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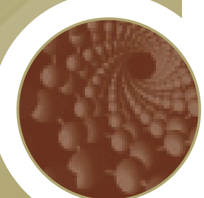
*Project on Emerging
Nanotechnologies*

# NANOTECHNOLOGY:
## A Research Strategy *for* Addressing Risk

*Andrew D. Maynard*



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## A Research Strategy *for* Addressing Risk

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# Foreword

"Are nanotechnology products safe?" is a question that is not going away. It is being asked with increasing frequency by journalists, environmental and consumer groups, scientists and engineers and increasingly by the public. Nanotechnology innovations are made possible because researchers have learned how to deftly manipulate matter at the atomic level, opening the way for the creation of a vast array of new materials and products possessing a variety of novel and exciting properties. However, many of the same novel properties that give nanotechnologies the capacity to transform medicines, materials, and consumer products, may also present novel risks.

With Lux Research reporting over $32 billion worth of products incorporating nanotechnology sold in 2005, we still know little about the potential risks, and how they should be managed.[1] Despite a current annual worldwide investment of over $9.6 billion in nanotechnology research,[2] not very much is being spent on investigating what is safe and what is not. With a sound, science-based and sensible research strategy, we can provide nano-businesses—large and small—with the tools they need to identify and reduce or remove possible dangers to health and the environment. But without the right research plan and investments, the safety and sustainability of emerging nanotechnologies is uncertain at best.

The United States government has been a key driver of nanotechnology innovation through the National Nanotechnology Initiative (NNI). It has spent billions of dollars to encourage the development and use of nanotechnology in practical, commercial applications. And yet, the risk research underpinning this investment is weak.

As noted in this report, according to a 2005 study presented by the Project on Emerging Nanotechnologies, funding of "highly relevant" nanotechnology risk research is just one percent of the annual NNI budget—totaling just an estimated $11 million in 2005.

This number increases to about $30 million when research generally relevant to health and safety issues is included. But this is below the $40 million that the NNI claims is being allocated yearly on research looking at risks as it is strictly defined by the Office of Management and Budget.[3] It also is far short of the NNI assertion that more like $100 million annually is being spent on risk research, if you consider other parts of the government's research portfolio which the NNI argues—but does not document—is relevant to understanding nanotechnology's implications.

More important than the level of funding is the fact that the government's research into the environmental, safety and health implications of nanotechnology lacks strategic direction and coordination. As a result, researchers are unsure about how to work safely with new nanomaterials, nano-businesses are uncertain about how to develop safe products, and public confidence in these emerging applications is in danger of being undermined.

1. Lux Research, *How Industry Leaders Organize For Nanotech Innovation,* Lux Research Inc., New York, NY, (2006)
2. Lux Research, *The Nanotech Report, 4th Edition,* Lux Research Inc., New York, NY, (2006)
3. Duke, W. In *Government Executive* (Washington, DC, 46–52) (June 15, 2006)

Clearly, a strategic framework is needed for risk-based research, and it is needed *now*. A recent inventory developed by the Project on Emerging Nanotechnologies indicates that approximately 300 nanotechnology-enabled consumer products identified by companies from 15 countries are presently on the market.[4] Currently, there also are an estimated 600 nanotechnology raw materials, intermediate components, and industrial equipment items used by manufacturers.

This report is a first attempt to offer a blueprint for systematically exploring the potential risks of nanotechnology. Drawing from previously published scientific papers and reports, it identifies critical research gaps and develops a framework within which effective risk-based research can proceed over the next two years and beyond. It makes recommendations on what research should be done and who should lead the research efforts.

The paper calls for two major changes in the status quo, specifically:

Leadership. A shift in leadership and funding for risk research to federal agencies that have a clear mandate for oversight and for research of environment, safety and health issues (such as the National Institute for Occupational Safety and Health [NIOSH], and the Environmental Protection Agency [EPA]).

Funding. An estimated minimum federal investment of $100 million over the next two years devoted to highly relevant, targeted risk-based research. According to the Project's data, this would require a $40 million annual increase over what is currently spent and significant increases in the research budgets of agencies like NIOSH, EPA, and the National Institute of Environmental Health Sciences (NIEHS). The amount of federal monies allocated beyond the initial two years would depend on the strategic framework developed and adopted by the government, and its ability to form risk research partnerships with business and other countries.

Nanotechnology is moving forward, and it is moving fast. We no longer have the luxury of waiting for risks to appear in the workplace or marketplace before beginning our research. We must ensure that adequate research is funded, and that it is the right research done at the right time, if we are to develop safe, sustainable nanotechnologies. This paper provides a starting point to do just that.

**David Rejeski**
**Director, Project on Emerging Nanotechnologies**

4. Project on Emerging Nanotechnologies: *A Nanotechnology Consumer Products Inventory* www.nanotechproject.org/consumerproducts. Accessed June 2006

# Executive Summary

Emerging nanotechnologies are unlikely to succeed without appropriate research into understanding and managing potential risks to health, safety and the environment. Despite current research, significant knowledge gaps exist in all areas of nanotech risk assessment.

These gaps will be filled only through targeted and strategic research. This report addresses the current state of nanotechnology risk research and what needs to be done to help ensure the technology's safe development and commercialization. A strategic research framework is developed that identifies and prioritizes what the author believes are the critical short-term issues. Recommendations are made on how a viable strategic research plan might be implemented.

Changes need to be made in risk research responsibility within the federal government. The report's principal conclusions are that the federal government needs to assume top-down, authoritative oversight of strategic risk-based research, and that nanotechnology risk research should be carried out by federal agencies with a clear mandate for oversight and for research of environment, health and safety issues.

Adequate funding must be provided for highly relevant risk research. The appropriate agencies to lead risk research—which include the Environmental Protection Agency (EPA), the National Institute for Occupational Safety and Health (NIOSH), the National Institutes of Health (NIH) and the National Institute of Standards and Technology (NIST)—will require an estimated minimum budget of $100 million over the next two years devoted to highly relevant, targeted risk-based research, if critical knowledge is to be developed. This should be supported by a complementary and identifiable investment in basic research and applications-focused research that has the potential to inform our understanding of risk. Mechanisms should be developed to make full use of this complementary research.

Short-term research priorities. Over the next two years, nanotechnology risk research should focus on ensuring the safety of technologies already in use or close to commercialization. Top priorities should include identifying and measuring nanomaterials exposure and environmental release, evaluating nanomaterials toxicity, controlling the release of and exposure to engineered nanomaterials and developing "best practices" for working safely with nanomaterials. There should also be a strong research investment in longer-term issues such as predictive toxicology.

Mechanisms are needed for joint government-industry research funding. Government research funding should be leveraged with joint-industry funding within a strategic risk-research framework. The Health Effects Institute—which has successfully addressed particulate pollution through joint government-industry funding—should be considered as a possible model for addressing nanomaterials risk.

International coordination is essential. Ways of coordinating research activities, sharing costs and exchanging information between countries and economic regions should be explored.

A new interagency oversight group is needed. Development and oversight of a fully funded strategic research plan will require a new interagency group to be established. This group should have the authority to set and implement a strategic research agenda and assure agencies are provided with appropriate resources.

Long-term research needs and strategies should be assessed on a rolling basis. Finally, an independent study effort should be established to identify future research needs, provide advice on how to incorporate them into a strategic research framework and evaluate progress towards achieving strategic research goals.

# Setting the Scene

Nanotechnology has become something of a catch-all phrase for an incredible variety of innovations that are being incorporated into a wide range of applications—cosmetics, car parts, drugs, food packaging, sports equipment and electronics, to name but a few. Specific nanotechnologies can be vastly different in form, function and implementation, but they share one common feature: all take advantage of a new (or at least greatly improved) ability to manipulate physical matter down to the atomic level. Scientists are now able to arrange atoms and molecules into precise configurations almost as if they were using a child's building blocks.

For example, scientists have constructed carbon "nanotubes" that are only about a nanometer—one-billionth of a meter—in diameter, which is tens of thousands of times smaller than the width of a human hair. These nanotubes possess unusual properties, such as incredible strength and the ability to conduct heat and electricity, that appear to make them ideal for improving everything from televisions and tennis rackets to solar cells and water filters.

## Nanotechnology, "the new industrial revolution"

Nanotubes are just one of many innovations percolating in the world of nanotechnology. There are nanometer-sized particles (nanoparticles) being developed that could greatly improve pharmaceuticals because their size, structure and behavior can be used to combat illnesses beyond the reach of conventional drugs. Nanometer-scale materials (nanomaterials) that can repel stains or kill bacteria are being built into clothing fabric. Food companies are experimenting with nanoparticles that can be incorporated into packages to detect spoilage or pathogens. Cosmetics companies have developed products with nanoparticles that, because of their microscopic size and novel properties, allow sunscreens and moisturizers to perform better. And these are just some of the current and near-to-market applications. Because nanotechnology gives us the tools to do things differently, the list of potential applications is almost endless. For example, the next few years will see nanotechnology leading to stronger, lighter materials in cars and airplanes, high performance batteries, cheap solar cells, highly efficient water filtration and desalination processes, and smaller, more sensitive sensors. Overall, experts estimate that innovations sparked by various types of nanotechnology will soon encompass a global market in goods and services worth $1 trillion. Clearly, today, small is big.

But as the public and private sectors in the U.S. and, increasingly, the rest of the world, invest billions into what many nanotechnology boosters like to call "the new industrial revolution," it is fair to ask whether there are any perils in what is usually portrayed as an area of limitless promise. After all, if this is the new industrial revolution that some claim, it might be worth reflecting on the hazards that emerged in the wake of the first industrial revolution.

## New technologies mean different risks

While on balance they have greatly raised our living standards, industrial processes can cause harm. Witness such problems as "brown lung" among textile workers, pulmonary illness caused by asbestos exposure and air pollution, environmental damage from acid rain, and the wide variety of cancers linked to industrial chemicals and emissions. There is no reason to assume that nanotechnology will be different from other industrial innovations when it comes to having the potential to present both benefits and risks to human and environmental health.

While there has not been much research into risks posed by the many implementations of nanotechnology, there has been enough to reasonably conclude that there are some applications that will present problems. For example, carbon nanotubes can cause lung inflammation and granulomas in animals, and some nanoparticles seem to be more harmful mass-for-mass than their larger counterparts. While not intended as an alarmist statement, the fact remains that certain applications of nanotechnology will present risks unlike any we have encountered before. Saying they will be different does not mean they will be *more* threatening. This discussion of risks is not intended to give credence to sensational fears of nanotechnology, such as the science-fiction fantasy of self-replicating nanobots or "grey goo" taking over the world. But acknowledging that nanotechnology presents new kinds of risks means that we need reliable information to understand what the real dangers are—from the insignificant to the life threatening—and to learn how they can be minimized.

One reason that each week seems to bring another breakthrough application of nanotechnology is that scientists have moved beyond conventional capabilities and into a brand new world of making industrial materials and substances. But these same new processes that so excite public and private sector scientists also challenge our conventional understanding of threats to safety and health and how to manage them.

## Understanding risk through research

If there is a silver lining in our past experience with industrial hazards, it is that we now know that an important first step in safeguarding the public from such threats is to invest in objective research that can properly define the nature of the risk. Everyday, in a variety of situations, hazardous chemicals and materials are used safely because we have invested in the scientific research that shows us how to avoid their dangers. Most likely, the risks of nanotechnology also can be safety managed, if we understand what those risks entail.

But today, while billions are being invested by government and industry to quickly capitalize on the commercial potential of nanotechnology, there seems to be little interest in uncovering and exploring potential risks. One reason for the lack of attention is a view often expressed in both the public and private sectors—that nanotechnology does not present a new set of dangers, and if threats do emerge, we have the regulatory review and safety oversight systems in place to protect the public from harm.

Of course, this begs the question: how can we be confident that nanotechnology applications are likely to be safe and any threats that emerge will be manageable when there has been so little research exploring risks?

For example, it appears it appears that only one percent of the billions of dollars the U.S. federal government has invested in nanotechnology research has focused directly on exploring risks. Yet hundreds of products incorporating nanotechnology innovations already are on the market and over the next few years, thousands of additional applications are expected to be unveiled.

Today, there are those who dismiss any concerns about nanotechnology as the musings of "Luddites" who harbor irrational fears of technology in general. But, in fact, anyone who wants to see nanotechnology achieve its full potential has a vested interest in the establishment of a comprehensive nanotechnology risk research program. A thorough and open exploration of nanotechnology's potential threats to humans and the environment is the best way to keep concerns about nanotechnology rooted in objective, scientific review. Without such data, the promoters of nanotechnology will have difficulty responding effectively to even the most outlandish statements about nanorisks.

This paper explores the need to develop a better understanding of the risks presented by nanotechnology in all its diversity, and how to develop a responsible approach to risk research. Essentially, it considers the question of what to do and how to do to it, to support "safe" nanotechnology.[1] It represents one scientist's personal perspective, and is aimed at stimulating discussion on research prioritization and the implementation of a strategic research agenda. In particular, it focuses on short-term research needs that are critical to assessing and managing risks associated with nanotechnologies already on the market, or on the cusp of commercialization.

1. "Safe" is used here as a relative term—"Safe" nanotechnology refers to nanotechnology where the possible risk of harm to people and the environment is understood and minimized.

# A Reason for Caution

When it comes to considering a risk research program focused specifically on nanotechnology, we need to ask the question: should we anticipate that certain applications of nanotechnology will introduce risks that are substantially different from those we encounter with conventional products? The answer appears to be yes. The complexity of engineered nanomaterials means that their impact will depend on more than chemistry alone. Size, shape, surface chemistry and surface coatings (for example) can all influence how these materials behave. In some cases, the microscopic size alone of nanoparticles might allow them to more easily enter and affect human organs. In other instances, the fact that nanoscale materials can have unusual properties—properties that do not conform to "conventional" physics and chemistry—may influence the potential for risks. Indeed, the dependency of nanomaterials' properties on chemistry *and* structure has prompted one commentator to call for new product-based nano-regulation that is responsive to this distinction.[2]

Of course, it is often argued that by their very nature, engineered nanomaterials will only be produced and used in minute quantities and that exposures will be insignificant. This possibly is true for new nanotechnologies in their infancy. However, putting aside the question of what "insignificant" means (and so far there has been no general consensus), commercially successful nanotechnologies will depend on producing and using sizeable quantities of materials. The 2004 *Royal Society and Royal Academy of Engineering* report anticipates that the quantities of engineered nanomaterials in use will increase rapidly over the next few years, with an estimated production rate of 58,000 metric tonnes per year between 2011–2020 (Figure 1).[3] It is sobering to think that, if (as we suspect) the number or surface of particles making up these materials determines the hazard they represent, the impact of these materials *might* be the equivalent of between 5 million and 50 billion metric tonnes of conventional materials.[4]

## Rethinking exposure and toxicity

When it comes to potential hazard, size can matter. Compared to conventionally sized particles, certain nanoparticles may move easily into sensitive lung tissues after inhalation, and cause damage that can lead to chronic breathing problems.[5] There is also evidence that some nanoparticles may be able to move from the lungs into the bloodstream. Although it is not fully clear what happens if a nanoparticle goes from the lungs into the blood, we do know that larger inhaled particles do not normally get into the bloodstream. The possibility that nanoparticles

2. Davies, J. C., *Managing the Effects of Nanotechnology*, Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies, Washington DC, (2006) 2006–1
3. *Nanoscience and Nanotechnologies: Opportunities and Uncertainties*, The Royal Society and The Royal Academy of Engineering, London, UK, (2004)
4. Comparing a "conventional" material made up of 2 μm diameter particles, to a nanomaterial comprised of 20 nm diameter particles, and assuming that hazard is associated with either particle number or surface area, not mass.
5. Ferin, J. & Oberdörster, G., *Journal of Aerosol Medicine-Deposition Clearance and Effects in the Lung* (1992) 5 (3), 179–187

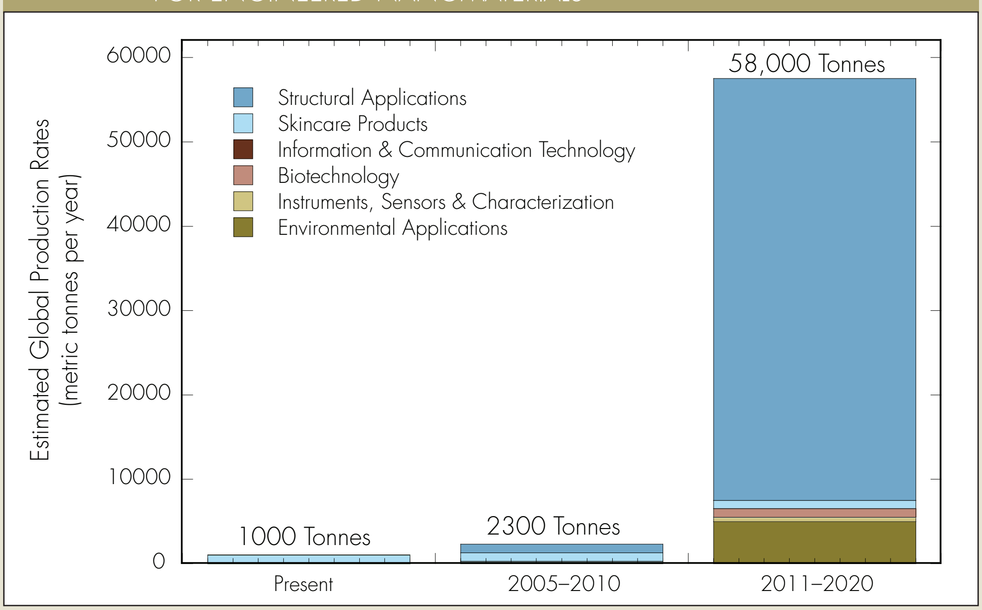
might have an easy route to the body is the kind of nanorisk that deserves more study.[6]

It is also known that some nanoparticles are small enough to get inside cells. In fact, both food and drug companies are looking at the ability of nanoparticles to significantly enhance the biological activity of foods and medicines precisely because they can deliver drugs and nutrients to parts of the body they previously could not reach. But there is some evidence that when certain types of particles penetrate cells, they can cause damage.[7]

Some substances and materials at the nanoscale also may exhibit new properties that make them more harmful than they would be at a more conventional size. For example, in one study, scientists were surprised to find that rats died a mere 30 minutes after being exposed to an amount of nanosized particles that, if the material were in a more conventional form, would be considered a safe daily dose.[8] It appears that both the size of the particles and the changes in their "surface chemistry" that occurred in their diminutive state made the nanosized materials much more toxic than the larger form of the same material.

In this case, the finding was a serendipitous discovery. The researchers did not set out to evaluate nanotechnology risks. And while

FIGURE 1. ESTIMATED ANNUAL GLOBAL PRODUCTION RATES FOR ENGINEERED NANOMATERIALS




Values are based on estimates in the 2004 *Royal Society and Royal Academy of Engineering* report on nanotechnology.[9] They are intended for guidance only, as validated figures are commercially confidential.

6. Ibid., ; Oberdörster, G. et al., *J. Toxicol. Env. Health Pt A* (2002) 65 (20), 1531–1543
7. Li, N. et al., *Environ. Health Perspect.* (2003) 111 (4), 455–460; Oberdörster, G. et al. in American Toxicological Society (Orlando, Fl, 2004).
8. Oberdörster, G., Gelein, R. M., Ferin, J. & Weiss, B., *Inhal. Toxicol.* (1995) 7, 111–124
9. *Nanoscience and Nanotechnologies: Opportunities and Uncertainties*, The Royal Society and The Royal Academy of Engineering, London, UK, (2004)

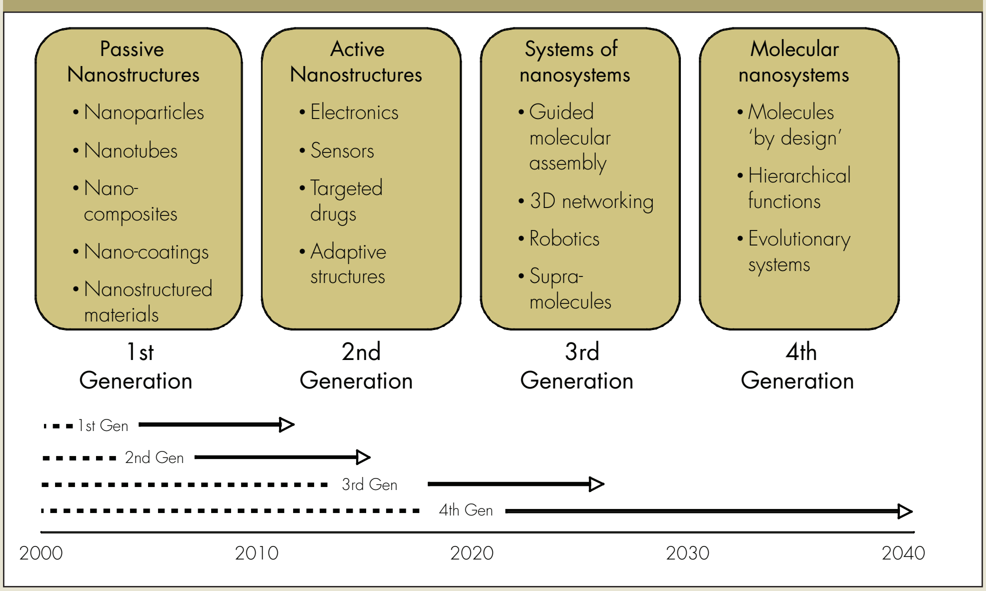
the particles that killed the rats are not being considered for any commercial applications of nanotechnology, the results still should serve as a warning that we may get some rude surprises if risks are not aggressively explored early on.

Beyond possible impact on human health, engineered nanomaterials present us with many challenges to understanding and managing environmental impact. Many nanomaterials are highly durable, meaning that they will remain in the environment long after the products they are used in are disposed of. Could this longevity lead to unanticipated accumulation in and harm to the environment? Even nanomaterials that are harmless to humans might affect other species—possibly upsetting delicate ecological balances. For instance, the increasing use of silver nanoparticles as an antimicrobial agent is raising concern over possible harm to beneficial microbes in the environment. And materials entering the bottom of the food chain have a habit of affecting organisms—including people—much higher up the chain. We certainly know from experience that the unanticipated impact of apparently "safe" materials on the environment can be significant, if not caught early on.

## New risks require new research

Overall, we know enough about the potential risks posed by nanotechnology to understand that there are at least some nano-materials and products that pose a different risk to human health and the environment compared to conventional materials.[10] However,

FIGURE 2. NANOTECHNOLOGY IMPLEMENTATION AND DEVELOPMENT




These timelines provide a somewhat subjective indication of when relevant research (dashed lines) and when commercialization (solid lines) is anticipated. Based on Roco (2004).[11]

10. Maynard, A. D. & Kuempel, E. D., *Journal Of Nanoparticle Research* (2005) 7 (6), 587–614; Maynard, A. D., *Nano Today* (2006) 1 (2), 22–33; Oberdörster, G., Oberdörster, E. & Oberdörster, J., *Environ. Health Perspect.* (2005) 13 (117), 823–840

11. Roco, M. C., *AIChE. J.* (2004) 50 (5), 890–897

we currently lack information to conduct the most basic risk analysis for simple (or first generation) nanomaterials. Even less is known about later generation nanomaterials now under development that may involve more complicated assemblages of molecules and may be far more powerful in terms of their abilities, for good or for ill, to affect humans and the environment (Figure 2).

Relying on existing knowledge to quantify the risks of engineered nanomaterials will engender false assumptions of safety. We need to think differently about at least some of these new materials and substances if we are to identify and manage their safe introduction into commercial markets.[12] With the rush in so many sectors to take advantage of the innovations of nanotechnology, it is a given that risk research inevitably will lag behind product development. But the goal at the moment should be to narrow what is now a wide gap between current and emerging commercial applications, and knowledge of their potential hazards.

The dearth of information on risks is particularly troubling because so many of the early applications of nanotechnology are by-design intended to achieve high exposure. About a third of the hundreds of nanotechnology-related consumer products now on the market are intended to be ingested, or applied to the skin.[13] In fact, the food and cosmetic industries are arguably moving as fast or faster than any other sector to reap the benefits of nanotechnology.

Most of these innovations likely will turn out to be relatively safe. Nonetheless, few appear to have come to market supported by independent research that specifically explores nano-related risks. And there is no indication at the moment that we are asking the right questions about future applications. As was noted before, existing knowledge of such things as toxicity, exposures and particle hazards will be insufficient for anticipating the risks posed by some nanotechnology applications. Yet government regulators expect to review and approve nanotech innovations with the same processes and benchmarks used to assess the safety of conventional products. Do we really want a situation where the *de facto* approach to health and safety of nanotechnology is "put the products on the market first and answer questions later"?

## Why nanotech boosters should fear a dearth of risk research

The inattention to nano-specific risk research puts more than consumers and the environment in danger. It also sets up a scenario in which the future promise of nanotechnology could suffer serious set-backs, as what could have been predictable and preventable problems instead emerge as market-jarring surprises.

The industry recently got a taste of this scenario when a German company was forced to recall an aerosol version of its glass and tile sealant, Magic Nano, after numerous reports that people using it suffered breathing problems, some serious enough to require hospitalization.[14] It appears now the product

12. Maynard, A. D., *Nano Today* (2006) 1 (2), 22–33; Maynard, A. D. & Kuempel, E. D., *Journal Of Nanoparticle Research* (2005) 7 (6), 587–614; Oberdörster, G., Oberdörster, E. & Oberdörster, J., *Environ. Health Perspect.* (2005) 13 (117), 823-840; Oberdörster, G. et al., *Part. Fiber Toxicol.* (2005) 2 (8), doi:10.1186/1743-8977-2-8

13. Project on Emerging Nanotechnologies, *Consumer Products Inventory.* www.nanotechproject.org/consumer-products. Accessed June 2006.

14. Weiss, R. In *Washington Post* (Washinghton, DC, April 06) A02; von Bubnoff, A. In *Small Times* (Ann Arbor MI, April 14)

did not contain nanoparticles (as was initially suspected) and it is not completely clear what kind of nanotechnology, if any, was used in the spray.[15] Nevertheless, Magic Nano went on the market widely promoted as a nanotechnology innovation. No one in government or industry sought to verify the claim, or require even rudimentary safety data that would show whether it involved an application of nanotechnology that might cause harm.

Now, almost every mainstream news story on nanotechnology prominently features the problems with Magic Nano as a cautionary tale from the cutting edge. For example, a recent front-page article in the *Los Angeles Times* called it "a case that highlights the murky definitions and poorly understood risks in one of the fastest-growing segments of science and technology."[16]

The next five years will bring a torrent of new nanotechnology applications to market. By putting almost all of their investments in product development without anything approaching a sufficient hedge in risk research, governments and industries are making a high stakes bet that nanotech will be largely devoid of problems, despite the evidence that nanotechnology could involve a range of poorly understood and significant hazards.

As yet, there is no well-documented evidence of ill health or environmental harm resulting from encounters with engineered nanomaterials. This fact, however, could be misleading, as appropriate surveillance has not been in place, and commercial applications—particularly of the more advanced nanotechnology innovations—are still not widespread. The prudent way forward, even if one wants to assume products generally will be safe, is to develop strategies and frameworks that identify and address potential risks that, if overlooked, could end up imperiling people, harming the environment and doing great harm to industry.

15. von Bubnoff, A. In *Small Times* (Ann Arbor MI, May 26)
16. Piller, C. In *Los Angeles Times* (Los Angeles, CA, June 1)

# Nanotechnology Research and Development in the United States

Any effort to craft a rational and comprehensive approach to nanotechnology risk assessment must be rooted in a thorough understanding of the existing research framework that has been so influential in the evolution of nanotechnology, from laboratory curiosity to transformative technology in the industrialized world.

The advancement of nanotechnology in the United States—and some would say the world—has been led by the U.S. National Nanotechnology Initiative (NNI). Formed in 2001 under the Clinton Administration, the NNI has been highly successful in promoting nanotechnology as a multidisciplinary concept for stimulating research, commercialization and economic growth. Although primarily established to encourage and coordinate basic and applied research, the NNI now serves as the nexus of all government-funded nanotechnology work and is supposed to be tracking research into understanding and managing potential risks. But compared to its efforts to encourage commercial applications of nanotechnology, the NNI's approach to risks has been somewhat unfocused and unenlightening, raising questions about whether a program whose primary mission is to pursue the economic benefits of nanotechnology will give safety issues proper consideration.

In other words, there is no question that the NNI has been of enormous value in making nanotechnology research a priority within the government's science portfolio. But from both a philosophical and organizational standpoint, is it positioned to explore the risks of nanotechnology as aggressively as it does the benefits? Or in such a forum, does risk research become something of an afterthought, a box to be checked on the road to realizing nanotech's considerable benefits? To answer these questions, one must first understand the history of the NNI.

## A short history of the National Nanotechnology Initiative

The NNI has its roots in an informal initiative that was established as a way to share information and coordinate nanotechnology-related endeavors across a number of government agencies. In 1996, staff members from several agencies decided to meet on a regular basis to discuss their nanotechnology plans and programs.[17] In 1998, this informal group became the Interagency Working Group on Nanotechnology (IWGN) of the President's National Science and Technology Council (NSTC). In 1999, the IWGN published its vision for nanotechnology research and development for the next 10 years.[18] In a supporting letter, Neal Lane, then assistant to the president for science and technology, underlined the long term scientific and economic goals of nanotechnology Research and Development (R&D) within the U.S. government, stating:

17. National Academies, *Small Wonders, Endless Frontiers. A Review of the National Nanotechnology Initiative*, National Academy Press, Washington, DC, (2002)
18. *Nanotechnology Research Directions: IWGN Workshop Report. Vision for Nanotechnology R&D in the Next Decade*, National Science and Technology Council Committee on Technology Interagency Working Group on Nanoscience, Engineering and Technology (IWGN), Washington DC, (1999)

"*Nanotechnology Research Directions* will help our nation develop a balanced R&D nanotechnology infrastructure, advance critical research areas, and nurture the scientific and technical workforce of the next century."[19]

At the time, the IWGN included representatives from the Executive Office and nine agencies, including the Departments of Commerce, Defense, Energy, Treasury, and Transportation, along with the Environmental Protection Agency, the National Institutes of Health, the National Science Foundation, and the National Aeronautics and Space Administration.

Two years later, the Clinton administration, seeking a higher profile for nanotechnology, officially launched the NNI. The NSTC established a new Nanoscale Science Engineering and Technology (NSET) subcommittee to oversee the NNI, under the chair of NSF's Dr. Mihail Roco.[20]

The role of the NNI was formalized and further strengthened in 2003 with the signing of the *21st Century Nanotechnology Research and Development Act*.[21] The Act lays out the scope of nanotechnology research and development within the U.S. government, and includes specific provisions for review and evaluation. It mentions the importance of U.S. global leadership in nanotechnology, advancing U.S. productivity and competitiveness, and accelerating the deployment and application of nanotechnology research and development in the private sector. The Act also notes the need for a research program and interdisciplinary centers that address ethical, legal, environmental and other societal concerns.

In 2004, the NNI published a strategic research plan that highlights, in addition to application-oriented efforts, the need for "responsible development" of nanotechnology.[22] To that end, the NNI calls for research that focuses on "(1) environment, health, and safety implications, and (2) ethical, legal, and all other societal issues." The official position of the NNI is that because "technological innovations can bring both benefits and risks to society, the NNI has made research on and deliberation of these two areas a priority."

The NNI deserves credit for making risk research a part of the program's strategic goals. However, there are two barriers that have kept these goals from being translated into a meaningful risk research program.

First, the NNI lacks the authority to compel greater investments in risk-related research. While the NNI is able to facilitate intergovernmental cooperation—and can articulate overarching goals for nanotechnology research—as a practical matter, it plays only an advisory function. It has no authority to set the nanotechnology research agenda for particular agencies, or ensure adequate resources are available to achieve specific aims. For example, while NNI officials may speak publicly about a $1 billion annual NNI R&D budget, in reality these funds are allocated by numerous congressional committees and administered at the agency level—not through the NNI—

19. Ibid.
20. NSET currently includes members from agencies involved in the NNI, as well as representatives from the White House Office of Science and Technology Policy (OSTP), and is administered by the National Nanotechnology Coordinating Office (NNCO). The subcommittee is currently jointly chaired by representatives from OSTP and the Department of Energy.
21. United States Congress, *21st Century Nanotechnology Research and Development Act (Public Law 108-153)*, 108th Congress, 1st session., Washington DC, (2003) S.189
22. NSET, *The National Nanotechnology Initiative Strategic Plan*, National Science and Technology Council, (2004)

and are invested in the service of agency agendas, not the NNI's strategic plan. In that sense, the NNI plan and, in particular, its stated commitment to risk research, is more a thought exercise than an actual plan for federal investment in nanotechnology R&D.

Second, the NNI has struggled to adequately promote risk research as a priority. Just because the NNI has no budget authority does not mean it is without influence. Through their regular contacts with agency officials, Congress, the broader scientific community, the press and the public, NNI officials have many opportunities to put the spotlight on neglected areas of nanotechnology research—such as understanding potential risk. However, there is little evidence of NNI using its influence to significantly boost the federal investment in and profile of risk-related endeavors.

## Environmental, safety and health (ES&H) research within the National Nanotechnology Initiative

To recap, the NNI is an initiative with its roots in basic and applied research. It was established to serve the economic interests of the United States, with little authority to enact a strategic research plan. Yet even with its shortcomings, the NNI offers a vehicle for pursuing a coordinated federal research agenda focused on the environmental, safety and health impacts of nanotechnology. And it has taken some steps in this direction.

In 2004, following informal agency discussions, the Nanoscale Science Engineering and Technology subcommittee established the Nanotechnology Environmental and Health Implications (NEHI) working group. NEHI's purpose is to coordinate agency efforts that involve considerations of nanotechnology risks. The working group provides a forum for agency discussions on risk related issues and is supposed to help promote risk-related research as a priority within the NNI.[23] According to the NNI, the NEHI goals are to:

- Provide for information exchange among agencies that support nanotechnology research and those responsible for regulation and guidelines related to nanoproducts;
- Facilitate the identification, prioritization, and implementation of research and other activities required for the responsible research and development, utilization, and oversight of nanotechnology and;
- Promote communication of information related to research on environmental and health implications of nanotechnology to other government agencies and non-government parties.[24]

These are largely supportive roles, and the working group has yet to use its forum to play a leadership role in establishing a strong risk research program. Like other NNI entities, the working group has no authority to mandate priorities or ensure that particular initiatives are properly funded by agencies. However, the working group is preparing an evaluation of research needed to address environmental, safety and health implications, that should be complete in mid 2006,

23. Ibid.; *The National Nanotechnology Initiative. Research and Development Leading To a Revolution in Technology and Industry. Supplement to the President's FY2006 budget*, Nanoscale Science Engineering and Technology subcommittee of the NSTC, Washington DC, (2005)

24. The National Nanotechnology Initiative. *Interagency Working Group on Nanotechnology Environmental and Health Implications (NEHI WG),* www.nano.gov/html/society/NEHI.htm. Accessed June 2006.

TABLE 1. U.S. FEDERAL GOVERNMENT ANNUAL SPENDING ON NANOTECH-RISK R&D ($MILLIONS)

| Agency | NNI-estimated risk-related annual R&D | PEN-estimated risk-related annual R&D (all relevant research) | PEN-estimated risk-related annual R&D (highly relevant research) |
|---|---|---|---|
| NSF | 24.0 | 19.0 | 2.5 |
| DOD | 1.0 | 1.1 | 1.1 |
| DOE | 0.5 | 0.3 | 0 |
| HHS (NIH) | 3.0 | 3.0† | 3.0† |
| DOC (NIST) | 0.9 | 1.0 | 0 |
| USDA | 0.5 | 0.5 | 0 |
| EPA | 4.0 | 2.6 | 2.3 |
| HHS (NIOSH) | 3.1 | 3.1†† | 1.9††† |
| DOJ | 1.5 | 0 | 0 |
| Totals | 38.5 | 30.6 | 10.8 |

Annual spending estimated from the National Nanotechnology Initiative and the Project on Emerging Nanotechnologies (PEN).[25] Highly relevant research (right hand column) is specifically focused on health and environmental risks associated with engineered nanomaterials, and is included in the broader analysis of all relevant research (middle column). NNI figures are estimated budgets for October 2005–September 2006, while PEN figures are estimated expenditure for January–December 2005. †Estimate, based on research within the National Toxicology Program. ††Based on aggregated funding. Reported by NNI †††Estimated from the percentage of projects highly relevant to engineered nanomaterials.

and that may conceivably form a basis for concerted government action to address nanotechnology risk research.

## Current federal government investment in ES&H research

Federal agencies are investing in nanotechnology risk-relevant research, and one must assume that this is coordinated to a certain degree through the NEHI working group. However, it is difficult to obtain a clear picture of what is being done, and how relevant it is. Initial funding estimates from NNI indicated that federal agencies are spending $100 million each year on research related to nanotechnology risks. But there were criticisms that this figure included research that was not obviously relevant to understanding risk.[26] Using more stringent criteria for identifying risk-relevant research, the NNI published a revised estimate in 2005 of $38.5 million per year.[27] No detailed information was released on the research being supported by this funding however.

Even if the revised NNI figure is an accurate reflection of federal spending—and there is little evidence to show that it is—one still cannot determine if there is a robust and coordinated nanotechnology risk research strategy, because there is no information on

25. *The National Nanotechnology Initiative. Research and Development Leading To a Revolution in Technology and Industry. Supplement to the President's FY2006 budget*, Nanoscale Science Engineering and Technology subcommittee of the NSTC, Washington DC, (2005); *Inventory of Research on the Environmental, Health and Safety Implications of Nanotechnology*, Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, Washington DC, (2005)

26. Stuart, C., *Small Times* (2006) 6 (2), 22–23

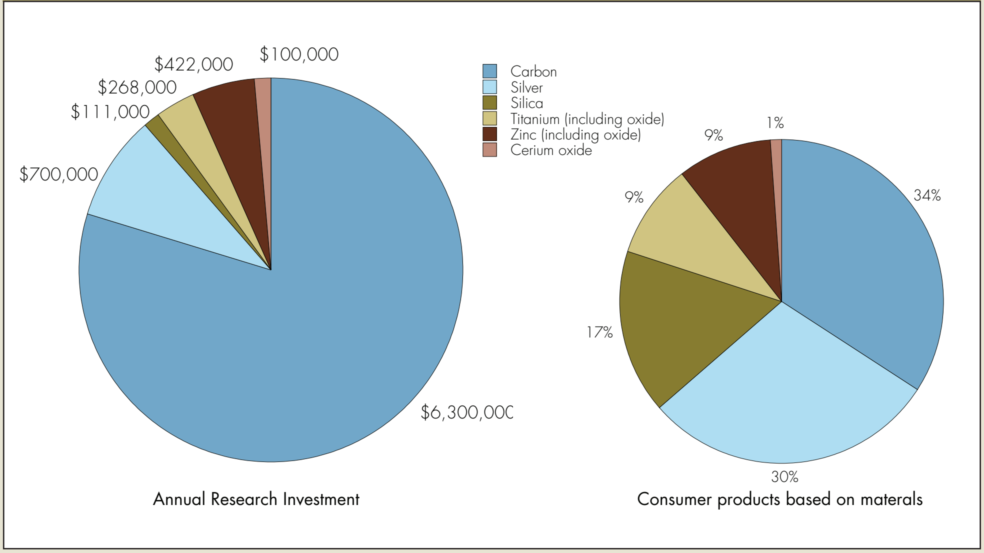
27. NSET, *The National Nanotechnology Initiative. Research and Development Leading To a Revolution in Technology and Industry. Supplement to the President's FY2006 budget*, Nanoscale Science Engineering and Technology subcommittee of the NSTC, Washington DC, (2005)

what research is being done and what is not. NNI representatives have noted that it is hard to tease out risk-related projects from the general mix of nanotechnology work. However, without a more precise understanding of what U.S. government-funded investigators are studying, the reported figures tell us nothing about whether the right questions are being asked—and answered—that will ensure nanotechnology's safe management.

Although the NNI is reticent to provide more details on risk-related research projects, a substantial amount of information is available from funding agencies. In 2005, the Project on Emerging Nanotechnologies (PEN) compiled an inventory of current government-funded risk-related research.[28] In the absence of clear information from the NNI, PEN sought to collect and categorize agency-supported research that is relevant to nanotechnology's risks to humans and the environment. Acknowledging that risk-relevant work is indeed sometimes embedded within broader efforts, projects were categorized as being either generally or highly relevant to health and safety issues. The inventory is not comprehensive, as a number of agencies were not forthcoming in providing information. It is, however, currently the most comprehensive information source of its kind.

Comparing PEN's estimate of federal spending on nanotechnology risk research with the NNI's estimate tells an interesting

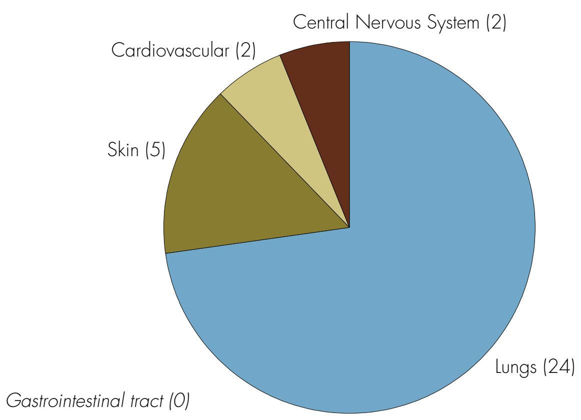
FIGURE 3. NANOTECHNOLOGY ES&H RESEARCH FUNDING FOR SIX CLASSES OF ENGINEERED NANOMATERIALS, COMPARED TO CONSUMER PRODUCTS USING THOSE MATERIALS[29]




28. *Nanotechnology. Health and Environmental Implications: An Inventory of Current Research*. Project on Emerging Nanotechnologies. www.nanotechproject.org/18/esh-inventory. Accessed June 2006.

29. *The Nanotechnology Consumer Products Inventory*, Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, Washington DC, (2006); *Inventory of Research on the Environmental, Health and Safety Implications of Nanotechnology*, Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, Washington DC, (2005)

FIGURE 4. NANOTECH-RISK RESEARCH PROJECTS ON SPECIFIC AREAS OF THE BODY




The number of current research projects specifically focused on the impact of engineered nanomaterials on five target areas within the body (lungs, skin, cardiovascular system, central nervous system, gastrointestinal tract).[30]

story. Table 1 compares estimated annual funding for research which is highly relevant to understanding risk, against research which has some degree of relevance. The periods over which the estimates are based are slightly mis-aligned, although there are no indications that there have been major changes in funding levels between 2005 and 2006.

Although the NNI funding estimate purports to represent research *highly relevant* to understanding risk, there is actually a close agreement between this figure (column 2 in table 1) and the PEN estimate of *all research* with risk-relevance. This includes research projects developing nanotechnology applications, and projects addressing incidental nanoparticles such as welding fume. The $8 million difference between NNI's $38.5 million per year estimate and PEN's $30.6 million per year estimate could reflect the different reporting periods or, more likely, agency reticence to fully disclose the details of current research. Differences in accounting will also influence the comparison—for instance, NNI-reported EPA funding in table 1 includes investment in risk-focused research grants over a three-year period, while PEN figures just reflect active research in 2005.

When PEN's estimate of research that is *highly relevant* to engineered nanomaterials is compared to the NNI estimate, the gap widens: PEN estimates that approximately $11 million per year is being spent on research that is highly relevant to nanotechnology risks, compared to NNI's estimate of $38.5 million per year. That gap is too large to be explained by the different reporting periods or a lack of agency disclosure, and raises questions about the validity and the basis of the NNI figures.

To recap, a detailed analysis of U.S. government-funded research specifically addressing the risks associated with nanotechnology amounts to approximately $11 million dollars per year, or about 1% of the $1.06 billion requested in the fiscal year 2006 nanotechnology research and development budget.[31]

Of further significance is the fact that the two government agencies mandated to carry out research in support of protecting human health and the environment (EPA and

30. I*nventory of Research on the Environmental, Health and Safety Implications of Nanotechnology*, Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, Washington DC, (2005)

31. *The National Nanotechnology Initiative. Research and Development Leading To a Revolution in Technology and Industry. Supplement to the President's FY2006 budget*, Nanoscale Science Engineering and Technology subcommittee of the NSTC, Washington DC, (2005)

NIOSH) only represent around $4 million, or just over one third, of all spending on *highly relevant* nanotech risk research. This naturally raises questions about what other agencies are doing, and whether this balance between different agencies is appropriate. It also begs the question whether research currently underway is sufficient to answer some of the most critical questions related to nanotechnology. Again, it is hard to say without more detailed information from the agencies or the NNI. But it is reasonable to conclude the low investment and the lack of specifics indicate that, at best, strategic, highly relevant risk-related research has been a low priority within the NNI.

## Connecting research activities with research needs

Two examples serve to further highlight an apparent disconnect between the approach to risk research within the NNI and what is needed to illuminate any hazards related to nanotechnology.

The first example draws on another inventory compiled by PEN that lists consumer products purporting to be based in some way on nanotechnology.[32] Figure 3 summarizes funding for risk-related research addressing six types of nanomaterials, based on carbon, silver, silica, titanium, zinc and cerium, and compares it to the number of consumer products known to be using these materials. Although this is a very subjective exercise, it shows that most of the risk research is focused—disproportionately it would seem—on carbon-based nanomaterials. In the consumer products market, carbon-based nanomaterials account for 34% of listed products, while silver is used in 30% of products and silica and metal oxides such as silica, titanium dioxide, zinc oxide and cerium oxide are uses in 36% of listed products. In other words, risk research does not appear to be in step with current market realities.

The second example considers the number of research projects that are probing the potential effects of nanomaterials on different parts of the body—the lungs, the skin, the central nervous system, the cardiovascular system, and the gastrointestinal tract (see Figure 4). Current human hazard research appears to focus heavily on nanomaterials in the lungs (24 projects), while no projects are specifically addressing the potential effects of nanomaterials in the gastrointestinal tract. Given the large number of current nanoproducts that are supposed to be eaten—such as food and nutritional supplements—this is a curious and serious omission.[33]

These examples indicate that current federally funded research is not addressing the general range of risks that may already be present in the market, and that risk research is not guided by a careful consideration of needs—present or future. Why is there so little research on nanomaterials in use now? Is the emphasis on lung impact due to careful consideration of relative risks, or because pulmonary toxicologists are more active in this field?

An apparent disparity between risk research, nanomaterials in use and where they might impact on the body naturally leads to the question "are there real gaps in our knowledge that are not being adequately addressed?" And the answer is clearly yes. This document, and the papers it draws on,

32. *A Nanotechnology Consumer Products Inventory.* Project on Emerging Nanotechnologies. www.nanotechproject.org/consumerproducts. Accessed June 2006

33. *The Nanotechnology Consumer Products Inventory*, Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, Washington DC, (2006)

is a testament to the vast tracts of nano-risk knowledge that remain undiscovered. This essential knowledge will not be developed by chance, but by strategic, targeted research. For example, there is little evidence that the current nanotechnology risk research portfolio will provide rapid answers to questions like:

- Are buckyballs (C60) in cosmetics harmful?
- What are the risks in releasing nano-silver into the environment?
- Do nanomaterials in foods and food packaging present a risk?
- Will exposure to engineered nanomaterials lead to ill health?
- What happens to engineered nanomaterials at the end of a nano-product's life?

Individual agencies such as NIOSH, EPA and NIH have small research programs addressing risk. But overall, as a federal government initiative that otherwise closely tracks the federal government's $1 billion annual investment in nanotechnology research, the NNI seems to have something of a blind spot when it comes to focusing on risk-related research. As the NNI coordinates research that will help the U.S. realize the benefits of nanotechnology, one should also expect it to ensure that federal efforts protect the public from possible risks. And if the NNI finds those efforts are insufficient, it should take the lead in a high-profile push to craft an agenda and promote the collaborations and partnerships required to develop a thorough understanding of any safety concerns that may emerge from this exciting new era of industrialization.

# Developing a Strategic Nanotechnology Risk Research Framework

Clearly, a strategic research framework is needed that will underpin the roll-out of "safe" nanotechnologies. Without proper consideration of risk assessment and management needs, it is likely that harmful technologies and products will result. And that, in turn, could slow down product development across the board as regulators and users pause to reconsider potential dangers. But drawing up a blueprint for nanotech risk research will not be easy. In addition to identifying what needs to be done and when, a viable risk research framework must focus on how resources are allocated and indicate how participating organizations and agencies should be involved in the decision-making process. The framework also should reflect the multidisciplinary nature of nanotechnology, which crosses established boundaries of scientific inquiry and agency jurisdictions.

To function efficiently, such a framework should be overseen and implemented at a very high level. If strategic research plans are developed only at the individual organizational or agency level, risk research would lack the necessary breadth, coordination, and authority that only an overarching framework can provide. Such a framework for nanotechnology risk research should be international in scope. However, a more realistic expectation would be for a national framework that includes the necessary provisions for full and effective international collaboration and coordination.

An effective risk research framework also would address regulatory and oversight needs, in addition to the generation of new knowledge. Ensuring risk research supports the oversight of nanotechnology requires government leadership in establishing a relevant and workable framework. Nevertheless, an effective framework would also incorporate partnerships and coordination with industry and other stakeholder groups.

## An immediate short-term research strategy is needed

Advances in nanotechnology and its implementation are predicted to continue for many years,[34] and an effective strategic framework for risk-based research will necessarily need to address long-term needs. However, nanotechnology-based products are a reality now. The Project on Emerging Nanotechnologies has published an inventory listing over 275 nanotechnology-enabled consumer products.[35] These products are seen as the tip of the nanotechnology-application iceberg. Many researchers and nanotechnology industry workers already are producing and handling engineered nanomaterials on a day-to-day basis, with little information on assessing and managing risk.[36] These products and materials are being released into the environment (intentionally or unintentionally) with little understanding, at least in some cases, about what the long-term impacts might be.

Recognizing the urgency with which coordinated action is needed, this paper deals specifically with short-term strategic research

34. Roco, M. C., *AIChE. J.* (2004) 50 (5), 890–897
35. Project on Emerging Nanotechnologies. *A Nanotechnology Consumer Products Inventory.* www.nanotechproject.org/consumerproducts. Accessed June 2006
36. Maynard, A. D. & Kuempel, E. D., *Journal Of Nanoparticle Research* (2005) 7 (6), 587–614

needs. It addresses what can and should be done over the next two years to understand possible dangers posed by products, processes and materials either in use now or soon to be introduced. The recommendations that result address immediate needs, while robust long-term research strategies are developed.

## Identifying and prioritizing research needs

Over the past two years, many groups, government agencies and organizations have published their perspectives on the research required to support safe nanotechnology. However, there have been no attempts to use this information to develop a strategic research plan that identifies critical questions and asks how and when those questions are going to be answered.

This report for the first time presents and analyzes the recommendations on needed risk research contained in nine of the most significant published perspectives. In the analysis presented here, the identified research needs are prioritized over a ten-year period, allowing short-term research requirements to be highlighted that are informed by immediate needs and longer-term developments. Although identifying research priorities 10 years out is somewhat speculative, it is an exercise that helps focus on immediate needs, while also highlighting longer-term issues that must begin to be addressed soon, if we are to stay abreast of emerging nanotechnologies.

## Nanotech environment, safety and health research needs

The nine sources of information used for this analysis—all published in the past two years—are listed in Table 2. While these sources do not form a comprehensive list on the subject of risk and nanotechnology, they do provide many different stakeholder perspectives and represent a diversity of scientific opinions.

TABLE 2. SOURCES USED TO IDENTIFY RESEARCH NEEDS

| | Source | Year | Document |
|---|---|---|---|
| A | G. A. Oberdörster, A. Maynard et al. | 2005 | Principles for characterizing the potential human health effects from exposure to nanomaterials: elements of a screening strategy. *Part. Fibre Toxicol.* 2(8): doi:10.1 186/1743-8977-2-8 |
| B | Environmental Protection Agency | 2005 | U.S. Environmental Protection Agency Nanotechnology White Paper: *External Review Draft.* |
| C | U.K. Government | 2005 | *Characterizing the Potential Risks Posed by Engineered Nanoparticles. A first U.K. government research report.* |
| D | The Royal Society and The Royal Academy of Engineering | 2004 | *Nanoscience and Nanotechnologies: Opportunities and Uncertainties.* |
| E | A. D. Maynard and E. D. Kuempel | 2005 | Airborne Nanostructured Particles and Occupational Health, *Journal of Nanoparticle Research* 7(6): 587-614 |
| F | National Institute for Occupational Safety and Health | 2005 | Strategic plan for NIOSH Nanotechnology Research, *Draft, September 28, 2005.* |
| G | European Commission | 2005 | *Communication from the Commission to the Council, the European Parliament and the Economic and Social Committee. Nanoscience and Nanotechnologies: An Action Plan for Europe 2005 –2009.* |
| H | R. A. Dennison (Environmental Defense) | 2005 | *A Proposal to Increase Federal Funding of Nanotechnology Risk Research To at Least $100 Million Annually.* |
| I | Chemical Industry Vision 2020 Technology Partnership and SRC | 2005 | *Joint NNI-ChI CBAN and SRC CWG5 Nanotechnology Research Needs Recommendations.* |

Each of the documents listed in Table 2 addresses nanotechnology and risk to some extent, although in each case the perspective and aims are different. Taken individually, no single document provides a comprehensive view of what needs to be done to assess and manage risks. However, taken together, they represent a broad multi-stakeholder perspective on critical risk issues.

Research needs explicitly identified in each of the nine documents were collected together. To these were added additional research needs that were suggested through a reasonable interpretation of the text. The research needs were then grouped into distinct categories. This process guided the construction of a list of clearly-defined research areas and sub-areas.

Table 3 summarizes the information gleaned from the various sources. Overarching areas are shown in bold, while component sub-areas are bolded, indented, and italicized. Each research area (left column) is mapped onto the sources where it is highlighted (right columns). For example, the need for exposure research in general is noted in all documents, whereas just two sources highlighted the need for research into methods for measuring nanomaterials in the environment.

While the table does not represent an exhaustive analysis of research needs, it provides a valuable starting point for identifying critical short-term research issues, and for beginning to address longer-term strategic research.

The analysis yielded 11 overarching categories of research needed:

Human Health Hazard. Research is needed into how nanomaterials get into and behave within the body, and how toxicity can be tested for and predicted.

Health Outcomes. Research is needed on disease resulting from exposure to engineered nanomaterials within the workforce, the general population, and sensitive groups such as children and the elderly.

Environment. Research is needed on how engineered nanomaterials enter the environment, where they go and how they behave once there, the impact they have, and how they might be controlled.

Exposure. Research is needed to identify sources of engineered nanomaterials exposure and how changes in nanomaterials over time might affect exposure. In particular, research is needed into how exposure should be measured.

Characterization. Research is needed on how significant characteristics of engineered nanomaterials, such as size, shape, surface area and surface chemistry, should be measured when evaluating risk.

Control. Research is needed into where engineered nanomaterials might potentially escape into the environment, and ways of preventing such escapes. In particular, research into the efficacy of personal protective equipment (including respirators) is needed, and how to deal with releases when they occur.

Risk Reduction. Research is needed into new ways of assessing risk, and new ways of working safely with engineered nanomaterials.

Standards. The development of appropriate nanotechnology standards is needed—in particular, standards that develop an appropriate language for describing nanomaterials and standards for measuring exposure. Standard materials are also needed for developing an understanding of potential risk, and for benchmarking toxicity evaluations.

## TABLE 3. NANOTECH RISK-RESEARCH AREAS THAT NEED ADDRESSING

| Research areas | Sources A | B | C | D | E | F | G | H | I |
|---|---|---|---|---|---|---|---|---|---|
| **Human health hazard** | ■ | ■ | ■ | ■ | ■ | ■ | | ■ | ■ |
| *Toxicity evaluation* | ■ | ■ | ■ | ■ | ■ | | | ■ | ■ |
| *Screening tests* | ■ | | | ■ | | | | | ■ |
| *Endpoints* | ■ | ■ | | | | | | | |
| *Testing methods* | ■ | ■ | ■ | | | | | ■ | |
| *Predictive toxicology* | ■ | ■ | | | | ■ | | ■ | |
| *Structure activity relationships* | ■ | ■ | | | | | | | |
| *Role of material physicochemistry* | ■ | ■ | | | | | | | ■ |
| *Computational toxicology* | ■ | ■ | | | | | | | |
| *Mechanisms of toxicity* | ■ | | ■ | | | | | | |
| *Behavior in the body* | ■ | ■ | ■ | ■ | | ■ | | ■ | ■ |
| *Routes of entry* | ■ | | | ■ | | | | | |
| *Dose* | | ■ | | | | ■ | | | ■ |
| *Transport, transformation and fate* | ■ | ■ | ■ | | | | | ■ | |
| **Health outcomes** | | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ |
| *Health impact* | | ■ | ■ | | | ■ | | | |
| *Epidemiology* | | | | ■ | ■ | ■ | ■ | | |
| *Sensitive populations* | | ■ | | | | | | | |
| **Environment** | | ■ | ■ | ■ | | | ■ | ■ | ■ |
| *Life cycle analysis* | | ■ | | ■ | | | ■ | ■ | |
| *Dispersion (including sources)* | | ■ | ■ | | | | | | ■ |
| *Transformation* | | ■ | ■ | | | | | ■ | |
| *Fate* | | ■ | ■ | ■ | | | | | |
| *Persistence and bioaccumulation* | | ■ | ■ | ■ | | | | | |
| *Exotoxicology* | | ■ | ■ | | | | | ■ | ■ |
| *Toxicity testing* | | ■ | ■ | | | | | | |
| *Toxic mechanisms* | | ■ | ■ | | | | | | |
| *Environmental control* | | ■ | | | | | | | |
| **Exposure** | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ |
| *Sources* | ■ | ■ | ■ | | ■ | ■ | | ■ | |
| *Exposure routes* | ■ | | ■ | | | ■ | | | |
| *Exposure metrics* | | | ■ | ■ | ■ | | | | |
| *Measurement methods* | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ |
| *Nanomaterials in the environment* | | ■ | ■ | | | | | | |
| *Nanostructured material behavior* | ■ | ■ | ■ | | ■ | | | | |
| **Characterization** | ■ | ■ | | | | | | ■ | |
| **Control** | | ■ | ■ | ■ | ■ | ■ | ■ | | |
| *Potential release routes* | | | | | ■ | | | | |
| *Engineering control* | | ■ | ■ | ■ | ■ | ■ | ■ | | |
| *Substitute materials* | | | | | | ■ | | | |
| *Personal protective equipment* | | ■ | | | | ■ | | | |
| *Respirators and filters* | | ■ | | | ■ | ■ | | | |
| *Process/material based control* | | | | | | | | | |
| *Spills* | | ■ | | | | | | | |
| **Risk reduction** | ■ | | | ■ | ■ | ■ | ■ | ■ | ■ |
| *Risk assessment* | | | | ■ | ■ | ■ | ■ | ■ | ■ |
| *Best practices* | ■ | | | ■ | ■ | ■ | | ■ | |
| **Standards** | ■ | ■ | ■ | ■ | ■ | ■ | ■ | | ■ |
| *Terminology* | | | ■ | | ■ | | ■ | | ■ |
| *Measurement* | ■ | | | ■ | | | | | |
| *Materials* | ■ | ■ | ■ | | ■ | ■ | | | |
| **Safety** | | | ■ | ■ | | | | | |
| **Informatics** | ■ | | | ■ | | ■ | | | |
| **Research approaches** | | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ |

Research areas as identified in nine sources (Table 2)

Safety. Research into the potential for engineered nanomaterials and nano-products to cause physical harm is needed. In particular, more research is required into explosion and fire hazards.

Informatics. Research is needed into how to collect, sort and use the vast and diverse amount of data being generated on engineered nanomaterials that is relevant to understanding risk.

Research approaches. Research is needed into how to do research. Put simply, the challenges being faced by some nanotechnologies are so new that conventional research approaches and tools are sometimes not sufficient. For example, it is now known that some conventional ways of evaluating toxicity are inappropriate for nanomaterials, requiring new approaches to be developed. The complexity of nanomaterials is forcing cross-disciplinary collaboration across previously rigid scientific divides, and researchers are having to find new approaches to working together effectively.

While perhaps not comprehensive, table 3 captures most critical areas of research needs. Two areas that were not captured well by the sources used however, but are nevertheless important, include:

Transportation. The movement of engineered nanomaterials from one place to another—in raw, intermediate or highly processed forms—will involve specific risks of release, exposure and impact. Research is needed into the potential for release and the exposure hazard for different types of material, containment requirements, hazard labeling, and specific transportation requirements and limitations.

Emergency responders. In the case of an accidental release of engineered nanomaterials, emergency response teams will need specific information on how to respond effectively—and in particular how procedures and protocols may differ from incidents involving conventional materials. Research is needed to develop appropriate advice, guidance and protocols.

## Prioritizing research

Ideally, all research needs—from immediate to long-term—should be prioritized by the science and policy communities, and should represent the perspectives of multiple stakeholders. This could be a somewhat lengthy process, given the need to consult widely and review recommendations extensively. At the same time, immediate research is needed to address concerns about materials and technologies close to commercialization or already in the market. This report suggests a method by which critical short-term needs can be identified and acted on while longer-term research strategies are developed.

## Overarching objectives for prioritization

To guide prioritization of research needs, two overarching objectives were used:

- Oversight. Research supporting the development of risk oversight frameworks, paradigms, and mechanisms that protect human health and the environment as far as is practicable in the absence of complete information, while not unnecessarily stifling innovation.

- New Knowledge. Research leading to the development of new knowledge that will further enable risks to be reduced and managed appropriately.

Within these objectives, research areas were aligned with immediate, medium-term or long-term needs, using the following definitions as guidelines:

- *Immediate needs* – Ensuring current nanotechnologies are as safe as possible, that appropriate workplace practices for handling engineered nanomaterials exist and appropriate ways of using and disposing of nanotechnology-based products are understood.

- *Medium-term needs* – Establishing associations between nanomaterial exposure and disease or environmental impact, and developing an understanding of how to minimize impact. This research would include human health outcomes; ecotoxicity; toxicity screening; risk management systems; control methods; life-cycle assessment; and exposure methods.

- *Long-term needs* – Developing ways of predicting and preemptively managing the potential risk of emerging nanotechnologies, including mechanistic toxicology; predictive risk assessment and management of later generation nanotechnologies; emergent behavior and convergence between different technologies.

Common to all three definitions is an understanding that research must relate to technologies and materials that will be developed in the future (for example, see Figure 1), as well as current nanotechnologies.

## Managing risk will be a complex process

Understanding and managing potential risks associated with nanotechnologies will be a complex process. One cannot develop a robust approach to assessing and managing risk through a linear sequence of research where one project begets another. Rather, many parallel research threads must be followed simultaneously to ensure that appropriate knowledge is developed and applied efficiently. To put it bluntly, people are being exposed to nanomaterials now and risk research is playing a game of catch-up. We do not have the luxury of researching every aspect of nanomaterials toxicity for the next 10 years before proceeding on to research into exposure measurement and control. Therefore, we need to move rapidly with a comprehensive approach to understanding the nanotechnology risks that we may be facing, if we are to have any hope of predicting and managing the impact of new nanotechnologies 10 years down the line.

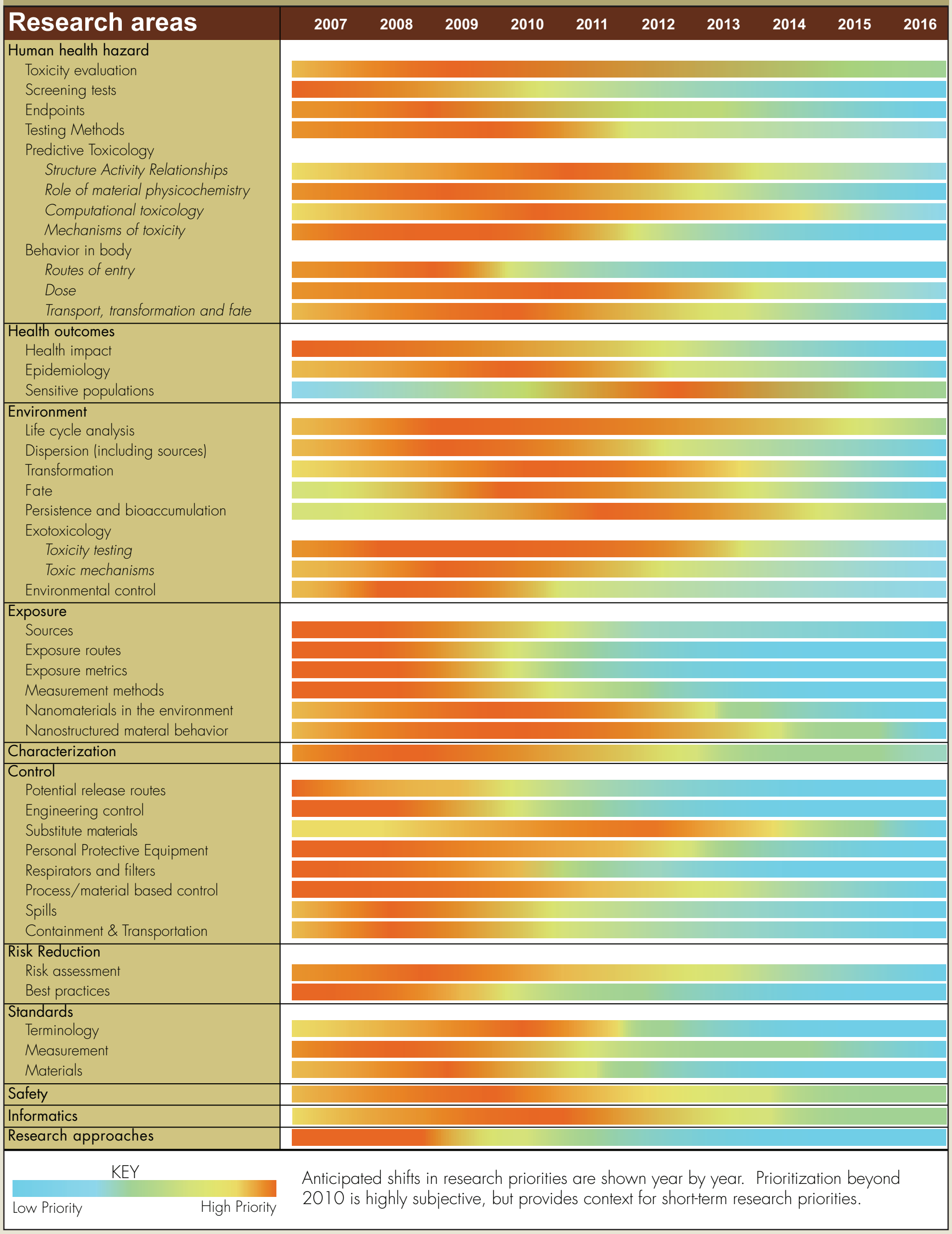
Responding to this challenge, the research prioritization presented here provides my conclusions about what research should be done and when. It recognizes that research addressing long-term needs should be started now but that research addressing short-term critical issues should be given a higher priority.

## Prioritizing research—a 10-year perspective

Table 4 provides a visual representation of research priorities over the next 10 years. Following the criteria outlined previously, it reflects shifting priorities over time, from ensuring emerging nanotechnologies are as safe as possible within our current limited understanding, through establishing associations between nanomaterials and health and environmental impact, to being able to predict and prevent potential risk farther down the road.

Table 4 provides an extensive amount of information. At the most basic level, it highlights research needs "hot spots" (denoted by "hot" colors)—showing what type of research needs to be done when over the next 10 years. For instance, research to develop toxicity screening tests is urgently needed now, while understanding how nanomaterials change in the environment is something that will become more critical in the next two years.

TABLE 4. A 10-YEAR NANO-RISK RESEARCH PRIORITIZATION




A personal evaluation of research priorities. Hot/dark colors (red, orange) indicate high priority, while cooler/lighter colors (green, blue) represent lower priorities.

Table 4 also pinpoints when certain areas of research are likely to increase in prominence (for instance, the impact on sensitive populations like children and the elderly is anticipated to increase in relevance in the next few years), allowing some degree of forward planning in research strategies.

Finally, Table 4 identifies when some areas of research should perhaps be de-emphasized (shown by cooler colors), although this, of course, becomes increasingly speculative the further out one goes. An example is research into predicting the toxicity of new nanomaterials—which will become a high priority in a few years' time, but is superceded by more pressing matters in the short term.

The research priorities beyond 2010 in table 4 are probably too speculative to form the basis of a long-term strategic research plan, but do help provide a context for short-term research needs. However, identified research priorities for 2007–2009 provide a useful basis for highlighting and acting on short-term research needs that address critical questions, as well as identifying research that will increase in relevance in coming years.

## Short-term research priorities

Short-term research needs identified in table 4 are listed in table 5. The table is divided into three categories—immediate research issues, and research that is needed now to begin addressing medium and long-term issues.

Immediate issues include those that need to be addressed as soon as possible, and represent the highest priority areas. But in choosing where to invest in the short-term, it is also important to develop capacity to address medium and long-term priorities. This relationship between short-term and longer-terms needs is particularly important in fields that may take many years to produce useable results, such as predictive toxicology. The medium to long-term research areas highlighted in Table 5 are those we should begin addressing now, if a long-term sustainable research program is to be developed.

Immediate research needs include investigations concerned with reducing risks encountered by people handling nanomaterials and addressing risk posed by products already in commercial use, or close to commercialization. The top tier of research needs identified in Table 5 address:

- Research methods—ensuring diverse research expertise is used to the full;
- Toxicity testing—screening new nanomaterials for potential toxicity;
- Measurement—charactering nanomaterials releases and exposure;
- Control—Preventing nanomaterials release and exposure; and;
- Best practices—developing ways of working as safely as possible with engineered nanomaterials.

Investments in medium- and long-term research areas over the next two years should support a variety of endeavors, including research addressing environmental impacts, developing a systematic approach to understanding and managing risks from nanotechnologies, and developing the capabilities to better predict risks posed by new nanomaterials. By supporting this work now, we can begin to build research capacity, and develop the knowledge base needed to anticipate how the unique properties of emerging materials and technologies might affect biological systems in the future.

TABLE 5. SHORT-TERM RESEARCH NEEDS (NOMINALLY 2007–2009)

| Category | Research Needs |
|---|---|
| Immediate research needs | • Appropriate measurement methods<br>• Best practices for working with engineered nanomaterials<br>• Engineering controls<br>• Exposure routes<br>• Instrument-based exposure metrics<br>• Personal protective equipment and respirator development and evaluation<br>• Potential release routes<br>• Process-based controls<br>• Responsive and effective methods of doing risk research<br>• Sources of exposre<br>• Toxicity screening tests |
| Early investment in medium-term research | • Control and management of spills<br>• Dose-metrics relevant to target organs<br>• Ecotoxicity - toxicity testing<br>• Health outcomes associated with exposure<br>• Life cycle analysis<br>• Measurement standards<br>• Nanomaterial characterization<br>• Predictive toxicology - role of physicochemistry and mechanisms of toxicity<br>• Risk assessment<br>• Routes of entry into the body<br>• Safety (risk of physical harm)<br>• Toxicity evaluation, including identification of appropriate endpoints and testing methods |
| Early investment in long-term research | • Computational toxicology<br>• Control - substitute materials<br>• Dispersion, transformation, fate, persistence and bioaccumulation in the environment<br>• Ecotoxicity - toxic mechanisms<br>• Informatics<br>• Nanomaterials release into the environment<br>• Standards - terminology, reference materials<br>• Structure activity relationships<br>• Transport, transformation and fate in the body |

Research is categorized as addressing immediate needs, or laying the groundwork for medium-term and long-term priorities, based on Table 4. Research needs are listed in alphabetical order, and are not further prioritized.

# Implementing a strategic research framework

Now that a short-term research agenda has been identified, how do we ensure that it is carried out in an efficient and timely manner? This will entail developing appropriate strategic action plans within the agencies and organizations that provide funding. However, as was discussed earlier, these plans must be tied to an overarching strategic research framework if they are to be effective. In these final pages, I consider what a viable framework might look like.

An effective framework for strategic nanotechnology risk-based research will have a number of attributes. It will provide a relevant link between the implementation of nanotechnologies and the research necessary to ensure appropriate oversight of risk. It will ensure that research conducted within different agencies and organizations is coordinated at the national level. It will enable coordination and partnerships between international initiatives. It will allow resources to be allocated appropriately to address critical issues. It will ensure research capacity is built up to address new risks. And it will provide broad strategic research priorities for assessing and managing potential risk. A successful strategic risk research framework that underpins "safe" nanotechnologies will also be responsive to the increasing sophistication of these technologies, and through regular review and revision will keep the priorities in line with emerging issues.

## Responsibility for a strategic research framework

Who should be responsible for such an overarching framework? Some might suggest it should be the industries that stand to gain from nanotechnology.[37] It is certainly in industry's best interest to ensure that appropriate risk research frameworks are put in place, as a way to maintain public and commercial confidence in their products and minimize the chances for adverse impacts. However, one would not expect them to conduct more general and basic research into the broad challenges posed by nanotechnology. Additionally, since industry also has an economic incentive to sell products, their research is not always made public, and findings might be considered suspect by some groups, if not supported by independent studies.

The most viable alternative to an industry-led strategic research framework is a government-led framework. A strategic research framework developed and administered by the federal government would combine societal accountability with a high level overview of research needs. Government science policy experts also are experienced with developing research agendas that deal with broad, generic issues, and they are routinely involved in projects that emphasize partnerships and interagency coordination. It is also fair to assert that the federal government has a social responsibility for developing and implementing an effective strategic research framework: The federal government is investing a significant sum of money into nanotechnology research and development—over $1 billion dollars in 2006.[38] With this investment must come a certain degree of social responsibility to ensure that

37. *Sizing Nanotechnology's Value Chain*, Lux Research Inc., New York, NY, (2004)
38. *The National Nanotechnology Initiative. Research and Development Leading To a Revolution in Technology and Industry. Supplement to the President's FY2006 budget*, Nanoscale Science Engineering and Technology subcommittee of the NSTC, Washington DC, (2005)

any new risks associated with the applications it is helping usher into existence are assessed and managed appropriately. The government has a responsibility to protect people who may be directly or indirectly affected by new nanotechnology materials, processes and products. It also has a responsibility to the business community, to help it understand the social and technical risks associated with the technologies the government is encouraging it to support.

## Components of a government-led strategic research framework

A successful government-led strategic research framework will need to address four areas:

Linking research to oversight. Ultimately, the aim of a strategic risk research framework would be to minimize and manage risk through applying existing knowledge and developing new knowledge. However, it will be ineffective in the long-term if research is not linked to oversight, whether this takes the form of regulation, voluntary programs, best practices or other risk management tools and approaches.

Balancing different approaches to research and research funding. Answers to short-term critical research questions require targeted and applied research, while understanding mechanisms of risk and risk management must be underpinned by basic (and investigator-driven) research. All types of research have their place. However, an effective strategic research framework will ensure that different approaches to funding and managing research match the research needs.

Authority to direct and support research. An effective strategic research framework must have teeth. It will not be sufficient merely to suggest areas of research to respective agencies, or to rely on agency resources to support the necessary investigations. While research organizations require a certain level of autonomy, an effective strategic research framework would include mechanisms that ensure that work is done by the appropriate organizations, and that resource levels are adequate to the task.

Coordination and partnership. As well as directing and coordinating research within the federal government, a successful strategic research framework would include provisions to coordinate and partner with industry, international governments, and non-government organizations. With such provisions, both private and public resources can be allocated to maximize returns and minimize redundancy.

Development and execution of such a strategic framework within the federal government will require oversight across agencies. The Nanotechnology Environmental and Health Implications (NEHI) working group of the Nanoscale Science, Engineering and Technology subcommittee (NSET) is well positioned to address some aspects of a strategic research framework, but it is restricted in its ability to address issues related to oversight, or to direct research and resources. An existing governmental coordination group between The Occupational Safety and Health Administration (OSHA), the Mine Safety and Health Administration (MSHA), the National Institute for Occupational Safety and Health (NIOSH) and the Environmental Protection Agency (EPA) (called the OMNE group) includes two of the key research agencies addressing nanotechnology, but again has only limited scope and authority. It is also doubtful whether the limited membership of OMNE makes it suitable for overseeing a broad strategic research framework. In their current configurations, neither the NEHI or the OMNE would appear to be adequate for developing and implementing the type of strategic risk research framework necessary for the development of sustainable nanotechnologies.

Unless significant changes are made to the scope and structure of NEHI, a new interagency group will be necessary to oversee an appropriate strategic framework. It should ideally be established outside the structure of NSET—which does not have a clear mandate to consider oversight issues—although it should coordinate with NSET. The group should be comprised of representatives from the key regulatory and oversight-focused research agencies, including NIOSH, EPA, OSHA, FDA, CPSC, USDA DOT and NIEHS. Representation from agencies such as NIH, NSF, DOD, and DOE who are now funding basic or applied research that can offer insight into risks (even if risk assessment is not the primary objective) also should be considered, as long as a bias away from risk-specific research does not result.

The group must have authority to ensure sufficient funding and resources are available through various mechanisms. Maintaining the current situation where agencies such as EPA and NIOSH—entities with the primary responsibility to protect people and the environment from risks—receive little support for nanotechnology risk research is untenable, if critical questions are to be answered in a timely fashion.

## What might a short-term strategic research plan look like?

Having considered research that is needed in support of "safe" nanotechnology—along with the prioritization of this research in the short-term and a strategic framework within which this research can be carried out—two key questions remain: while the federal government would oversee the initiative, who would do the actual work, and how much would it cost? Although these are complex questions to answer, I have attempted to construct a proposed action plan that addresses short-term risk research needs. This action plan is not so much a set of recommendations as a perspective to stimulate dialogue. It does, however, serve three tangible purposes: It provides an estimate of how much the research might cost, identifies lead agencies, and describes a division of labor between these agencies.

## Targeted research

Targeted research is research aimed at addressing a specific question or issue. It may be conducted inside an agency, or externally through grants and contracts. The common theme is that it starts with a specific question, and applies resources as appropriate to obtain timely and relevant answers.

In table 6, a plan to address the short-term research areas previously developed is presented. It incudes estimates of how much the research might cost, and who should lead in implementing it. Three things are apparent from this table:

Cost. If significant progress is to be made, ***at least*** $50 million a year over the next two years should be invested in targeted, highly relevant research into nanotechnology risks. This figure is five times more than current government spending in this area.

Lead Agencies. Targeted research is most appropriately led by four agencies—EPA, NIH (mainly through the National Institute of Environmental Health Sciences or NIEHS), NIOSH and NIST.

Collaboration. Some research needs can be successfully accomplished only through cross-agency collaboration. This includes the

TABLE 6. SHORT-TERM RESEARCH GOALS

| Lead Agency | Short Term Research Goals | Estimated Funding† |
|---|---|---|
| Cross Agency | • Develop research methodologies to proactively address risk<br>• Begin developing appropriate risk assessment tools<br>• Preliminary development of informatics systems for nanomaterials | 7 |
| EPA | • Identify sources and routes of exposure and release - environment<br>• Develop and evaluate environmental measurement methods<br>• Preliminary development of appropriate methods for evaluating ecotoxicity<br>• Preliminary development of life cycle analysis tools for engineered nanomaterials<br>• Preliminary investigation of ecotoxicity mechanisms<br>• Preliminary investigation of nanomaterial release into the environment<br>• Begin to study dispersion, transformation, fate, persistence and bioaccumulation in the environment | 20 |
| NIH | • Begin to evaluate the toxicity of representative nanomaterials<br>• Preliminary development of appropriate toxicity testing endpoints<br>• Preliminary development of appropriate toxicity testing methods<br>• Begin developing predictive toxicology capabilities<br>• Begin developing computational toxicology for engineered nanomaterials<br>• Preliminary investigation of nanomaterial structure activity relationships | 24 |
| NIOSH | • Develop and evaluate human exposure measurement methods<br>• Develop guidance on best possible working practices<br>• Develop and evaluate personal protective equipment<br>• Develop and evaluate respiratory protective equipment<br>• Develop and evaluate process-based controls<br>• Identify sources and routes of exposure and release - workplaces<br>• Develop instrument-based exposure metrics<br>• Develop and evaluate appropriate toxcity screening tests<br>• Develop a preliminary understanding of organ-specific dose<br>• Preliminary research exploring associations between nanomaterials exposure and human health outcomes<br>• Begin to develop methods to control and manage spills<br>• Study the role and significance of routes of entry into the body<br>• Preliminary investigations of nano-specific safety issues<br>• Begin studying transport, transformation, and fate in the body<br>• Preliminary evaluation of risk reduction through material substitution | 46 |
| NIST | • Preliminary development of appropriate nanomaterials characterization methods<br>• Begin developing measurement and characterization standards<br>• Begin developing standards for terminology and reference materials | 9 |
| Total | | 106 |

Proposed lead agencies and minimum targeted federal funding levels to address identified short-term research goals. Estimated funding is in $millions (USD) over a two-year period, and includes intramural and extramural funding of risk-specific research. Research goals addressing immediate, medium-term and long-term areas are shaded from dark to light (based on Table 5).

†Estimated funding over 2 years.

development of research methodologies to proactively address risk.

Short-term research goals fall within five general areas:

Risk assessment. This includes research methodologies, risk assessment tools and information management. This area is so diverse and crosses so many boundaries that cross-agency leadership will most likely be needed.

Environmental impact. High priority research goals include identifying routes of release and exposure, and measurement methods. This research falls within EPA's mandate and competency, and indeed the agency has already demonstrated leadership in addressing the environmental impact of nanotechnologies.

Human health impact. High priority research goals include exposure measurement methods, controlling release of material and preventing exposure, and developing toxicity screening tests. These goals lie within the scope of NIOSH's mission, and the agency has been active in developing a robust research portfolio addressing human health impact.

Predicting hazard. The ability to predict the hazard of a new engineered nanomaterial, and even to reduce its toxicity through careful engineering, is a long-term goal that needs an initial research investment now. The foundational research needed into toxicity, including mechanisms of action, is most appropriately led by NIH. A comprehensive research program addressing the toxicity of select nanomaterials has been established by the National Toxicity Program under the administration of NIEHS, further supporting NIH leadership in this area.

Materials characterization. An ability to characterize nanomaterials appropriately when evaluating potential risk will require investment in basic research now. NIST is ideally positioned to lead the development of characterization methods and standards, building on extensive expertise and experience in this area.

It is important to distinguish between agencies that should lead research, and those that are capable of doing the work. Agencies such as DOE, DOD and NSF are already supporting fundamental research addressing the potential impact of nanotechnology (table 1), and they will no doubt continue to provide valuable support for this research. However, it must be asked whether these and similar agencies should be taking a leadership, as opposed to a supporting role, in strategic targeted risk-focused research, which may lead to nanotechnology oversight and regulation.

The Food and Drug Administration (FDA) clearly has a critical role to play in determining the direction and relevancy of strategic risk-based research, and yet it is not listed in table 6 as a key research agency. While FDA does have a limited research capacity in this area, current activities are predominantly coordinated through the National Toxicology Program (NTP) and NIEHS. Although this may change in the future, the agency is best positioned to advise on strategic research directions, while continuing to participate in active research through the NTP.

## Indirect research

As has already been noted, research into basic nanoscience and nanotechnology applications has the potential to inform an understanding of the impact of nanotechnologies. Examples include the development of characterization methods that enable the advancement of nanotechnology as well as risk evaluation, and the transfer of knowledge from the development of medical therapeutics to an understanding of toxicity. Relevant research will most likely be led by pure and applied research agencies such as NSF and NIH, along with DOD, DOE, USDA and NIST. A strategic research plan must find ways to tap into this kind of work to provide answers to risk-related questions.

Placing a value on how much indirect research is needed is a near-impossible task. It is clear that a comprehensive understanding of risk will not be developed as quickly or effectively if this source of information is overlooked. And yet, it is dangerous to assess the value of indirect research solely on its *potential* to inform an understanding of risk. Returning to the example given above: Research into new characterization methods might lead to technologies that can be used to measure nanomaterial exposure. But unless this latent potential has been realized through targeted research, the work will be worthless to understanding and addressing risk.

## Partnerships

An effective strategic research plan will leverage resources through collaboration and partnerships. For the federal government, this would include working with industry and international partners, as discussed above. This is an area where there already has been considerable activity within the federal government: The NNI has been working closely with industry through the Consultative Boards on Advancing Nanotechnology (CBAN),[39] and was responsible for initiating the International Dialogue on Responsible Nanotechnology in 2004. In addition, NIOSH is developing partnerships with nanotechnology industries to evaluate methods of assessing and controlling risk,[40] EPA is partnering with three other agencies to support risk-focused research, and the agency is also developing a voluntary program for industry to provide and develop risk-related information on new materials.[41]

Within the broad and diverse range of partnership opportunities in this area, three specific aspects should be included within a short-term strategic research plan:

### Transparency and information sharing.

Mechanisms should be put in place whereby industry and government can openly share internal information relevant to understanding and addressing risk. Where this can be achieved without compromising sensitive business information, it will facilitate the rapid development of robust standards of care across nanotechnology industries, as well as ensuring that researchers and policymakers have access to the best possible information on risk assessment and management. Willingness to share information also will support public trust in nanotechnology.

### Coordinated strategic research plans.

Effective mechanisms are needed to ensure coordination between international research

39. Chemical Industry Vision 2020 technology Partnership & SRC, *Joint NNI-ChI CBAN and SRC CWG5 Nanotechnology research needs recommendations*, (2005)

40. National Institute for Occupational Safety and Health. *NIOSH to Form Field Research Team for Partnerships in Studying, Assessing Nanotechnology Processes*. www.cdc.gov/niosh/topics/ nanotech/newsarchive.html#fieldteam. Accessed June 2006.

41. *Overview Document on Nanoscale Materials, 11/22/05*, National Pollution Prevention and Toxics Advisory Committee (NPPTAC). A federal advisory committee to the U.S. Environmental Protection Agency, Washington DC, (2005)

efforts, and between industry and government strategic research plans. In the United States, CBANs have been partially successful at developing a constructive dialogue between industry and government.[42] However, these boards have had limited success so far in coordinating actual research projects, as opposed to advising on research needs. In the broader research community, channels of communication certainly exist between countries. The challenge is to take these relationships to the next level and implement coordinated strategic research plans so that work is complementary, not duplicative, and all necessary avenues of investigation are pursued. Two possible models for such international collaboration are the sequencing and mapping of the human genome and Arabidopsis genome.

Joint government-industry funding of research. A powerful and proven approach to leverage government and industry research funding is to establish a research institute jointly funded by government and industry. A model example is the Health Effects Institute (HEI)[43] which was established to address the health impact of air pollution. This public-private effort has been tremendously successful since its inception in supporting high quality independent and authoritative research.[44] A number of people have suggested, informally, establishing a similar institute for addressing the health and environmental impact of engineered nanomaterials. Such an endeavor would extend the range of research undertaken, ensure research is closely tied to commercial products, and support capacity building within the research community. Whether it would involve working through the existing HEI, or establishing a new Nanotechnology Effects Institute (NEI), this type of partnership would make maximum use of government and industry resources and expertise to support targeted independent research.

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42. Chemical Industry Vision 2020 Technology Partnership & SRC, *Joint NNI-ChI CBAN and SRC CWG5 Nanotechnology Research Needs Recommendations*, (2005)
43. The Health Effects Institute is a nonprofit corporation chartered in 1980 as an independent research organization to provide high-quality, impartial, and relevant science on the health effects of air pollution. Typically, HEI receives half of its core funds from the U.S. Environmental Protection Agency and half from the worldwide motor vehicle industry. Further details can be found at www.healtheffects.org
44. Health Effects Institute, Boston MA, (2005)

# Summary

Nanotechnology is a reality now, and our ability to produce ever-more sophisticated materials, processes and products by engineering at the nanoscale will only increase over the coming years. Yet our understanding of the potential health, safety and environmental impacts of these emerging technologies is rudimentary at best. Current risk-based research is poorly directed and funded, and is unlikely to provide answers where they are most needed. And needed they are, since a proper understanding of risks is the only way to assure the emergence of economically viable technologies that do not harm people, animals, or the environment.

In this paper, I have presented a strategy for risk research that encompasses what needs to be done in the short term, who needs to do it and how much it will cost, if we are to understand and address risks in a systematic manner. Some of this research is already being supported by the federal government. But without the context of a strategic research framework, it is difficult to judge where it is making a significant contribution.

No doubt some of these ideas will be embraced, while others will be dismissed out of hand. Yet when all is said and done, the truth remains that without a viable strategic research framework, we will not be able to provide the answers that businesses, workers and the public deserve and, increasingly, demand. My hope is that this paper will stimulate a dialogue that leads to much greater emphasis on risk research through a strategic, coordinated and above all, relevant, framework for action.

# Recommendations

**1.** Changes need to be made in risk research responsibility within the federal government. There should be top-down authoritative oversight of strategic risk-based research within the federal government, and nanotechnology risk research needs to shift to federal agencies with a clear mandate for oversight and for research into environment, health and safety issues.

**2.** Adequate funding must be provided for highly relevant risk research. Key lead agencies, including the Environmental Protection Agency, the National Institute for Occupational Safety and Health, the National Institutes of Health and the National Institute of Standards and Technology, will require an estimated *minimum* budget of $100 million over the next two years devoted to highly relevant, targeted risk-based research if critical knowledge is to be developed. In addition, there should be a complementary and identifiable investment in basic research and applications-focused research that has the potential to inform our understanding of risk. Mechanisms should be developed to make full use of this indirect but complementary research.

**3.** A short-term strategic risk-research plan should be developed and implemented. The research plan should address issues critical to ensuring the safety of nanotechnologies in or close to commercial use. Top priorities should include identifying and measuring nanomaterials exposure and environmental release, evaluating nanomaterials' toxicity, controlling the release of and exposure to engineered nanomaterials, and developing "best practices" for working safely with nanomaterials. Strategic research investment in longer-term issues such as predictive toxicology should also be undertaken now, to build research capacity and provide the scientific basis for addressing new risks.

**4.** Mechanisms should be developed for joint government-industry risk research funding. A research institute should be established along the lines of the Health Effects Institute, enabling government and industry funding to be leveraged in the service of strategic nanotechnology risk research.

**5.** Nanotechnology risk research must be coordinated internationally. Mechanisms should be established to achieve effective global coordination of government-funded research into the environmental, safety and health implications of nanotechnology. There should be mechanisms facilitating the free exchange of information on research needs, activities, and priorities. There also should be mechanisms for sharing costs and resources, which can be pursued in the context of coordinating strategic research agendas and by jointly funding specific projects. In addition, there is a need for international coordination of research conducted by non-governmental groups. Finally, the need for a global focus on nanotechnology risks could justify establishing an independent secretariat, funded by member countries, to oversee international risk research.

6. An interagency oversight group should be established with authority to set, implement and review a strategic risk research framework. The group would be responsible for developing a top-level strategic framework that would serve as a guide for the coordination and conduct of risk-related research in relevant agencies. It would have the authority to set and implement a strategic research agenda and assure agencies are provided with appropriate resources to carry out the work. The group would direct efforts to provide a strong scientific basis for regulatory decisions, thus bridging the existing gap between the need for oversight and our poor technical understanding of nanotechnology risks. It would also ensure that the results of risk-relevant research are put to practical uses, including education and outreach programs. In addition, the group would ensure risk-related research is coordinated between industry and government, and between the U.S., other countries and international organizations.

7. A rolling, independent assessment of long-term research needs and strategies should be established. An independent study effort is needed to identify future research needs, provide advice on how to incorporate them into a strategic research framework, and evaluate progress toward achieving strategic research goals. The study would be carried out by an authoritative organization such as the National Academies. It would ideally run for five years, with an option that would allow it to be extended for an additional five years. The first set of strategic recommendations should be released within two years of the study's inception. The scope of the study would include methods of stimulating and managing risk-focused research that are responsive to rapidly developing and complex technologies, and developing effective collaboration between industry, academia, international governments and other stakeholders.

The **PROJECT ON EMERGING NANOTECHNOLOGIES** was launched in 2005 by the Wilson Center and The Pew Charitable Trusts. It is dedicated to helping business, governments, and the public anticipate and manage the possible human and environmental implications of nanotechnology.

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