether dermally applied titanium dioxide that may be in the nanoscale can penetrate the skin, and if so, whether there may be toxicities associated with these particles. The majority of evidence to date suggests that titanium dioxide nanoparticles do not penetrate intact skin (Nohynek et al. 2007). Nevertheless, research continues through the National Toxicology Program and through other Federal efforts on this and other questions regarding exposure to and toxicity of nanoscale metal oxides.[6]

In consideration of the issue, some have called for responses from industry and government ranging from product withdrawal or labeling to a full-scale moratorium on all nanotechnology-related consumer products.

[6] In recently proposed rulemaking, the FDA has issued a call for public input and data on this specific issue.

Although most of these calls focus on the possible risks that may be associated with nanoscale materials, they fail to consider the broader relative risks and benefits of sunscreens—nano-based and otherwise—to human health.

In contrast, one non-governmental organization conducted a detailed and broad evaluation of sunscreens, including evaluation of other chemical contents and functional benefits. Contrary to their stated expectations, the group found that sunscreens containing nanoscale titanium dioxide or zinc oxide are some of the safest, most effective sunscreens available (EWG 2007). The extent of absorption and associated risk was higher for the non-nanoscale active ingredients than for nanoscale metal oxides. Indeed, the data on titanium dioxide suggests no exposure and better reduction of UV risk, whereas many other active ingredients are known hazards with less UVA blocking benefit.

All relative risks and benefits considered, the overall health benefits (better adhering formulations that better block UVA that consumers are more likely to use since they go on transparently) evidently outweigh the overall health risks, both known (UV-exposure carcinogenicity and/or chemical toxicity) and unknown.

Biomedicine

Simultaneous detection of multiple biomarkers of disease. Polymerase chain reaction (PCR) technology revolutionized diagnostic medicine and basic research through its ability to amplify and detect minute amounts of specific DNA sequences. Researchers at Northwestern University have developed a diagnostic nanotechnology known as the biobarcode assay that works like PCR for proteins (Figure III-2). The biobarcode assay can simultaneously detect trace levels of multiple biomarkers (including DNA and proteins) associated with human cancers using oligonucleotide- and antibody-coated gold nanoparticles.

In 2007 the Northwestern team developed nanoparticle-tagged oligonucleotide biobarcodes to detect three cancer-related protein biomarkers: prostate specific antigen (PSA); human chorionic gonadotrophin (HCG), a marker for testicular cancer; and α-fetoprotein (AFP), a liver cancer marker. In this case, the investigators used three pairs of nanoparticles, each containing a different DNA barcode. The biobarcode assay was able to detect each of the three markers simultaneously at concentrations multiple orders of magnitude below that detectable by the standard immunoassay (Stoeva et al. 2006).

The ability to detect low-levels of protein biomarkers directly in serum in a multiplexed manner will enable more powerful diagnostic methods to detect early-stage malignancy. The biobarcode assay nanotechnology has been commercially developed by Nanosphere, Inc.; to date, the FDA has cleared its use for two molecular diagnostic tests associated with blood disorders (Nanosphere, Inc. 2007).

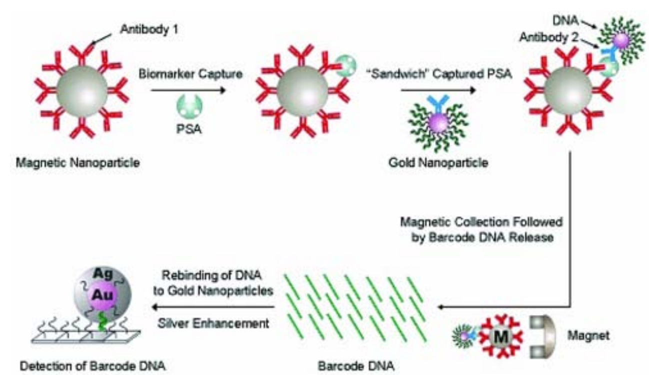


Figure III-2. The biobarcode assay uses two particle probes that are each specific to the targeted biomarker. One is a magnetic particle probe that captures the target from complex media. The other is a gold nanoparticle probe that is specific to the target of interest but that also carries with it hundreds to thousands of DNA sequence barcodes chosen to be specific to the target of interest. Released biobarcodes can be detected using common DNA detection methods (microarray, fluorescence, electrochemistry). (Image credit: Chad Mirkin, Northwestern University.)

Nanoparticles transport cancer-killing drug into tumor cells with greater efficacy and lower toxicity. Dendrimers (branched spherical nanoscale polymers) have shown promise as targeted delivery vehicles for anticancer therapy. Researchers at the University of Michigan have shown for the first time that a targeted dendrimer can indeed deliver anticancer drugs into tumor cells and that this nanotechnology-based treatment is effective in treating tumors growing in living animals and in prolonging life (Kukowska-Latallo et al. 2005). The study is the first to demonstrate a nanoparticle-targeted drug actually leaving the bloodstream, being concentrated in cancer cells, and having a biological effect on tumors.

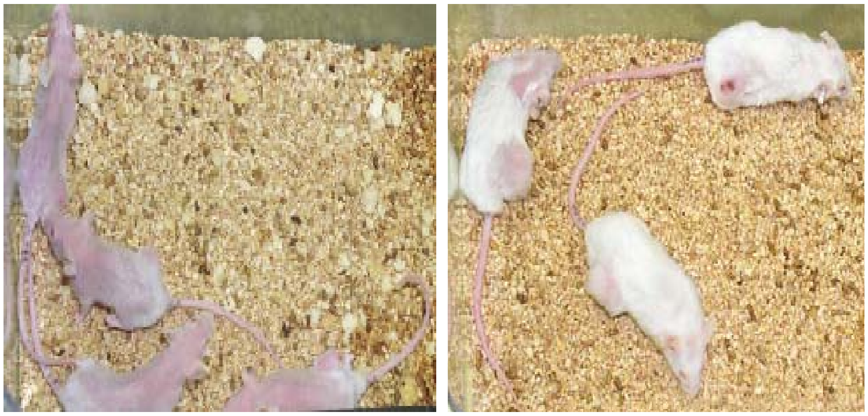


Figure III-3. On the left, mice receiving free methotrexate (30 mg/kg) alone lost their hair, lost weight, and experienced other toxic side effects from the drug. On the right, mice given nanoparticle-delivered methotrexate to shrink their tumors did not lose their hair—a common side effect of anticancer drugs. (Image credit: Kukowska-Latello, Michigan Nanotechnology Institute for Medicine and Biological Sciences.)

The Michigan research team integrated expertise from across a broad range of disciplines to develop multifunctional dendrimers as targeted carriers of anticancer drugs. These branched polymers form compact nanoparticles of well-defined size, ranging from less than 2 nanometers in diameter to greater than 13 nanometers in diameter, with reactive chemical groups on their surfaces that can be used to attach targeting molecules, therapeutic drugs, and imaging agents, either alone or in combination.

The investigators used a G5 dendrimer, which has a diameter of approximately 5 nanometers and room to attach as many as 110 targeting, therapeutic, and imaging molecules. The investigators attached folate as a targeting molecule and methotrexate as the therapeutic agent. Folate targets a high-affinity folic acid receptor that cancer cells overexpress, and methotrexate is an effective but highly toxic anticancer drug. The researchers also attached a fluorescent molecule to the dendrimer to act as an optical imaging probe to enable the investigators to track the dendrimers' distribution in the body by measuring fluorescence in various tissues.

When tested in laboratory mice that had received injections of human epithelial cancer cells, the targeted, methotrexate-loaded dendrimer was 10 times more effective than methotrexate alone at delaying tumor growth. Nanoparticle treatment also proved to be far less toxic to mice than the anticancer drug alone (Figure III-3). In the longest trial reported, which lasted 99 days, over 30 percent of the mice given the multifunctional nanoparticle survived. In contrast, all of the mice receiving free methotrexate died, either from tumor growth or from drug toxicity. Tumor growth also proceeded unabated when mice received a folate-targeted G5 dendrimer that did not contain methotrexate. The presence of a fluorescent label on the dendrimer had no effect on anti-tumor activity.

Biodistribution studies using the fluorescent tag showed that folate-targeted nanoparticles concentrated in tumors and liver, and tumor concentrations of the dendrimer remained high for four days after injection. These studies also revealed that the kidneys quickly filtered any nanoparticles that remained in circulation—they either did not bind to a target or were eventually released from their target—and eliminated them in urine. The researchers found no evidence that nanoparticles were able to leave the bloodstream and enter the brain. The nanoparticles did not appear to generate an immune response in mice in the study. Confocal microscopy studies, again utilizing the fluorescent tag on dendrimers, confirmed that the targeted nanoparticles were taken up by tumor cells.

In future research, scientists at the Michigan Nanotechnology Institute and Avidimer Therapeutics will determine the maximum therapeutic dose, in research animals, of targeted nanotherapy with methotrexate[7] and will complete other preliminary studies in preparation for human clinical trials.

Energy

Light, thin solar cells manufactured with printing presses. Thin-film photovoltaic technology has improved over the last decade to a point where it can now convert sunlight to electricity as efficiently as all but the most expensive silicon-based solar cells. New low-cost production methods could help make these thin-film cells an important contributor to the Nation's energy needs. Nanosolar, Inc. is using printing presses instead of vacuum deposition equipment to make solar panels based on a semiconducting material called copper indium gallium diselenide (CIGS). The presses deposit nanostructured ink, which is then processed to create the light-absorbing nanoarchitecture at the heart of the solar cell. Employing a range of innovative technologies developed in part with the support of the Department of Energy, the National Science Foundation, and the Defense Advanced Research Projects Agency, Nanosolar has recently shipped its first utility-scale panels. The company was one of several recipients of major awards under DOE's Solar America Initiative that are using nanotechnology to drive down the cost of renewable energy, with the ultimate goal of achieving price parity with the major energy sources now feeding the electric grid.

Titanium-studded carbon nanotubes hold promise for fuel cells with high-capacity hydrogen storage. Quantum calculations and computer models show that carbon nanotubes (CNTs) "decorated" with titanium or other transition metals can latch on to hydrogen molecules in numbers more than adequate for efficient hydrogen storage (Figure III-4), a capability key to long-term efforts to develop fuel cells as an affordable alternative transportation technology (Yildirim and Ciraci 2005).

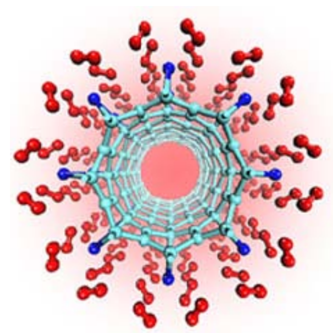


Figure III-4. This computer model shows how titanium atoms (dark blue) can attach above the centers of single-walled carbon nanotubes (light blue). Each titanium atom can bond with four hydrogen molecules (red), which could lead to efficient fuel cells for future automobiles. (Image credit: T. Yildirim, NIST, and S. Ciraci, Bilkent University, Turkey.)

Using established quantum physics theory, NIST researchers and international collaborators predict that hydrogen can amass in amounts equivalent to 8 percent of the weight of titanium-studded singled walled carbon nanotubes—better than the 6 percent minimum storage capacity requirement set by the FreedomCar Research Partnership involving DOE and U.S. automakers. As important, the hydrogen molecules that link to a titanium atom are readily relinquished when heated. Such reversible desorption is another requirement for practical hydrogen storage.

Resembling exceedingly small cylinders of chicken wire, single-walled CNTs are among several candidate materials eyed for hydrogen storage. Reaching the 6 percent minimum target, however, has proved difficult. With structural and computational models of the materials, researchers showed that positioning a titanium atom above the center of hexagonally arranged carbon atoms (the repeating geometric pattern characteristic of CNTs) appears to enable sufficient, reversible storage. Surprisingly, interactions among carbon, titanium, and hydrogen seem to give rise to unusual attractive forces. The upshot is that four hydrogen molecules can dock on a titanium atom, apparently by means of a unique chemical bond of modest strength. Several forces at work within the geometric arrangement appear to play a role in the reversible hydrogen binding. The findings demonstrate a potential way to engineer novel nanostructured high-capacity hydrogen storage materials and catalysts.

[7] See http://www.avidimer.com/productportfolio/leadproductcandidate.html for a more detailed description of the nanostructured methotrexate product.

Electronics

Researchers at IBM, a pioneer in nanotechnology research, published work in *Science* magazine reporting on novel computational approaches based on nanoscale science and engineering. Researchers demonstrated progress in developing the ability to measure the magnetic anisotropy of single atoms—and thus their potential ability to store information magnetically at the atomic level (Hirjibehedin et al. 2007). Such capability would dramatically shrink the space currently needed for computational memory—the equivalent of holding all the video contents of YouTube on an iPod.

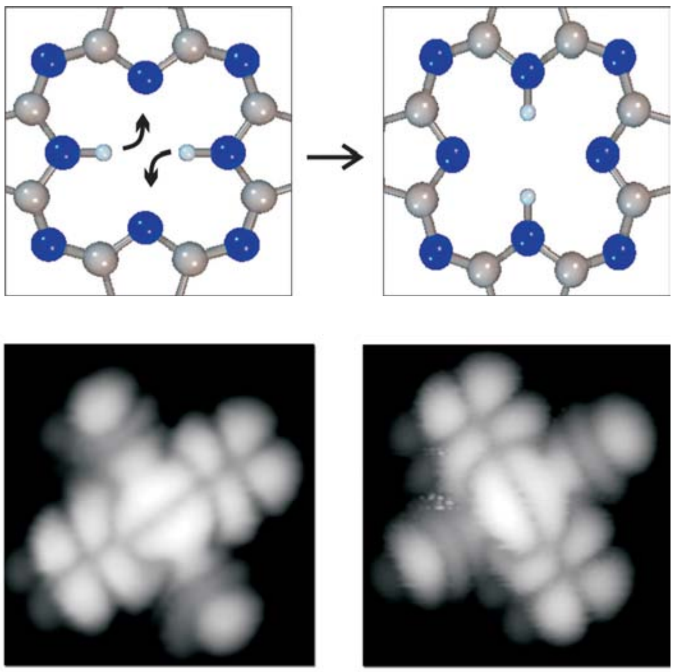


Figure III-5. Molecular switch in stable framework. (Image credits: IBM, 30 August 2007, available online: http://www-03.ibm.com/press/us/en/presskit/22242.wss.)

Furthermore, IBM researchers also have developed the first molecular switch that preserves the external framework of the molecule (Liljeroth, Repp, and Meyer 2007). Because the external framework does not change shape when the switch is "on" or "off" (Figure III-5), this opens the possibility of integrating this novel molecular switch (which functions as a logic gate) as a component in a larger circuit.

Platform Technology

Carbon nanotubes. Although not the first commercialized nanoscale materials, CNTs have gained broad public recognition as an embodiment of nanotechnology and a prime example of development through government, academia, and industry cooperation. Due to beneficial properties that include exceptional tensile strength, unique current conduction mechanisms, and their vessel-like shape, CNTs have multiple potential applications. They are already impacting commercial electronics and composites, are demonstrating promise for use in energy storage and conservation, and are being explored for use in gene and drug delivery within the body.

Although perhaps best known for their use in composite materials for consumer products such as car bumpers and sporting goods, CNTs can only improve material characteristics to a degree that is limited by manufacturing challenges (e.g., ability to control uniformity, length, and disaggregation). Revolutionary advantages enabled by CNTs over the composite materials that are currently on the market will depend on improving manufacturing controls (Eklund et al. 2007).

There are many different types of CNTs, with a variety of diameters, number of walls (single or multiple), and functional additives, as well as impurities. Pure, single-walled CNTs are extremely difficult and expensive to manufacture, and the market for these (as compared to cheaper multi-walled CNTs) is not yet evident. Asia and Japan in particular far surpass the United States and Europe in manufacturing capability for multi-walled CNTs. The primary market for multi-walled CNT manufacturing is currently for use in lithium-ion battery electrodes, whereas the primary market for single-walled CNTs is field emission devices (used, for example, in field emission microscopes for surface science studies and in vacuum microelectronic devices).

Challenges to Commercialization

Along with the many opportunities that presently exist in the innovation and development process for technologies like those described above, there are also challenges. The following barriers to commercialization are pronounced with respect to nanotechnology, given the scope of potential applications and the many unknowns associated with various nanomaterials constructs:

- Lack of standards
- Questions about EHS implications: unknown risks (cf. publications in environmental law), attention by insurers, anecdotal evidence of companies avoiding "nano" in their product descriptions, or worse, shelving their nanotechnology development efforts
- Limited/restricted venture capital: an investor community uncomfortable with many nanomaterial-dependent startups due to their relative earlier stages of development and longer development cycles (i.e., greater time to applications and products)
- Insufficient education and workforce preparation

The Federal Government plays a central role in overcoming the barriers in the process of nanotechnology innovation and commercialization. The NNI serves to coordinate Federal agency efforts in this regard. The NNI directly supports the broad spectrum of basic nanotechnology research and development and also stimulates private sector commercial investment with targeted, application-focused research and development programs. Furthermore, the unparalleled research infrastructure and interdisciplinary training programs built at a national level through the NNI are clearly accelerating the process of U.S. nanotechnology innovation and seeding regional efforts to do the same. Limited dissemination of knowledge/skill/expertise in nanotechnology is a continuing barrier to commercialization of the cutting-edge ideas that come out of the lab. Transfer of nanotechnology know-how and ideas from university research labs to industry occurs primarily when students are hired by existing companies or start new ones. The importance of the Government role in educating scientists and engineers through investment in R&D cannot be overemphasized.

As described in the updated NNI Strategic Plan of December 2007, the NNI aims to continue fostering technology transfer by creating a favorable business environment for nanotechnology developers by a variety of means. Key approaches include coordinated engagement with industry, clear intellectual property protections, and better defined development pathways and oversight expectations. NNI participating agencies also are working to facilitate sharing of precompetitive data on nanomaterials domestically and internationally, which will help to address EHS concerns.

IV. Implications: Addressing Environmental, Health, Safety, and Ethics Issues Responsibly

Principal Findings

- *The Federal Government is highly active and widely supporting nanotechnology EHS planning and R&D, and is coordinating with industry and international stakeholders to that end.*
- *Manufacturers have a unique responsibility for product and workplace safety.*
- *Companies that make and use nanomaterials must also be involved wherever possible in developing and widely sharing information about the properties of the nanomaterials in their products.*
- *Negative public perceptions threaten the development and subsequent economic and societal benefits of nanotechnology.*
- *Although no ethical concerns appear to be fundamentally unique to nanotechnology today, all stakeholders have a shared responsibility to carefully evaluate the ethical, legal, and societal implications raised by the development of novel science and technology.*

Context of and Perspective on EHS Considerations

Many nanotechnology-enabled products are already available today, including medical applications and devices, electronics, and a broad range of consumer goods. The impact of nanotechnology will certainly increase in the future as more innovations enabled by nanotechnology are developed into commercial applications. The NNAP anticipates that nanotechnology will have a net positive effect on the environment and human health.

As with any emerging technology, responsible nanotechnology development and application should be a universally shared goal of researchers, developers, manufacturers, regulators, and consumers. However, applying this principle can be challenging, because nanoscale materials have unique physical and chemical properties that can be difficult and/or costly to fully characterize, and their effects on health or the environment are not known or are poorly understood. The NNI stance should continue to be appropriately cautionary, not precautionary, and NNI member agencies should maintain a proactive approach to developing and disseminating relevant risk-related information.

The Federal agencies recognize that there is much that is unknown about the possible health effects from exposure to nanomaterials. Therefore, in order to cultivate a growing body of baseline information, the NNI and its member agencies should continue to (1) strategically fund priority EHS research and (2) support collaborative EHS activities with industry and with research agencies in other countries. The NNI has a vital role in supporting the regulatory agencies by providing such research.

The NNAP examined the nature and scope of the NNI investments in research to assess the environmental, health, and safety implications of nanotechnology as well as in research to identify the ethical, societal, legal, and related workforce concerns that arise in connection with nanotechnology research, development, and commercialization. These implications need to be carefully examined continuously to ensure responsible development and appropriate balancing of risks versus benefits. Such ongoing, thorough examination of EHS implications, within the proper framework and incorporating broad stakeholder input, will enable sustainable development and maximum realization of the potential of nanotechnology.

In making its review, the NNAP is aware of the growing number of articles and publications suggesting that EHS efforts in the United States are inadequate and might lead to environmental, health, and safety risks that are unacceptable. In general, these reports suggest that insufficient funding and focus on EHS concerns are the primary problem. The NNAP has paid particular attention to EHS funding and current research efforts in this review. The panel finds that from a scientific point of view, while there is still plenty to learn, the research being funded is leading to an ever-increasing body of knowledge about EHS issues. Budgetary support for EHS has been growing at a rate well above that of the entire NNI program and, as such, the panel believes it is of the right order of magnitude to continue building knowledge of EHS issues as knowledge of the science increases. The panel does note that if expenditures of other countries in the global economy were as significant in the EHS field as those in the United States, and with ongoing, appropriately multinational communication efforts, the entire field would benefit greatly.

Having said this, there is little question that nanotechnology development is facing an important threshold, in that public acceptance of nanotechnology may deteriorate if some of the more frightening speculations of some writers reach common acceptance. The NNAP is concerned that nanoscience is losing a public relations contest. The value of nanotechnology to the U.S. economy and the contribution of nanotechnology to actually improve EHS conditions in our country are being drowned out by the emphasis on uncertainties and by speculation that is unconstrained by examination of actual exposure and hazard in realistic use settings. These concerns have led the NNAP to pay close attention to EHS and related activities and implications in this report.

Federal EHS Activities

In September 2006, the NNI issued a report titled *Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials*, developed under the auspices of the Nanotechnology Environmental and Health Implications (NEHI) Working Group of the NSET Subcommittee (NSTC/NSET 2006). The report incorporates perspectives of several different Federal agencies that have a role in assuring the responsible development of nanotechnologies. Carrying out the research specified in the report over the next several years is a fundamental responsibility of the Federal effort in nanotechnology research. The report also provides guidelines for State agencies, the private sector, and international entities involved in nanotechnology-related EHS research.

In August 2007, the NNI released for public comment an interim document that prioritizes EHS research needs. The prioritization was based on (1) the value of information and (2) the ability to leverage relevant research funded by other governments and the private sector. The NNAP views the NNI reports to date as an important first step in identifying the many research areas that are encompassed by the need for responsible development of nanotechnology, and in prioritizing research areas that must necessarily follow to ensure research resources are appropriately deployed.

Input gained from public comment on the NEHI research needs and prioritization documents as well as from detailed analyses of current Federal nanotechnology EHS research by the NEHI has informed the development of the NNI's February 2008 publication, *Strategy for Nanotechnology-Related Environmental, Health, and Safety Research* (NSTC/NSET 2008b). This document includes a process for regular progress review and transparent reevaluation of the stated EHS research needs and priorities. Because this report was completed and released at the close of the NNAP's current review process, the NNAP intends to issue a brief addendum to this report commenting on the strategy.

Since the 2005 NNAP report called for special attention to be directed toward EHS research and assessment, NNI member agencies responsible for oversight of human health and the environment have been proactive in addressing the EHS information needs. Several NNI agencies have been actively evaluating their approach to regulation and oversight of nanotechnology products, manufacturing, and workplace safety, as indicated by the following examples:

- The OSTP and the Council on Environmental Quality (CEQ) issued in November 2007 a memorandum identifying principles for nanotechnology environmental, health, and safety oversight based on interagency consensus (OSTP 2007).

- The National Institute of Occupational Safety and Health (NIOSH) issued a call in July 2006 for information on *Approaches to Safe Nanotechnology* (NIOSH 2006) inviting expert feedback from private industry and other government entities, and in June 2007 it issued the report *Progress Toward Safe Nanotechnology in the Workplace* (NIOSH 2007).
- The Environmental Protection Agency (EPA) produced in February 2007 a white paper (EPA 2007) summarizing the agency's anticipated approach to nanotechnology EHS research, followed in February 2008 by a nanomaterial research strategy (EPA 2008). The agency also has launched a Voluntary Nanoscale Materials stewardship program.
- The Food and Drug Administration (FDA) released in July 2007 the report (FDA 2007) of its Nanotechnology Task Force's efforts to clarify a predictable pathway for application of existing regulatory approaches on a case-by-case basis for developers of nanotechnology-enabled products under its jurisdiction.
- NIST is producing standard reference materials for nanoscale gold and carbon nanotubes.

Considered along with the full interagency coordination of EHS activities and planning through NEHI, these activities further demonstrate active involvement and participation by the Federal agencies responsible for public health and safety to inform regulatory approaches and policy development.

The total funding of research in nanotechnology EHS has grown since the last NNI report from $34.8 million in 2005 to a requested $76.4 million in the President's proposed budget for nanotechnology R&D in 2009. This accounts only for research that is specifically and primarily focused on environmental and health effects of nanotechnology. In 2007, the NSET Subcommittee coordinated with the Office of Management and Budget to collect a broader account of research under the five priority categories identified in the NEHI 2006 report *EHS Research Needs for Engineered Nanoscale Materials* for research that not only examines EHS issues directly but that supports such examination, including research in instrumentation, in fundamental understanding of the behavior of key nanomaterials, and in risk management methods. When such research is included, the total investment amount related both directly and indirectly to EHS in FY 2006 was over $68 million, compared to reported research spending of $37.7 million primarily addressing EHS. Though not practical for regular reporting, this data snapshot likely represents more closely the Federal investment in nanotechnology-related EHS research. The NNAP feels that this amount of research is appropriate; however, it does recommend that the funding level for EHS continue to grow consistent with the needs and approach identified in the NNI research strategy for nanotechnology EHS as well as the available capacity for quality research.

While the Federal Government establishes and provides appropriate regulatory oversight, manufacturers have a responsibility for product and workplace safety. Therefore, companies that make and use nanomaterials must also be involved in developing information about the properties of their products.

As the 2005 NNAP report stated, the greatest likelihood of exposure to manufactured nanomaterials is in the manufacturing environment. Currently the exposure to consumers and the environment is relatively low. NIOSH has various resources available at its nanotechnology website, http://www.cdc.gov/niosh/topics/nanotech/default.html, including the two documents mentioned above, that provide interim guidance on safe handling of nanomaterials in the workplace.

Although the following sections separately address the NNI-sponsored research in the areas of environmental impact, human health effects, and safety considerations, the context of EHS issues must be understood in order to properly evaluate and manage risk. Most EHS areas are highly interrelated. Environmental issues can impact the health of humans and other living organisms. Safety considerations can also affect health. This review discusses environmental issues as those directly impacting the environment; health issues include those directly intended to improve human health but that may have unintended consequences; safety issues include possible consequences of exposure to nanomaterials in the workplace and elsewhere where activities involving nanomaterials might have a deleterious effect on the persons connected with the activity. As previously noted, Federally sponsored EHS research should be coordinated not only with the States and with

U.S. industry, but also with the international community. The NNAP commends NNI efforts to cooperate on EHS issues with OECD and other international bodies.

Nano EHS Research Today and Tomorrow

A large body of both domestic and international research on EHS implications of nanotechnology already exists and is growing, which is consistent with the continuing growth rate of Federal support in the area. For example, a recent search of the International Council on Nanotechnology's Virtual Journal on nanoEHS—a representative database of publications worldwide—shows well over 1,000 peer-reviewed scientific papers as well as technical reviews and other articles that have been published in this area since 2003 (http://www.icon.rice.edu/virtualjournal.cfm). In addition, Government agencies, corporations, and a handful of non-government organizations are conducting extensive targeted research as well. One organization, the Environmental Working Group, studied over 900 sunscreen products based on over 400 studies on efficacy and toxicity of relevant materials in the scientific literature (EWG 2007b). Targeted efforts like these properly assess nanomaterials in product- and life-cycle-specific contexts and complement fundamental research and baseline characterization of nanomaterials.

However, growing research in nanotechnology EHS must be strategic, guided by (1) a comprehensive set of scientifically determined priorities and needs rather than arbitrary percentages or funding figures, and (2) standardized methods and data sets for nanomaterial characterization to enable reproducible and progressive research. For example, a recent review of over 400 publications showed that the vast majority of studies did not adequately characterize the nanomaterials under study, making it virtually impossible to specify the hazard-determinative properties of those nanomaterials (Hansen et al. 2007). In the absence of guidelines for appropriately standardized materials and analyses, EHS research on nanomaterials will not move forward. Arbitrary funding increases will only lead to more confusion (instead of 80 nonreproducible, noncomparable studies on various types of carbon nanotubes, we could have 800) and will hinder the necessary, relevant research that can only be built on clearly characterized, reproducible, standardized, comparable research on specific materials in specific, relevant applications.

Environment

The presence of nanoscale materials in the environment is not new; in fact, nanoscale materials occur naturally. However, as engineered nanoscale materials are developed, the potential environmental effects may be unique for specific nanoscale substances. The NNI, and the Federal Government in general, has a central role to play in the development of tests to assess environmental effects of nanoscale materials. In many cases, it is not yet clear if existing protocols are sufficient, although they should be used as a starting point. The NNI is working to collaborate with other stakeholders (industry, academia, and international peers such as the OECD Working Party on Manufactured Nanomaterials) to share the burden of development of analytical tests and risk assessment methodologies and to ensure broad acceptance of tests worldwide. As new nanomaterials come to market in products, it is also the fundamental responsibility of industrial developers to perform appropriate and relevant studies to assure environmental neutrality, guided by scientifically founded assessments of associated risks and benefits.

There is an increasing recognition that the characterization of test materials is not always as complete as needed to fully understand the basis for observed effects. At the nanoscale, there can be profound differences between chemical entities otherwise thought to be of the same basic material, based on shape, charge, and other characteristics. For example, as particles become smaller and the ratio of surface area to mass greatly increases, the contribution of the surface chemistry to observed effects may greatly increase as well. However, any surface contamination is also magnified—a factor often overlooked. A resulting observed effect may be due to a contaminant and not to the material being evaluated. The NNI is uniquely positioned to have an impact on improving awareness of the need for robust physical characterization of nanoscale materials through the participation of agencies such as NIST, EPA, and FDA, as well as through international cooperation. The NNI must continue to be diligent in filling this role.

Health

The application of nanotechnology to health maintenance and improvement is one of its most promising areas of use. Much of the work with nanoscale materials is being performed to develop new pharmaceuticals and medical devices or to improve food preservation techniques. This is an exciting area, and some of the work has shown that nanoscale medications may provide enhanced benefits over conventional forms of the same medications and can in some cases provide improved targeting with fewer side effects (see examples cited earlier in III, Applications). Clearly, these benefits, if fully realized, will have great social value. But because nanomaterials are being actively used in biomedical and healthcare products, and marketing claims for the improved performance of these products proliferate as new compounds are used, the FDA, consistent with its regulatory scope, must remain vigilant and proactive in assessing approval for and use of products that incorporate nanomaterials.

In cancer therapy, colloidal gold and nanoscale gold-coated particles have been shown to be effective in targeting and reducing tumors. Thousands of citizens receive hip, knee, or other bone replacements, stents, heart valves, and a wide variety of other medical implants each year. Research and development continues apace using nanomaterials to further improve the performance of and further reduce the risks associated with these structures. Novel delivery mechanisms and implantable devices have raised legitimate concerns about the longer-term effects of nanomaterials in the body. Studies to determine these impacts are being funded by the NNI and must continue as more targeted, nanotechnology-enabled drugs and devices are designed.

The NNI, in conjunction with participating agencies such as FDA and USDA, is increasingly looking at this expanding role of nanotechnology-based products for healthcare and food. Though there is no evidence at present of negative human health outcomes from use of these products, continued diligence in testing and approving these products will be necessary as their use continues to grow.

Safety

As described in the 2005 NNAP report, the greatest present safety concern remains in the workplaces where nanotechnology products are being produced. Developing and communicating information about potential health effects and minimizing unintended exposures to workers and users of nanoscale materials is of critical importance. As noted above, NIOSH is very active in assessing workplace factors with respect to nanoscale materials. It has established a robust program to work with those developing nanoscale materials, both to collect more data about existing workplace practices and to provide guidance to workers and employers via its website and upon request (see *Approaches to Safe Nanotechnology*, http://www.cdc.gov/niosh/topics/nanotech/safenano/) to help reduce potential exposure along the lines of current good manufacturing practices. EPA's Voluntary Nanoscale Materials Stewardship Program (http://www.epa.gov/oppt/nano/stewardship.htm) encourages industry submission of data that may have a safety impact. While respecting confidential business information, these data should be regularly published where possible and incorporated into the literature identifying best practices.

Ethics

Concerns about ethical, legal, and societal implications (ELSI) have naturally arisen as nanotechnology has developed and as products have proliferated in the marketplace. The following are examples of findings from the many scholarly articles that have been written in the recent past defining and assessing societal benefits:

- New drugs that may be more active, using less material, and produced at lower cost, may enable use by a broader segment of an affected population.
- Application of nanoscale materials in environmental remediation may facilitate work in areas of greatest need and economic disadvantage.
- Superior energy production through the use of nanoscale materials may be possible due to more active catalysts in petroleum refining or battery electrodes improved through the addition of nanoscale materials.
- Improved efficiencies in manufacturing processes may result in less waste.

At the same time, ethical issues identified in the context of nanotechnology applications and implications are a growing area of debate. Besides the safety issues—both from a human and an environmental health perspective—some have asked whether some potential applications of nanotechnology would pass meticulous ethical consideration. For example, bioethical questions have been raised regarding access to benefits and uses, many of which may ultimately go beyond therapeutic use into performance enhancement and challenge core concepts of what it means to be human.

As noted earlier in this report, in many ways, these concerns do not differ from those raised as any new technologies come into existence. It is not clear whether the concerns raised are exclusively related to nanotechnology or, more likely, to the generally increasing penetration of technology into the fabric of our daily lives.

The NNI has funded some research in this area, particularly through the NNI/NSF Centers for Nanotechnology and Society located at universities around the country. In addition, the NNAP in performing this review has engaged the President's Council on Bioethics (which conducted an independent study and has published a brief summary of its examination and thoughts on these issues[8]) as well as other experts in the field of ethics to discuss these issues. Numerous ethical issues common to emerging technologies could be the subject of further examination, including, among many others, development of codes of conduct for emerging technologies, risks to marginalized people, therapeutics vs. enhancement, privacy issues invited by the use of nanosensors, confidentiality issues, nanotechnology-related policies for developing countries, and many more.

Based on input from the nTAG, the President's Council on Bioethics, and numerous thought leaders, the assessment of the NNAP is that there are no ethical concerns that are unique to nanotechnology today. That is not to say that nanotechnology does not warrant careful ethical evaluation. As with all new science and technology development, all stakeholders have a shared responsibility to carefully evaluate the ethical, legal, and societal implications raised by novel science and technology developments. However, the NNAP, in consultation with the President's Council on Bioethics, sees no apparent need at this time to reinvent fundamental ethical principles or fields or to develop novel approaches to assessing societal impacts with respect to nanotechnology.

Managing and Coordinating Implications Research

The NNAP is pleased with the degree of coordination taking place among the agencies through the NNI. The great strength of the NNI's consensus-based interagency approach is that it successfully leverages the broad expertise resident in the various agencies, consistent with their respective missions. For example, Federal assessment of risks associated with diesel exhaust and other incidental nanomaterials has informed planning for how to assess engineered nanomaterials. This argues against the notion of creating a centralized, top-down management structure that would duplicate or, worse, exclude contributions from key mission agencies.

The panel expects that the NNI's current EHS, education, and societal dimensions planning and coordination processes, under NSET Subcommittee and NNCO leadership, will continue to strategically guide nanotechnology-related EHS research across NNI member agencies. While there is much to learn, the process is certainly not "broken." In fact, the coordination process used at the NNCO and the similar process used to manage the Networking and Information Technology Research and Development (NITRD) program could well be considered models for similar coordination in fields such as K–12 education, where spending for hundreds of programs is spread over many agencies without any formal mechanism whereby the spending agencies might be informed of activities in their sister Government departments. The NNAP anticipates an expeditious review of the final nanotechnology EHS research strategy and how the interagency coordination will functionally implement it as a forthcoming addendum to this report.

---

[8] See http://www.bioethics.gov/topics/nanotech_index.html.

V. Recommendations: Sustaining Leadership Through Coordination, Strategy, Communication

Nanotechnology in many ways represents a new age of research, development, and commercialization. It is one of the first broad-based technology areas in which the United States has had a research lead and where development and market applications have been clearly defined as essential aims from the beginning. It is in large part due to the formal coordination and prioritization work of the NNI that the United States has been an early leader and continues to be a global leader in nanotechnology. However, nanotechnology is also one of the first areas where European and Asian countries have approximately matched U.S. investments at the earliest stages of development. Nanotechnology is one of the core drivers of interdisciplinary collaboration, which is becoming more and more essential for all science R&D today. And nanotechnology still presents a distinct opportunity in the history of innovation to get technology development "right" from the outset by establishing and maintaining strong, sound, proactive policies to guide public and private R&D and responsible, sustainable innovation of a wide spectrum of materials and products for use in commercial applications.

Overall, the members of the NNAP feel that the NNI is well organized and well managed. The NSET Subcommittee, supported by an interagency-funded coordination office (the NNCO), is effectively coordinating nanotechnology activities across the Federal Government, while allowing agencies to leverage their efforts aimed at supporting their individual agency missions. The panel believes that the NNI's eight program component areas, currently designated in the updated NNI Strategic Plan to track areas of investment, are well conceived and the categories are sufficient to assess and manage the program. The NNAP notes that its overall positive assessment is consistent with those of planning and advisory bodies in other countries, based on the number of nanotechnology programs around the world intentionally modeled after the NNI.

Like the NNAP, the National Academies also bears responsibility for oversight of the NNI. The NNAP members feel these two oversight efforts should be more appropriately timed and more closely coordinated with the NNI schedule (i.e., both reviews should be every three years after the strategic plan is revised) to avoid overlap and to get more out of both activities, particularly in terms of increasing public awareness of their activities and those of the NNI agencies. More timely coordination will enhance the effectiveness and objectivity of both panels.

The members of the NNAP feel that U.S. leadership in nanotechnology is due in large part to the formal framework of the National Nanotechnology Initiative. However, in order to ensure that the Nation remains competitive, the NNAP has the following recommendations to improve and further strengthen the NNI.

1. Infrastructure, Management, and Coordination

Maintaining the world-class R&D infrastructure and strong interagency coordination created under the NNI is essential to achieving broad societal benefits from nanotechnology innovation.

1.1. Ensure continuing support from NNI member agencies and from Congress for NNI multidisciplinary centers, networks, and user facilities for nanoscale research. The NNI infrastructure of user facilities, centers, and networks is an unparalleled resource for the nanotechnology R&D community, but it requires sufficient funding to maintain and operate. Having had the foresight to establish these centers, DOE, NSF, NIH, and NIST should provide ongoing strong support for these vital assets. In particular, NSF and NIH should continue to fund large centers and collaborative research groups that enable the multidisciplinary approaches that are essential to advances in basic nanotechnology research. Such multidisciplinary research remains especially vital because many applications will emerge from research at the convergence of historically disparate fields of science and technology. The NNI should continue to foster both "curiosity-driven" researchers and "applications-driven" developers, and their interaction.

1.2. **Seek to improve *intra-agency* coordination.** Due to the scope and breadth of nanotechnology's impact, the NNAP recommends that each department and agency with numerous operating divisions impacted by nanotechnology (including DOC, DOD, EPA, HHS, and USDA) establish a cross-cutting task force or some similar mechanism to coordinate and optimize nanotechnology activities and policies more uniformly within the agency as a whole. Where such groups already exist, they should be supported at all levels and should be strengthened horizontally and vertically within the agency. The FDA's Nanotechnology Task Force, which incorporates representation from each of its centers, is a notable example. These intra-agency groups, which should include policy, communications, and budget specialists, will foster improved communication within the agency, across the Federal Government, and with outside stakeholders and agency customers.

1.3. **Strengthen participation in the NNI by DOC (beyond NIST), DOEd, and DOL** in light of their respective departmental missions. Interdisciplinary training, broad-based education, workforce preparation, market assessment and evaluation, and standards development are critical challenges for nanotechnology and are essential for the United States to achieve the expected societal and economic benefits of nanotechnology research, development, and commercialization. These needs warrant closer involvement from these agencies in the NNI than has existed to date.

1.4. **Coordinate NSET Subcommittee and working groups activities more broadly with related NSTC interagency working groups**, especially the Interagency Working Group on Manufacturing R&D, which has identified nanomanufacturing as an area of opportunity.

1.5. **Continue to function as the central coordination structure for nanotechnology R&D—including nanotechnology EHS research.** The NSET Subcommittee, its working groups, and the NNCO have been, and should continue to be, the locus of coordination for all nanotechnology-related activities. Congress, to the extent that it engages these issues, should support the current interagency coordination and management structure of the NNI through the NSET Subcommittee and the NNCO.

2. Standards Development

Progress across the breadth of NNI-supported R&D critically depends upon the development and implementation of standards for nanomaterial identification, characterization, and risk assessment.

2.1. **Participate in the development of voluntary consensus-based standards,** which are crucial to research, commercialization, and safe handling and use of nanotechnology. The NNI agencies, individually and jointly through the NNCO, should participate in and support standards development activities. In particular, the NNI should support U.S. participation at key international standards bodies, such as the International Organization for Standards (ISO). Through Federal agency participation, the NNI should seek to avoid duplication of standards development work at organizations that have overlapping areas of activity.

2.2. **Develop materials and analytical standards for nanotechnology EHS research**. Such standards are critical to characterizing and monitoring effects of nanomaterials. NIST should lead the development work, in consultation and collaboration with agencies that use such standards, including EPA and FDA. The initial focus should be on nanomaterials that have or are moving toward broad commercial use (e.g., nanoscale gold, silver, metal oxides, carbon nanotubes, and other materials such as those identified in the OECD list of fourteen most common nanomaterials in current applications).

2.3. Work towards development of minimum data sets of physical and chemical properties of nanomaterials. If properly defined, adoption of a minimum set of data for research on nanomaterials would ensure accurate communication of research results and product properties. It would also enable comparison and reproducibility of EHS testing. This is essential to ensure that evaluations are meaningful and that the assessments of potential EHS impacts are sound. NIST should take a leading role in coordinating efforts to this end among the interagency NNI members.

3. Technology Transfer and Commercialization

Nanotechnology innovation through to commercialization depends on maintaining and strengthening cross-sector collaborations and cross-fertilization of technology development and business development expertise.

3.1. Expand efforts to assess national and international innovation and commercialization activities. While the NNAP commends current and ongoing efforts, the NNI—led by DOC—should identify metrics and obtain data that will allow accurate assessment of the economic impact of nanotechnology development. This will require closer and more coordinated involvement from DOC and continued engagement with OECD to obtain better data at the national and international levels. The downstream impact of nanotechnology development on the economy remains difficult to quantitatively assess, but market projections based on well-defined categories of nanomaterials and devices and specific classes of products will allow for some reasonable estimates, if properly qualified. In any case, since so many industries are involved in nanotechnology development, it appears clear that nanotechnology will have a large economic impact, and continuously monitoring that impact is an important role DOC should play.

3.2. Continue to build connections across the innovation ecosystem, including requiring that multidisciplinary centers partner with industry or with economic development organizations. NSF, NIH, and other major supporters of multidisciplinary nanotechnology-focused centers should explicitly support, maintain, and strengthen cross-sector linkages.

3.3. Educate more scientists and engineers to become entrepreneurs and skilled technology workers. Transfer of know-how and ideas from university labs to products and processes with commercial value and public benefit occurs primarily through college and university education and research activities. Funding world-class research is the best "training program" for top-notch nanoscale scientists and engineers.[9] The NSF Integrative Graduate Education Research and Traineeship (IGERT) program is a notable model in this regard, particularly with respect to interdisciplinary nanotechnology training and R&D.

4. Environmental, Health, and Safety Implications

Nanotechnology EHS research must be strategically guided, integrated, and coordinated across agencies, sectors, and countries, and include balanced assessment of risks and benefits in the context of specific, real-world applications.

4.1. Coordinate the nanotechnology EHS strategy with industry and international stakeholders. EHS research is noncompetitive; therefore, the NNI should coordinate efforts in this area with the activities of industry and other countries so as to avoid duplication and to leverage investments. NNI member agencies should work centrally through the NNCO and/or consensus lead agencies designated in the NNI nanotechnology EHS research strategy to coordinate their respective research activities with other relevant entities.

---

[9] While this report focuses on nanotechnology, the NNAP references useful reports with regard to the nature of engineering education, including the November 2006 workshop by the National Science Board (http://www.nsf.gov/pubs/2007/nsb07122/nsb07122_4.pdf).

4.2. Do not segregate implications research and applications research. In many instances, nanotechnology EHS research cannot be separated from the particular application(s) research and from the context for which a specific nanomaterial is intended. Such division is unproductive and neglects the whole benefit of research. Consequently, the NNAP expects that a substantial fraction of nanotechnology research related to EHS will continue to take place under the auspices of agencies that fund applications R&D and may not be uniquely or exclusively identified as nanotechnology EHS research. Risk research that is performed independent of applications development should nevertheless be carried out with consideration of overall risks and benefits associated with the particular material or technology. Furthermore, detailed reporting on the degree of relevance to EHS of such research is not necessarily critical to (and may actually hinder) overall prioritization and coordination.

4.3. Continue developing joint programs among NNI agencies that leverage expertise and resources to conduct nanotechnology EHS research and to support agency missions. The NNI member agencies should proactively seek to collaborate on priority EHS research, where appropriate, in order to expedite progress and take advantage of competency and knowledge that is distributed across the Federal Government.

4.4. Support wide distribution and availability of new nonproprietary information about the properties of nanomaterials. Such information should include methods for risk/benefit analysis that can be implemented by researchers, as well as by developers and manufacturers.

4.5. Note: As mentioned earlier in the report, in the near future the NNAP will be adding an addendum to this report with its review of the just-published NNI EHS research strategy.

5. Societal and Ethical Implications

5.1. Research on the societal and ethical aspects of nanotechnology should both be integrated with technical R&D and take place in the context of broader societal and ethical scholarship. Societal research should continue to be addressed in conjunction with technical research activities. However, these discussions will also be advanced by involvement of researchers who are primarily engaged in social science, ethics of technology, and other members of the broader academic community with expertise on science, technology, and society.

6. Communication and Outreach

Public perception of and expectations related to nanotechnology should be informed based on sound science and balanced assessment of risks and benefits (known and anticipated) of specific innovations and their implications for society.

6.1. Demonstrate more clearly to the public the value of nanotechnology and NNI-supported research and development. Broader communication and outreach efforts are an essential part of successful innovation. A lack of information and basic understanding of nanotechnology by the general public fosters susceptibility to exaggerated claims and to miscommunications that generate unfounded hopes or fears; these in turn may inhibit future nanotechnology innovation and societal benefit. While communication is a fundamental responsibility of all researchers, a number of specific NNI programs are pursuing efforts to address this both broadly (e.g., the NSF Nanoscale Informal Science Education Network, or NISE Net[10]) and more narrowly, in areas of application (e.g., the model communications efforts of the Alliance for Nanotechnology in Cancer program at NCI[11]). Nonetheless, the NNI should undertake a more explicit and direct outreach approach to better inform and engage policymakers, stakeholders of all types, and the general public in a dialog as to the application-specific status and associated risk-benefit ratio of relevant near-commercial and commercial nanotechnologies; and to convey the significance of nanotechnology-

[10] See http://www.nisenet.org/.

[11] See http://nano.cancer.gov/.

based capabilities to address grand challenges and future opportunities across industry sectors. Failing to effectively communicate the complete risk-benefit pictures with respect to various specific nanotechnology applications as they exist to date will hinder realization of the significant societal benefits, both demonstrated and promised, of nanotechnology advancements.

6.2. Enhance communications efforts within the NNCO. As an interagency office, the NNCO is well positioned to serve as a central point for much of the communication activity outlined above. In addition, the office also should coordinate among NNI agencies to enhance their agency-specific communication efforts. Member agencies should provide for greater resources to be directed toward these activities.

Appendix A: List of Acronyms

Agencies	Departments, agencies, and commissions within the Executive Branch of U.S. Federal Government
AML	Advanced Measurement Laboratory (NIST)
CDC	Centers for Disease Control and Prevention (DHHS)
CEQ	Council on Environmental Quality (Executive Office of the President)
CMOS	Complementary-symmetry metal-oxide-semiconductor (integrated circuits)
CNST	Center for Nanoscale Science and Technology (NIST)
CNT	Carbon nanotube
CPSC	Consumer Product Safety Commission
DHS	Department of Homeland Security
DHHS	Department of Health and Human Services
DOC	Department of Commerce
DOD	Department of Defense
DOE	Department of Energy
DOEd	Department of Education
DOJ	Department of Justice
DOL	Department of Labor
DOS	Department of State
DOT	Department of Transportation
EPA	Environmental Protection Agency
FDA	Food and Drug Administration (DHHS)
GIN	Global Issues in Nanotechnology Working Group (NSET)
IGERT	Integrative Graduate Education Research and Traineeship awards (NSF)
ISO	International Organization for Standardization
NASA	National Aeronautics and Space Administration
NCI	National Cancer Institute (DHHS/NIH)
NCL	Nanotechnology Characterization Laboratory (DHHS/NIH/NCI)
NCTR	National Center for Toxicological Research (DHHS/FDA)
NEHI	Nanotechnology Environmental and Health Implications Working Group (NSET)
NIEHS	National Institute of Environmental Health Sciences (DHHS/NIH)
NIH	National Institutes of Health (DHHS)
NILI	Nanomanufacturing, Innovation, and Liaison with Industry Working Group (NSET)
NIOSH	National Institute for Occupational Safety and Health (DHHS/CDC)
NISE	Nanoscale Informal Science Education (NSF-supported network)
NIST	National Institute of Standards and Technology (DOC)
NNAP	National Nanotechnology Advisory Panel (PCAST)
NNCO	National Nanotechnology Coordination Office
NNI	National Nanotechnology Initiative
NNIN	National Nanotechnology Infrastructure Network (NSF program)

NPEC	Nanotechnology Public Engagement and Communications Working Group (NSET)
NRC	National Research Council of the National Academies
NRI	Nanoelectronics Research Initiative
NSEC	Nanoscale Science and Engineering Centers (NSF program)
NSET	Nanoscale Science, Engineering, and Technology Subcommittee of the NSTC Committee on Technology
NSF	National Science Foundation
NSRC	Nanoscale Science Research Centers (DOE program)
NSTC	National Science and Technology Council
OECD	Organisation for Economic Co-operation and Development
OMB	Office of Management and Budget (Executive Office of the President)
OSTP	Office of Science and Technology Policy (Executive Office of the President)
PCA	Program Component Area
PCAST	President's Council of Advisors on Science and Technology
R&D	research and development
USPTO	U.S. Patent and Trademark Office (DOC)
USDA	U.S. Department of Agriculture
UVA	ultraviolet radiation, long wave (400 nm–320 nm wavelength)

Appendix B: NNI Program Component Areas

Program Component Areas (PCAs) are the major subject areas under which related NNI projects and activities are grouped. Whereas the NNI goals embody the vision of the initiative and provide structure for its strategy and plans, the PCAs relate to areas of investment that are critical to accomplishing those goals. These areas cut across the interests and needs of the participating agencies and indicate where advancement may be expedited through coordination of work by multiple agencies. The PCAs are intended to provide a means by which the NSET Subcommittee, as the interagency coordinating body; the Office of Science and Technology Policy (OSTP) and the Office of Management and Budget (OMB); Congress; and others may be informed of and direct the relative investment in these key areas. The PCAs also provide a structure by which the agencies funding research and development can better direct and coordinate their activities. The eight PCAs are defined as follows:

1. Fundamental Nanoscale Phenomena and Processes: Discovery and development of fundamental knowledge pertaining to new phenomena in the physical, biological, and engineering sciences that occur at the nanoscale. Elucidation of scientific and engineering principles related to nanoscale structures, processes, and mechanisms.

2. Nanomaterials: Research aimed at the discovery of novel nanoscale and nanostructured materials and at a comprehensive understanding of the properties of nanomaterials (ranging across length scales, and including interface interactions). R&D leading to the ability to design and synthesize, in a controlled manner, nanostructured materials with targeted properties.

3. Nanoscale Devices and Systems: R&D that applies the principles of nanoscale science and engineering to create novel, or to improve existing, devices and systems. Includes the incorporation of nanoscale or nanostructured materials to achieve improved performance or new functionality. To meet this definition, the enabling science and technology must be at the nanoscale, but the systems and devices themselves are not restricted to that size.

4. Instrumentation Research, Metrology, and Standards for Nanotechnology: R&D pertaining to the tools needed to advance nanotechnology research and commercialization, including next-generation instrumentation for characterization, measurement, synthesis, and design of materials, structures, devices, and systems. Also includes research and development and other activities related to development of standards, including standards for nomenclature, materials, characterization and testing, and manufacture.

5. Nanomanufacturing: R&D aimed at enabling scaled-up, reliable, cost-effective manufacturing of nanoscale materials, structures, devices, and systems. Includes research and development and integration of ultra-miniaturized top-down processes and increasingly complex bottom-up or self-assembly processes.

6. Major Research Facilities and Instrumentation Acquisition: Establishment of user facilities, acquisition of major instrumentation, and other activities that develop, support, or enhance the Nation's scientific infrastructure for the conduct of nanoscale science, engineering, and technology R&D. Includes ongoing operation of user facilities and networks.

7. Environment, Health, and Safety: Research primarily directed at understanding the environmental, health, and safety impacts of nanotechnology development and corresponding risk assessment, risk management, and methods for risk mitigation.[12]

8. Education and Societal Dimensions: Education-related activities such as development of materials for schools, undergraduate programs, technical training, and public communication, including outreach and engagement. Research directed at identifying and quantifying the broad implications of nanotechnology for society, including social, economic, workforce, educational, ethical and legal implications.

NOTE: With the release at the end of 2007 of the updated NNI Strategic Plan, the original Societal Dimensions PCA (7) defined in the 2004 plan was divided into two PCAs as shown. This change aligns with budget-reporting practices since 2006.

[12] Environmental, health, and safety (EHS) research and development on the EHS implications of nanotechnology includes efforts whose primary purpose is to understand and address potential risks to health and to the environment posed by this technology. Potential risks encompass those resulting from human, animal, or environmental exposure to nanoproducts—here defined as engineered nanoscale materials, nanostructured materials, or nanotechnology-based devices, and their byproducts.

Appendix C: Planned 2009 Agency Investments by PCA

Table C-1. Planned 2009 agency investments by Program Component Area (PCA) in millions of dollars.

	DOD	NSF	DOE	DHHS (NIH)	DOC (NIST)	NASA	EPA	DHHS (NIOSH)	USDA (FS)	USDA (CREES)	DOJ	DHS	DOT (FHWA)	**Total**
Fundamental nanoscale phenomena & processes	227.8	141.7	96.9	55.5	24.5	1.2	0.2		1.7	0.4			0.9	**550.8**
Nanomaterials	55.2	62.5	63.5	25.4	8.5	9.8	0.2		1.3	0.8				**227.2**
Nanoscale devices and systems	107.7	51.6	8.1	125.8	22.7	7.7	0.2		0.7	1.5		1.0		**327.0**
Instrument Research, Metrology, & Standards	3.6	16.0	32.0	5.9	20.9				1.1		2.0			**81.5**
Nano-manufacturing	12.8	26.9	6.0	0.8	15.3				0.2	0.1				**62.1**
Major research facilities & instrumentation acquisition	22.1	32.1	101.2	0.0	5.7	0.2								**161.3**
Environment, Health, & Safety	1.8	30.6	3.0	7.7	12.8	0.1	14.3	6.0		0.1				**76.4**
Education & Societal Dimensions		35.5	0.5	4.6										**40.6**
NNI Total	**431.0**	**396.9**	**311.2**	**225.7**	**110.4**	**19.0**	**14.9**	**6.0**	**5.0**	**3.0**	**2.0**	**1.0**	**0.9**	**1,527.0**

Appendix D: Summary of Key Findings and Recommendations from the 2006 NRC Review of the NNI

In December 2006, the National Research Council (NRC) of the National Academies conducted its first triennial review of the NNI, largely in parallel to the initial NNAP review, but including specific one-time studies on the technical feasibility of molecular manufacturing and the responsible development of nanotechnology.[13] Some of the key findings may be summarized as follows:

- *NNI-related R&D is world-class and in many instances world-leading, and… is making invaluable contributions to the advancement of knowledge and innovation in the United States. [p. 22]*
- *Increased interagency cooperation—which has enhanced the development of interdisciplinary research, led to improvements in the R&D infrastructure, and stimulated new areas in research—is an important impact of the NNI. [p. 5]*
- *The articulation [in the NNI Strategic Plan] of the NNI's strategic goals and the development of the related PCAs are an important outcome of the NNI that has had a positive impact on the provision of Federal support for the fields and disciplines involved in R&D at the nanoscale... the strategy has led to the NNI contributing to the education of the 21st Century R&D workforce, as well as addressing societal issues such as health effects and environmental impact. [pp. 24–25]*
- *The flexible structure of the [NSET] working groups… help[s] to promote effective interagency communication, coordination, and joint programs development and enable the NSET Subcommittee to efficiently address societal issues by giving it ready access to regulatory experts and health professionals in various agencies. [pp. 25–26]*
- *… other outreach and coordination efforts stimulated by and established under the NNI have made a considerable contribution to coordination of R&D efforts in pursuit of realizing the full potential of nanotechnology. [p. 27]*
- *A significant impact of the NNI has been the development of new collaborations across agencies and between different units within agencies that are conducting R&D relevant to the broad goals articulated by the NNI… [p. 27]*
- *A critically important impact of the NNI has been the focused investment by the NNI-participating agencies in the establishment and development of multidisciplinary research and education centers devoted to nanoscience and nanotechnology. Many such centers are designated as user facilities available to researchers from academia and the private sector, and to scientists at the national laboratories. [p. 29]*
- *NNI-related science and technology R&D and the strong Federal support for discovery-based research and interdisciplinary collaborations at university centers are attracting and exciting students… [However, the] committee believes that the public's curiosity about nanotechnology could be leveraged more effectively to build public support for the Federal support of R&D in the physical and biomedical sciences, as well as attract new talent into U.S. undergraduate and graduate education. [pp. 34–35]*

---

[13] National Research Council (NRC) of the National Academies. 2006. A matter of size: Triennial review of the National Nanotechnology Initiative. Washington DC: National Academies Press. (See http://www.nap.edu/catalog.php?record_id=11752.)

- *Although good comparative indicators of investment in nanotechnology R&D, resultant innovation, and economic exploitation of nanotechnology do not exist, existing data point to worldwide growth in investment in nanoscale research and innovation. The United States appears to remain in the lead, but with other countries closing this gap. [pp. 58–59]*
- *It is too early to gauge the economic impact of nanotechnology… any future analysis of economic impact will be hindered unless data are collected and metrics developed that will facilitate a rigorous analysis of economic indicators such as jobs created or individuals employed as a result of nanotechnology development. [p. 69]*
- *Materials and devices of moderate complexity can be designed and manufactured by molecular assembly… [however,] the eventually attainable perfection and complexity of manufactured products, while they can be calculated in theory, cannot be predicted with confidence… Research funding that is based on the ability of investigators to produce experimental demonstrations that link to abstract models and guide long-term vision is most appropriate to achieve this goal. [p. 108]*
- *It is not possible yet to make a rigorous assessment of the level of risk posed by [engineered nanomaterials]. Further risk assessment protocols have to be developed, and more research is required to enable assessment of potential EHS risks from nanomaterials. [p. 90]*

Many of the report's findings are also associated with recommendations. The following is a summary of key recommendations:

- *The Federal Government [should] sustain [nanoscale science and technology] investments in a manner that balances the pursuit of shorter-term goals with support for longer-term R&D and that ensures a robust supporting infrastructure, broadly defined. Supporting long-term research effectively will require making new funds available that do not come at the expense of much-needed ongoing investments in U.S. physical sciences and engineering research. [pp. 7–8]*
- *The Federal Government [should] establish an independent advisory panel with specific operational expertise in nanoscale science and engineering; management of research centers, facilities, and partnerships; and interdisciplinary collaboration… [p. 8]*
- *Federal agencies participating in the NNI, in consultation with the NNCO and the Office of Management and Budget, [should] continue to develop and enhance means for consistent tracking and reporting of funds requested, authorized, and expended annually. The current set of PCAs provides an appropriate initial template for such tracking. [p. 9]*
- *The NSET Subcommittee [should] carry out or commission a study on the feasibility of developing metrics to quantify the return to the U.S. economy from the Federal investment in nanotechnology R&D. [pp. 9–10]*
- *Research on the environmental, health, and safety effects of nanotechnology [should] be expanded. [p. 11]*
- *The NSET Subcommittee [should] create a working group on education and the workforce that engages the Department of Education and the Department of Labor as active participants. [p. 40]*

References

108th Congress. 2003 (December). Public Law 108-153. An Act to authorize appropriations for nanoscience, nanoengineering, and nanotechnology research, and for other purposes. Washington, DC: GPO. Available online: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=108_cong_public_laws&docid=f:publ153.108.pdf.

Chen, H. and M.C. Roco. 2008. Mapping nanotechnology innovations and knowledge: Global, longitudinal patent and literature analysis. Private communication with the author(s). (Publication forthcoming.)

Eklund, P., P. Ajayan, R. Blackmon, A.J. Hart, J. Kong, B. Pradhan, A. Rao, and A. Rinzler. 2007. International assessment of research and development of carbon nanotube manufacturing and applications. Baltimore, MD: WTEC, Inc. Available online: http://wtec.org/cnm/CNM_final_report.pdf.

Environmental Protection Agency (EPA) Science Policy Council 2007. Nanotechnology white paper. Washington, DC: EPA. Available online: http://es.epa.gov/ncer/nano/publications/whitepaper12022005.pdf.

Environmental Protection Agency (EPA) Office of Research and Development 2008. Draft Nanomaterial Research Strategy (NRS). Washington, DC: EPA. Available online: http://es.epa.gov/ncer/nano/publications/nano_strategy_012408.pdf.

Environmental Working Group (EWG). 2007. Sunscreen: What's safe and what works. Available online: See http://www.cosmeticsdatabase.com/special/sunscreens/summary.php and the link "What about nanoparticles?" under "FAQ."

Environmental Working Group (EWG). 2007b. Sunscreen: What's safe and what works. Available online: See http://www.cosmeticsdatabase.com/special/sunscreens/summary.php and links on that page under "Investigation."

Food and Drug Administration (FDA) Nanotechnology Task Force. 2007. Nanotechnology. Washington, DC: FDA. Available online: http://www.fda.gov/nanotechnology/taskforce/report2007.pdf.

Hansen, S.F., B.H. Larsen, S.I. Olsen, and A. Baun. 2007. Categorization framework to aid hazard identification of nanomaterials. *Nanotoxicology* 1(3): 243–250.

Hirjibehedin, C.F., C.-Y. Lin, A.F. Otte, M. Ternes, C.P. Lutz, B.A. Jones, and A.J. Heinrich. 2007. Embedded in a surface molecular network large magnetic anisotropy of a single atomic spin. *Science* 317:1199–1203.

Hu, D., H.C. Chen, Z. Huang, and M.C. Roco. 2007. Longitudinal study on patent citations to academic research articles in nanotechnology (1976-2004). *Journal of Nanoparticle Research* 9:529–542.

Kisliuk, B. U.S. Patent and Trade Office (USPTO). 2008. Personal communication.

Kukowska-Latallo, J.F., Kimberly A. Candido, Z.Y. Cao, S.S. Nigavekar, I.J. Majoros, T.P. Thomas, L.P. Balogh, M.K. Khan, and J.R. Baker, Jr. 2005. Nanoparticle targeting of anticancer drug improves therapeutic response in animal model of human epithelial cancer. *Cancer Research* 65(12): 5317–5324.

Lewison, G. 2007. Personal communication: Data results of text search of the *Science Citation Index,* performed by Grant Lewison of Evaluametrics Ltd. at request of WTEC for NNCO.

Leydesdorff, L., and C. Wagner. 2006. Is the United States losing ground in science? A global perspective on the world science system. Scientometrics (forthcoming). Available online: http://users.fmg.uva.nl/lleydesdorff/us_science/index.htm.

Li, X., Y.L Lin, H.C. Chen, and M.C. Roco. 2007. Worldwide nanotechnology development: A comparative study of USPTO, EPO, and JPO patents (1976-2004). *Journal of Nanoparticle Research* 9(6): 977-1002.

Liljeroth, P., J. Repp, and G. Meyer. 2007. Current-induced hydrogen tautomerization and conductance switching of naphthalocyanine molecules. *Science* 317:1203–1206.

Lux Research. 2007. The nanotech report: Investment overview and market research for nanotechnology, 5th ed. New York: Lux Research.

Nanosphere, Inc. 2007. "Nanosphere announces FDA clearance of second molecular diagnostics assay." Press release: http://www.nanosphere.us/NanosphereAnnouncesFDAClearanceofSecondMolecularDiagnosticsAssay_4876.aspx.

National Institute for Occupational Safety and Health (NIOSH). 2007. Progress toward safe nanotechnology in the workplace. Washington, DC: NIOSH publication No. 2007-123. Available online: http://www.cdc.gov/niosh/docs/2007-123/.

National Institute for Occupational Safety and Health (NIOSH). 2006. Approaches to safe nanotechnology: an information exchange with NIOSH. Washington, DC: NIOSH draft for public comment. Available online: http://www.cdc.gov/niosh/topics/nanotech/safenano/.

National Research Council (NRC) of the National Academies. 2006. A matter of size: Triennial review of the National Nanotechnology Initiative. Washington DC: National Academies Press. (See http://www.nap.edu/catalog.php?record_id=11752.)

National Science and Technology Council, Nanoscale Science, Engineering, and Technology Subcommittee (NSTC/NSET). 2006. Environmental, health, and safety research needs for engineered nanoscale materials. Washington DC: NSTC. Available online: http://www.nano.gov/NNI_EHS_research_needs.pdf.

National Science and Technology Council, Nanoscale Science, Engineering, and Technology Subcommittee (NSTC/NSET). 2007. The National Nanotechnology Initiative: Research and development leading to a revolution in technology and industry. Supplement to the President's 2008 budget. Appendix A. Available online: http://www.nano.gov/NNI_08Budget.pdf.

National Science and Technology Council, Nanoscale Science, Engineering, and Technology Subcommittee (NSTC/NSET). 2008. The National Nanotechnology Initiative FY 2009 budget and highlights. Available online: http://www.nano.gov/NNI_FY09_budget_summary.pdf.

National Science and Technology Council, Nanoscale Science, Engineering, and Technology Subcommittee (NSTC/NSET). 2008b. Strategy for nanotechnology-related environmental, health, and safety research. Washington DC:NSTC. Available online: http://www.nano.gov/NNI_EHS_Research_Strategy.pdf.

Nohynek G.J., J. Lademann, C. Ribaud, and M.S. Roberts. 2007. Grey goo on the skin? Nanotechnology, cosmetic and sunscreen safety. *Crit. Rev. Toxicol.* 37(3):251-277.

Office of Science and Technology Policy (OSTP). 2007. Principles for Nanotechnology Environmental, Health, and Safety Oversight. (http://www.ostp.gov/galleries/default-file/Nano%20EHS%20Principles%20Memo_OSTP-CEQ_FINAL.pdf)

President's Council of Advisors on Science and Technology (PCAST). 2005. *The National Nanotechnology Initiative at five years: Assessment and recommendations of the National Nanotechnology Advisory Panel*. Available online: http://www.nano.gov/html/res/FINAL_PCAST_NANO_REPORT.pdf.

Qin, Y., X.D. Wang, and Z.L. Wang. 2008. Microfibre–nanowire hybrid structure for energy scavenging. *Nature* 451:809-813.

Roco, M.C., and H. Chen. 2008. Mapping nanotechnology innovations and knowledge: Global, longitudinal patent and literature analysis. Private communication with the author(s). (Publication forthcoming.)

Shelton, R.D. 2007. Personal communication: Data results from text search of the *Science Citation Index* as of 2006, performed by R.D. Shelton of WTEC for NNCO.

Stoeva, S., J.S. Lee, J.E. Smith, S.T. Rosen, and C.A. Mirkin. 2006. Multiplexed detection of protein cancer markers with biobarcoded nanoparticle probes. *J. Am. Chem. Soc.* 128(26):8378–8379. Available online: http://pubs.acs.org/cgi-bin/abstract.cgi/jacsat/2006/128/i26/abs/ja0613106.html.

Yildirim, T., and S. Ciraci. 2005. Titanium-decorated carbon nanotubes as a potential high-capacity hydrogen storage medium. *Phys. Rev. Lett.* 94:175501.

Ordering Copies of This PCAST Report

This report was prepared for publication by the National Nanotechnology Coordination Office (NNCO). To request additional copies of the report, please contact:

NNCO
4201 Wilson Boulevard
Stafford II, Suite 405
Arlington, VA 22230

703-292-8626 phone
703-292-9312 fax

info@nnco.nano.gov

This PCAST report is also available online at www.nano.gov and at www.ostp.gov/cs/pcast

President's Council of Advisors on Science and Technology • April 2008
www.ostp.gov