U.S. House of Representatives Committee on Science and Technology
Subcommittee on Research and Science Education
October 31, 2007 hearing on:
"Research on Environmental and Safety Impacts of Nanotechnology: Current Status of Planning and Implementation under the National Nanotechnology Initiative"

Questions for the Record to Dr. Richard A. Denison[1]
Senior Scientist
Environmental Defense

Introduction

Before addressing Subcommittee members' specific questions, Environmental Defense wishes first to elaborate on the recommendations we offered in our testimony on changes needed for the NNI to effectively identify and address the potential risks of nanoscale materials, as our recommendations bear directly on many of these questions. We also wish to address what we believe to be serious mischaracterizations of our positions provided by two other witnesses at the hearing. Finally, we describe a ***federal precedent and potential model for restructuring the NNI***. This model directly addresses our and others' mounting concern that nanotechnology's potential risks are not being sufficiently addressed because the same entity has been charged with both promoting and providing oversight of this technology. The restructuring we suggest would help to ensure that nanotechnology's risk implications get the attention they need, even as federal investment in nanotechnology development proceeds.

Our two main recommendations are as follows: First, we recommend creating a new entity, or elevating an existing entity, with the responsibility to develop and oversee a federal research strategy to identify, assess, and address the potential risks of nanomaterials. This entity should be provided with ample budgetary and independent management authority and sufficient resources, and should have a core public health and/or environmental mission. Second, we recommend establishing a clearer and stronger separation in decision-making and management between the parts of the federal government whose mission is to help develop and advance nanotechnology, and those parts charged with ensuring a thorough and objective examination of its potential risks and taking steps needed to mitigate those risks.

Hearing witnesses Dr. Clayton Teague and Mr. Floyd Kvamme inaccurately depicted Environmental Defense's recommendations in their prepared statements and in response to Subcommittee members' questions. They repeatedly and incorrectly stated or implied that we and other witnesses critical of their efforts (a) are calling for appointment of an EHS research "czar" and (b) intend for EHS research to be conducted in isolation (in a "silo"), wholly removed from research on nanotechnology applications. Neither is the case.

Environmental Defense is indeed very concerned about the NNI's continuing lack of sufficient direction, leadership, and authority to develop and implement an effective and coherent risk research strategy across the federal government. This lack of focus is not the result of

happenstance, in our view, but rather it is embedded in the origins and management structure of the NNI itself.

With apologies for the "alphabet soup," note that the National Nanotechnology Coordination Office (NNCO, headed by Dr. Teague) is managed under the Nanoscale Science Engineering and Technology (NSET) Subcommittee of the Committee on Technology (CoT), which is part of the National Science and Technology Council (NSTC). The NSTC is advised by the President's Council of Advisors on Science and Technology (PCAST, co-chaired by Mr. Kvamme). PCAST has been designated as the National Nanotechnology Advisory Panel (NNAP), which is charged with reviewing the federal nanotechnology research and development program.

The core mission of all of these entities is the advancement of technology in the U.S. The NNCO staff, the NSET and CoT chairs, and the PCAST/NNAP membership are populated almost entirely with *technologists* – individuals trained in materials sciences or with technology development expertise and experience.[2] From a historical perspective, this makeup is not surprising, as the NNI was created with the primary aim of advancing nanotechnology. (Of the eleven areas of activity delineated for the national nanotechnology program called for under the *21st Century Nanotechnology Research and Development Act of 2003*, only a small part of one of them addresses health or environmental implications; the other ten focus on advancing nanotechnology applications.[3])

Although the staffing and membership composition described above is quite appropriate for the NNI's work to develop and promote nanotechnology *applications*, it is entirely inappropriate when it comes to addressing nanotechnology's *implications* – its potential risks. Scientists trained and experienced in understanding health or environmental risks, rather than technologists, need to direct and implement the NNI's efforts to identify and address nanomaterial hazards and exposure potential. Delivering the right expertise is crucial, as is providing some distance from, and an effective counterbalance to, the inevitable boosterism of technologists charged with a promotional role.

The effect of the current imbalance is evident in the hearing statements of technologists Mr. Kvamme and Dr. Teague, defending the NNI's risk-related efforts. Even as they professed that the NNI is serious about addressing nanotechnology's potential risks, both witnesses claimed or implied that concerns about nanotechnology's risks are overblown. In his written statement, Mr. Kvamme stated the following:

> "Already, research is shedding light on some of the questions being asked. Specifically, a study at Purdue on the environmental impact of manufactured nanoparticles on ordinary soil showed ***no negative effects***; Georgia Tech scientists are doing similar work. Researchers at Dayton University are working on the health and safety aspects of the use of nanodiamonds as drug delivery vehicles ***with encouraging results***. University of Oregon chemists are looking at the use of nanomaterials to clean up toxic groundwater contaminants that have until now been difficult to remove. In vivo tests at Rice University have found ***no immediate adverse health effects*** from carbon nanotubes injected directly into the bloodstream and that the liver seems to collect these materials effectively for excretion." (emphases added)[4]

This "summary" of the available risk research on nanomaterials is highly selective and biased, as it over-generalizes findings and highlights only "exonerative" results while ignoring many other studies that indicate potential concerns. It is also entirely at odds with the far more balanced rendition of the facts provided by NNI Agency health and environmental scientists.[5]

Dr. Teague, in response to a Subcommittee member's question, stated the following:

> "A lot of the research that was done early on, even though it was certainly not coordinated and from the federal government, and I think that is why some of it did produce some very premature results and a lot of wrong conclusions were drawn from it. By the careful planning and by tapping into the depth of experts within the Federal Government, and our collaboration with others outside, I think that we have, by far, the best approach to trying to carry out appropriate research in a careful, deliberately planned way. If one doesn't do that, the result is typically bad research and research that leads to premature and often poor results, poor understanding and leading to, I think, a lot of misleading conclusions that have already been drawn there often, because the result was not planned, not well-conducted."[6]

While we certainly have no quarrel with the need for more and better coordinated research, Dr. Teague's implication that only "bad" research has indicated the potential for risks again reflects a very biased view of the available literature. It also is not indicative of what any good health or environmental scientist in the field would state to be the case.

Indeed, a review just published in *Nanotoxicology* found that the "vast majority" of nearly 430 journal papers reporting on toxicity testing of various nanoparticles identified adverse effects in laboratory animals or cell lines.[7]

What concerns Environmental Defense most about these statements, however, is that senior NNI and PCAST members seem to believe it is their role to downplay evidence that suggests that engineered nanomaterials may pose risks to health or the environment.

The mechanism the NNI is using to address nanotechnology's potential risks is the Interagency Working Group on Nanotechnology Environmental and Health Implications (NEHI). NEHI's stated mission is to:

- provide for ***exchange of information*** among agencies that support nanotechnology research and those responsible for regulation and guidelines related to nanoproducts (defined as engineered nanoscale materials, nanostructured materials or nanotechnology-based devices, and their byproducts);
- ***facilitate*** the identification, prioritization, and implementation of research and other activities required for the responsible research and development, utilization, and oversight of nanotechnology, including research methods of life-cycle analysis; and
- ***promote communication*** of information related to research on environmental and health implications of nanotechnology to other Government agencies and non-Government parties.[8]

Environmental Defense agrees with the importance and necessity of such "bottom-up" functions of interagency information exchange, facilitation, and communication, but we believe they are not enough to produce and effectively implement a risk research strategy. We think the record speaks for itself: a string of unmet promises to deliver the strategy, and near-universal disappointment in the scope and quality of the interim documents delivered to date by NEHI.[9]

We support retaining and continuing to use the "bottom-up" approach to gain input from the full range of agencies and individuals with expertise in relevant fields. This approach needs to be supplemented, however, with a "top-down" capacity, designating a smaller group of senior health and environmental scientists with the authority to direct and oversee both the EHS research budgets and associated activities within and across NNI agencies. These scientists should be drawn from NNI agencies with missions to protect human health and/or the environment and related research capabilities. ***Whether situated within the current NNI structure or outside of it, this executive body needs to have decision-making authority that is independent of those parts of NNI charged with advancing nanotechnology development.*** (Our written testimony elaborates further on why this separation of roles is needed.)

With regard to the claim of other witnesses that Environmental Defense favors somehow isolating implications research from applications research, we absolutely do not. We fully recognize both the need for and the benefits of "cross-fertilization," as well as the importance of simultaneously pursuing and sharing the results, from different lines of research. It would clearly be counterproductive to obstruct such opportunities for synergism or to impede the free flow of research ideas and results. Our point instead is that addressing risk implications requires conducting research that is both intended and directly targeted to answer specific risk-relevant questions. Such research should also be undertaken and directed by – and judgments as to its adequacy, quality and interpretation made by – scientists trained in the health or environmental sciences who work at agencies charged with the pursuit of health or environmental missions. It is equally important that the specifics of the projects and amount of funding spent on such research be transparently and clearly identified and accounted for separate from applications research, some of which may well yield findings relevant to understanding risk.

A federal precedent – and potential model – for our recommended approach

Our nation has faced similar situations in the past, when mounting concern that a technology's potential risks received insufficient attention because the same entity had been charged with both promoting and providing oversight of that technology. The Atomic Energy Commission (AEC), for example, first established by the *Atomic Energy Act of 1946*, was explicitly assigned the functions of both encouraging the use of nuclear power and regulating its safety. Concerns about this dual charge grew among both proponents and critics of nuclear power, coming to a head in the mid-1970s, when Congress abolished the AEC. Congress then assigned the oversight functions of the AEC to a new entity, the Nuclear Regulatory Commission (NRC), and shifted Federal nuclear energy research and development to the U.S. Department of Energy (DOE).[10]

The NRC's mission and work specifically includes risk research: "As part of its regulatory program, the NRC conducts an extensive research program to provide independent information and expertise to support its safety decision making."[11] This research is conducted through the

NRC's Office of Regulatory Research, which "[p]rovides leadership and plans, recommends, manages and implements programs of nuclear regulatory research." The Office also engages in considerable cooperative research with "DOE and other federal agencies, the nuclear power industry, U.S. universities, and international partners."[12] However, it operates and is managed independently, and the NRC has in place extensive guidelines and procedures intended to assure it avoids conflicts of interest (COI) that could arise from its use of DOE laboratories for technical assistance and research,[13] or from its hiring contractors who have also worked on or are competing for DOE contracts.[14]

Hence – far from operating in a "silo" and being unable to take advantage of the "cross-fertilization" arising from research conducted on applications – the NRC has established an approach intended to allow for safety research to be conducted in a manner that transparently manages COI, while also maintaining its independent decision-making. While we make no representation as to the NRC's performance, we believe the Committee should seriously examine the NRC example as a precedent and potential model for the kinds of changes that may be needed to reform the NNI. Such reform would, in our view, help to ensure that nanotechnology's risk implications get the attention they need, even as federal investment in nanotechnology development proceeds.

Our specific responses to Questions for the Record follow.

Questions Submitted by Subcommittee Chairman Brian Baird

1. *Dr. Maynard has suggested a mechanism for government to partner with industry to fund environmental, health and safety (EHS) research that would support the needs of government in formulating a regulatory framework for nanomaterials and the needs of industry on how to develop nanotechnology safely. The idea is to use the Health Effects Institute model, which studies the health effects of air pollution. Do you believe this would be a good model for developing a government/industry research partnership for EHS research related to nanotechnology?*

Response:
We agree that the Health Effects Institute (HEI) provides a good model for governing public-private research partnerships, for several reasons. First, because the research findings have implications for needed regulatory controls that may be controversial, it would be beneficial to have an objective, scientifically excellent third party, which neither makes nor is a stakeholder in policy-making (i.e., is outside of government and the regulated industry), conduct such research. Second, given the considerable technical demands of the research, the HEI model – which employs the finest academic scientists as research planners, performers and peer reviewers – will help assure high-quality and credible research results. Third, situating this research in a high-quality independent institution will help foster the development of a focused and consistent research strategy in a way that may be more difficult to achieve with multiple competing government agencies. Finally, HEI employs a number of governance and operational procedures to help ensure transparency, credibility and integrity in its research; these include a commitment

to release all research results (positive or negative), reliance on governance and advice by independent expert committees, and insulation of the review and release process from sponsor influence.

2. *The President's Council of Advisors on Science and Technology (PCAST) was assigned by the President to serve as the statutorily created outside advisory committee for the National Nanotechnology Initiative. How useful is PCAST as a means for private sector organizations to provide input to the planning and prioritization process for EHS research under the NNI? Are there other mechanisms available for stakeholders to have a voice in this process?*

Response:
As noted in our Introduction, PCAST, like the NNI itself, has as its core mission the advancement of technology in the U.S. Not surprisingly, PCAST's membership is therefore made up almost entirely of *technologists* – individuals trained in materials sciences or with expertise and experience in the area of technology development.[15] Only three of the 36 PCAST members have health science or environmental science expertise, and none has a risk science background. This mission and composition, while appropriate for overseeing NNI's primary goals related to developing and promoting nanotechnology *applications*, are inappropriate when it comes to overseeing or judging how well the NNI is addressing nanotechnology's *implications* – its potential risks. Scientists trained and with extensive experience in understanding health or environmental risks – not technologists – need to oversee and advise NNI's efforts to identify and address nanomaterial hazards and exposure potential. In our view, PCAST's ability to effectively execute its assigned advisory tasks is impeded by the same problem we have identified within the NNI itself: insufficient separation between the promotional and oversight roles it is being expected to play.

In addition to this structural or compositional constraint, the only mechanism PCAST seems to have developed for gaining outside input – its Nanotechnology Technical Advisory Group (NTAG) – operates virtually entirely out of sight. No description of the NTAG – its members, its mission or charge, its operating guidelines, whether or when it meets – is available on the PCAST website.[16] (In the interest of full disclosure, Environmental Defense was extended but declined an invitation to join the NTAG primarily because we were concerned that it appears to operate largely out of public view.) This approach is in marked contrast to the manner in which Federal advisory committees are structured and operate, pursuant to the Federal Advisory Committee Act (FACA).

3. *Dr. Maynard suggested the need for an individual to be designated to take a leadership role for EHS research under the NNI. Do you agree with this recommendation, and if so, how would you define the characteristics and functions of this leadership role and how could the proposal be implemented?*

Response:
We agree with the need for more centralized and independent leadership and increased decision-making authority sufficient to direct and oversee federal nanotechnology risk research, although

we think that designation of a small group of experienced individuals with a somewhat diverse set of backgrounds and expertise in health and environmental fields, rather than a single individual, may be preferable. In our Introduction, we have described in some detail the characteristics, functions and authorities such an entity would need to effectively direct a federal risk research program. We have also suggested that the Nuclear Regulatory Commission and its Office of Nuclear Regulatory Research provide both a precedent and potential model. Most important, such an executive body needs to have decision-making authority that is independent of those parts of NNI charged with advancing nanotechnology development.

4. *One of the key aspects of carrying out EHS research is to have agreed terminology and standards for characterization of nanomaterials.*

    a. *Is this getting sufficient attention under the NNI? What is the role of NIST in this area?*
    b. *Is there a role for NNI to provide direct assistance to nanotechnology companies, particularly small companies, to help them characterize new nanomaterials, which will thereby assist the companies in assessing the potential environmental and health risks of the new materials?*

Response:
While deciding on terminology and standards for characterization has proven challenging both domestically and internationally, we believe the NNI is devoting sufficient attention to these important matters. Because terminology and standards for characterization must be agreed upon by a variety of industry sectors, academic researchers, and government bodies in different countries, there is only so much the NNI can do to help the parties come to agreement. The National Institute of Standards and Technology (NIST) has an important role to play in both helping to set the standards and then developing and making available reference materials for those standards. To our knowledge, NIST is adequately engaged in these processes.

The federal government, through entities such as NIST and the Nanomaterial Characterization Laboratory of the National Cancer Institute, has been assisting both private sector and academic groups with nanomaterials characterization. This is indeed an important and useful role for the government to play, and the NNI should encourage its member agencies to assist with characterization. The NNI itself does not have the facilities to carry this out.

Question Submitted by Subcommittee Ranking Member Vern Ehlers

1. *On the issue of stovepiping EHS research versus integrating it into all research, do all current NNI grants currently include and EHS component? If not, should they? Why or why not?*

Response:
The choice need not be between either incorporating an EHS component into every research grant or stovepiping risk research into a completely separate program. Environmental Defense does not believe it makes sense to compel all researchers to add EHS research questions into

their projects, as many of them may lack the relevant EHS expertise. Rather, there ought to be a mechanism to ensure that federally funded investigators pursuing basic or applications-oriented research projects, which may provide insight into EHS questions (e.g., how nanomaterials interact with biologic systems), at least share their findings with EHS researchers. They should also coordinate their studies wherever possible (e.g., by conducting testing on the same materials, utilizing the same reference materials or methods for nanomaterial characterization).

As described in our Introduction, maximizing research coordination and sharing of results among investigators conducting applications and EHS implications research is highly beneficial and should be encouraged. However, in addressing EHS implications, it is essential to conduct research that is both intended and targeted to answer specific risk-relevant questions. Scientists trained in the health or environmental sciences who work at agencies charged with the pursuit of health or environmental missions should undertake and direct this research, and they should be the judges of its adequacy, quality and interpretation. It is equally important that the specifics of the projects and amounts spent on such EHS-targeted research be transparently and clearly identified and accounted for separate from applications research, even while fully acknowledging that some applications research will yield findings relevant to understanding risk.

Questions Submitted by Congressman Daniel Lipinski

Much of the EHS research to date has focused on exotic materials with unrealistic exposure scenarios. While that is useful in establishing information on an "upper bound" of the hazard, the context is rarely communicated and it creates fear. What is critical is that we make sure nano enabled products are as safe or safer than what we use today.

Response:
We will address the question of "upper bound hazard" and "unrealistic exposure scenarios" under the related Question 4 below.

We do not agree that current EHS research on nanomaterials is focusing on exotic materials. Most studies to date have focused on a range of engineered nanomaterials that are either already in commerce in significant amounts (e.g., titanium dioxide) or are now subject to considerable research interest and poised to enter commerce in the near future (e.g., carbon nanotubes). Some less common engineered nanomaterials (e.g., quantum dots) are confined mostly to biomedical research applications, but they are also being examined for use in a broader range of applications (e.g., photovoltaic cells, LED displays).[17]

1. *As I understand it, the hazard of a nanomaterial often depends upon much more than the size and type of material, but also surface properties, purity, etc. that relate to how it is made. How is the toxicology work underway controlling for this? Are researchers using standardized, well characterized materials? If not, how can we make use of the research findings?*

Response:

There is currently substantial variation in the degree and quality of physico-chemical characterization performed on nanomaterials used in toxicology studies.[18] The questioner is correct in suggesting that the results of studies with poor characterization are of limited use. Efforts to develop a scientific consensus are underway both domestically and internationally, and the government laboratories are setting a high standard for physico-chemical characterization in their own work. The development of international voluntary standards and characterization requirements for publication in scientific journals are both underway. Lastly, NIST and its international counterparts are developing and promoting the use of standardized reference nanomaterials. All of these efforts will improve the credibility and usefulness of research results.

One obstacle to sharing characterization data is the fact that manufacturers frequently consider such information to be Confidential Business Information (CBI), which greatly impedes the ability of the government, nanomaterial users, third-party researchers, and the public to independently conduct adequate toxicity testing or interpret the results. Ultimately, fully addressing the characterization issue will require both an understanding of the types of information that are most important for nanomaterials, as well as an agreement on what information needs to be released to strike the right balance between the need to sufficiently inform and to protect legitimate CBI.

2. *It seems that most of the early uses of nanotechnology and nanomaterials are for existing products and processes, many of which are far from ideal from a health and environmental safety perspective. What is being done to systematically compare the risks and benefits of the nanoscale alternative against the conventional approach in use today so that we accelerate the substitution of nanomaterials where they are superior? (e.g. when replacing a known toxin)*

Response:
We agree that most current nanomaterial applications represent incremental modifications of existing products and processes. We are not aware of evidence or analysis, however, indicating that such modifications have typically yielded any significant health or environmental benefits over the processes and products they are intended to replace. Indeed, most of the nanomaterial-containing products introduced onto the market to date have been intended to provide other consumer benefits (e.g., stain resistance, scratch resistance, strength enhancement, etc.), not to provide direct health or environmental benefits or replace of a specific toxic chemical. (Some producers may argue that the slew of recently introduced nanosilver-containing products claiming antimicrobial activity provide health benefits, but that assertion is far from established, in our view, and could easily be offset by the harm they could cause to beneficial microbes.) Nonetheless, there is no question that considerable nanotechnology research and development is underway that is intended to deliver products and processes that offer health or environmental benefits. Nanotechnology holds significant promise in this regard.

Determining whether and to what extent risks are reduced and environmental or health benefits are realized is complex. Virtually all experts agree that a systematic comparison will require considering the full lifecycles of the materials being compared, and that much of the information needed to perform such comparisons may be unavailable or difficult to compile. In many cases

there may also be tradeoffs: reduced energy consumption of a nano-enabled product during use might be offset by increased production energy, for example.

Proponents of Green Chemistry are already mounting efforts to ensure that its principles[19] are fully understood and applied by developers of nanomaterials.[20] While it cannot be assumed that nano-enabled products and processes will be inherently safer or yield health or environmental benefits, the potential for these outcomes exists and will be more likely to be realized through conscious design decisions.

3. *The discussion around nanomaterials tends to focus on "engineered" nanomaterials which are roughly defined as those that are purposefully created. However, the volume of naturally occurring and ultrafine particles produced by combustion, as well as those used as fillers in rubber tires or plastics is many orders of magnitude greater than the newly engineered nanomaterials. What are we doing to ensure that we leverage the body of EHS knowledge on these particles? Are we missing the forest from the trees by emphasizing only "engineered nanomaterials"? What efforts are there to assess the comparative hazard posed by engineered nanomaterials against incidental or naturally occurring nanomaterials?*

Response:
Newly engineered nanomaterials have both similarities and major differences with natural or incidental combustion particles and industrial ultrafine particles that have been around for decades or longer. Several points need to be made. First, there should be no assumption that non-engineered nanoparticles to which we are exposed, or even engineered nanoparticles that have been in use for some time, are "safe." It is precisely our recognition that inhaled ultrafine combustion particles can traverse the lungs and cause damage not only to the lungs but also elsewhere in the body (including to the cardiovascular system) that prompted much of the initial concern about engineered nanomaterials. The considerable literature and methods available on ultrafine combustion particles are indeed being used extensively to inform our efforts to understand the potential risks of engineered nanomaterials.

Second, in many cases, little or no testing of even large-volume "existing" engineered nanomaterials has been required as a condition to remain on the market, and for some of these so-called "legacy" nanomaterials, very few studies have been conducted. We would welcome greater scrutiny of such materials, as well as newer engineered nanomaterials, as well as comparisons among them.

Third, while it may be viewed as inequitable to hold newly engineered nanomaterials to a higher threshold of safety than older engineered nanomaterials, it would be an even more serious mistake to fail to ascertain the potential toxicity of newly engineered nanomaterials out of a belief that exposures will never be significant compared to more familiar materials. Some nanomaterials are being considered for use or already used in applications that will widely disperse them in the environment. For example, EPA's Office of Air and Radiation is evaluating an application for use of nano cerium oxide as a fuel additive. This application is eerily reminiscent of our experience with leaded gasoline, where initial assumptions that the lead would never be released from motor vehicle tailpipes in sufficient quantities to cause meaningful

exposure or harm turned out disastrously wrong. We should not repeat this mistake with insufficiently tested nanoparticle fuel additives.

Samsung's washing machines, which claim to infuse nanosilver particles into the washwater[21] (which then go down the drain), raised objections from operators of municipal wastewater treatment facilities, who were concerned about potential environmental effects of the resulting wastewater treatment plant influents and effluents, given that silver exhibits significant ecotoxicity.[22] Other nanomaterial applications already on the market entail direct human exposure, most notably sunscreens and cosmetics; the latter are not subject to any pre-market review despite the certainty of human exposure.[23]

Fourth, the precise and highly homogeneous composition of most engineered nanomaterials, and their intended use in specific applications, could well lead to exposures of a wholly different nature and magnitude than those associated with natural or incidental nanomaterials.

4. *To what extent is the toxicity research relevant to "real world" situations? To what extent are federally funded efforts using the routes of exposure or formulations that emulate the nanomaterials being used in available products?*

Response:
This question, like the preface to Mr. Lipinski's questions, is essentially asking whether the laboratory conditions used in toxicity testing realistically simulate conditions under which actual exposures occur.

There are important scientific and policy justifications for the approaches used to characterize the potential hazards of a substance, independent of how or in what form someone might be exposed to it. First, hazard characterization is intentionally conducted independent of exposure characterization (which are typically then combined to characterize risk); the former is used to identify the *inherent* hazards of a material, while the latter step is when factors affecting the nature and extent of exposure – e.g., form of the material, likely dose, etc. – are taken into account.

Second, the goal of hazard identification is to characterize the full extent of potential adverse affects that could be associated with exposure to a substance across an entire population. The exposed population will exhibit a range of responses even to the same exposure. In order to ensure that the most susceptible or vulnerable members of society are protected, hazard identification must be able to identify upper bound effects.

Third, toxicologists' obvious need to rely on animal rather than human studies requires, for sound scientific reasons, that they employ what the lay person may think are "unrealistic" exposure scenarios. Consider the very high doses typically used in animal studies. Certain adverse health effects, such as malignant tumors, are typically relatively infrequent events. Under "realistic" exposures, an effect seen in a human population at a frequency, say, of one in ten thousand to one in a million, would nevertheless be considered to occur at a high incidence. Given that it is unrealistic and unethical to use ten thousand or a million laboratory animals in a

study, we must rely on high-dose exposures to increase the chances that we will observe these rare events, should they be associated with the chemical being tested, in a much smaller number of laboratory animals, within a reasonable time span. We can then extrapolate the observed effects to predict what would occur in humans at much lower doses or over longer periods of time.

This is the risk-based approach to public health protection that has evolved over the last 60 years. Laboratory techniques have been developed to provide useful information for predicting toxicity in the "real world." While the resulting information is not perfect, and examples of inaccuracies are available, overall the information generated using validated, standardized laboratory tests allows scientists and policymakers to make informed decisions about the relative safety of different materials. All of these challenges inherent in developing a basis for predicting the effects of real world exposures apply equally to nanomaterials. They are among the reasons we are calling for more federal investment in, and a more strategic approach to, nanomaterial risk research.

With regard to our ability to know or predict what real world exposures will be, it is important to first recognize the complexity in defining what constitutes the "real world" for a class of materials like nanomaterials, the fate and behavior of which are presently poorly understood. Many nanomaterials are likely to take multiple forms when one considers the full value chain or lifecycle, from production through end use and disposal or post-use management. At each stage, the potential for releases into the environment or exposures to workers, consumers or the public are possible. Clearly, there is no single "real world" situation.

Seeking to limit testing at this early stage to only certain routes of exposure or certain formulations rests on the questionable assumption that we know exactly how these materials are produced, used and disposed of, now and for the foreseeable future. Most of this information is not available, and is almost certain to change. Before C60 fullerenes ("buckyballs") started showing up in skin creams offered for sale, few would have ever predicted such a use or the associated routes of exposure. Under our current regulatory system, except in limited circumstances, even new nanomaterials can be produced and used in any number of ways without the producer or user having to inform the government or gain its approval. There is essentially no tracking of the production and use of nanomaterials. This is another reason why it is so important to gain an understanding of the inherent hazard of a material, which is relevant no matter how it may be used or encounter people or the environment.

It is also premature to assume we know or can predict how nanomaterials behave in the body or the environment. As just one example, consider the conventional wisdom has been that, once released to the environment, nanomaterials would always aggregate and lose their "nano-ness." This assumption is already proving to be wrong. Because aggregation reduces or interferes with functionality and performance, developers of these materials are finding ways to modify or treat nanomaterials to better maintain them in a dispersed state. And recent studies of carbon nanotubes have revealed that mixing them with natural river water actually leads to a stable suspension of individual CNTs, due to their interaction with humic acids present in the water.[24]

5. *You and Dr. Maynard call for ten percent or more of the federal government's nanotechnology research and development budget be dedicated to goal-oriented EHS research. As pointed out in Dr. Denison's testimony, only 4.1% of NNI's 2008 budget is to be spent on EHS R&D. Would you please elaborate on this and explain how you came up with this 10% figure? Would the other panelists please comment on this recommendation?*

Response:
Our call to devote at least 10% of the Federal R&D nanotechnology budget to direct EHS research for the foreseeable future is based on an assessment of the scope, magnitude and complexity of the needed research.[25] It is also informed by reference to a number of analogous or related cost benchmarks, which are briefly noted below. Our full analysis and associated documentation is included here as Attachment 1; we prepared this analysis at the request of the National Academies' Committee to Review the National Nanotechnology Initiative.

Benchmarks we used to derive the minimum 10% figure include the following:

- Government and non-government experts' assessments of the costs of conducting the needed research – including basic material characterization, development of the needed infrastructure (e.g., methods, tools, instrumentation), and assessment of risks in specific exposure settings (e.g., workplaces). Each of these tasks by itself is estimated to require at least a major fraction of the 10% EHS investment we call for.
- Actual testing costs for identifying the hazard potential of conventional chemicals, which indicate the potential for testing costs *per substance* to extend into the millions of dollars.
- The budget – averaging $60 million annually – for a roughly analogous research program to characterize the risks of airborne particulate matter (PM), which EPA undertook based on a strategy developed and overseen by the National Academies' Board on Environmental Studies and Toxicology (BEST) between 1998 and 2004. As noted by BEST, this budget covered only a portion of EPA's and the nation's research needs to understand the risks of airborne PM. This task, while complex, is considerably more restricted in scope than what is expected to be needed to assess potential risks of nanomaterials.

6. *You mentioned in your testimony that over the past two years scientists at several NNI agencies and at NNI itself have published documents describing how little we know about nanomaterials' potential hazards and exposures and how much work will be needed both to address these gaps and to adequately assess risks. Yet everyday new nanotechnologies are entering the marketplace. Would you like to comment further on this finding? Would the other panelists care to address this issue?*

Response:
My written statement addresses this issue in considerable detail, and provides examples of the agencies' recognition of the magnitude of the research and regulatory task at hand, contrasted with the rather tepid actions being taken by those same agencies. These responses illustrate the growing disconnect between what most stakeholders- –, industry included – believe government should be doing in the face of nanotechnology's rapid commercialization, and what it is actually doing. This situation is at or near the point putting at risk the public's confidence in both government and

industry's ability or willingness to responsibly address the development of this technology. That, in turn, puts public acceptance – and the success – of nanotechnology itself at risk.

Question Submitted by Full Committee Ranking Member Ralph Hall

1. *Please share your thoughts on the idea of establishing a separate program office to oversee EHS research. Why is such an office needed for nanomaterials versus other materials? What authorities would such an office need to have? What are the possible pitfalls of such an approach? How would you prevent the perception of adding another level of federal bureaucracy to the mix? As an alternative to creating a new office, how can we improve the mechanisms we currently have in place to achieve the same goals?*

Response:
The Introduction to this document addresses these questions in detail.

Endnotes

[1] My colleagues Drs. John Balbus and Caroline Baier-Anderson assisted in preparing our answers to these questions for the record.
[2] See www.nano.gov/html/about/nnco.html (NNCO); www.nano.gov/html/about/nsetmembers.html (NSET); www.ostp.gov/nstc/html/_committees.html#cot (CoT); and www.ostp.gov/PCAST/membership2.html (PCAST). Only three of the 36 members of PCAST have a health science or environmental science expertise, and none has a risk science background.
[3] See Section 2(b) of the Act, available at frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=108_cong_public_laws&docid=f:publ153.108.
[4] Statement of Mr. Floyd Kvamme, Co-Chair of the President's Council of Advisors on Science and Technology, House Science Committee hearing held on 10/31/07, page 2, available at democrats.science.house.gov/Media/File/Commdocs/hearings/2007/research/31oct/Kvamme_testimony.pdf.
[5] For example, see: U.S. Food and Drug Administration, *Nanotechnology: A Report of the U.S. Food and Drug Administration Nanotechnology Task Force*, July 25, 2007, at www.fda.gov/nanotechnology/taskforce/report2007.pdf ; and U.S. Environmental Protection Agency, *Nanotechnology White Paper*, February 2007, at www.epa.gov/osa/nanotech.htm; National Institute for Occupational Safety and Health, *Strategic Plan for NIOSH Nanotechnology Research: Filling the Knowledge Gaps*, at www.cdc.gov/niosh/topics/nanotech/strat_planINTRO.html.
[6] Transcribed from the webcast of the hearing, starting at approximately 1 hour 29 minutes, available at science.edgeboss.net/real/science/scitech07/103107.smi.
[7] See Hansen, Steffen Foss, Larsen, Britt H., Olsen, Stig I. and Baun, Anders, "Categorization framework to aid hazard identification of nanomaterials," *Nanotoxicology*, published online November 13, 2007.
[8] See www.nano.gov/html/society/NEHI.htm.
[9] See testimony of non-government witnesses at the Committee's hearings held on November 17, 2005 (science.house.gov/publications/hearings_markups_details.aspx?NewsID=979); September 21, 2006 (science.house.gov/publications/hearings_markups_details.aspx?NewsID=1186); and October 31, 2007 (science.house.gov/publications/hearings_markups_details.aspx?NewsID=2021).
[10] See "NRC – Regulator of Nuclear Safety" (www.nrc.gov/reading-rm/doc-collections/nuregs/brochures/br0164/r4/) and "Our History" (www.nrc.gov/about-nrc/history.html) on the NRC's website.

[11] See "Regulatory Research" (www.nrc.gov/about-nrc/history.html) on the NRC's website.
[12] See webpage for the Office at www.nrc.gov/about-nrc/organization/resfuncdesc.html.
[13] See NRC memoranda titled "Organizational Conflict of Interest Regarding Department of Energy Laboratories" dated January 6, 1998 (www.nrc.gov/reading-rm/doc-collections/commission/secys/1998/secy1998-003/1998-003scy.html) and February 5, 1999 (www.nrc.gov/reading-rm/doc-collections/commission/secys/1999/secy1999-043/1999-043scy.html).
[14] See NRC memorandum titled "Memorandum Report: Audit of NRC Oversight of Its Federally Funded Research and Development Center," May 28, 2002 (www.nrc.gov/reading-rm/doc-collections/insp-gen/2002/02a-011.pdf).
[15] See www.ostp.gov/PCAST/membership2.html.
[16] This situation with the NTAG is in partial contrast to PCAST itself, whose members and meeting agendas are posted at ostp.gov/pcast/pcast.html.
[17] See, for example, Evident Technologies, the self-described "leader in quantum dot product development" (www.evidenttech.com/applications.html).
[18] One review just published in *Nanotoxicology* of nearly 430 nanoparticle toxicology papers found that, while the vast majority showed evidence of adverse effects, there was also a serious lack of characterization of the tested materials. See Hansen *et al.*, 2007, *op. cit.*
[19] See "12 Principles of Green Chemistry," www.epa.gov/greenchemistry/pubs/principles.html, originally developed by Paul Anastas and John Warner, *Green Chemistry: Theory and Practice* (Oxford University Press: New York, 1998).
[20] See, e.g., Paul Anastas and Julie Zimmerman (2007). "Green Nanotechnology: Why We Need a Green Nano Award & How to Make it Happen." Washington, DC: Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, at www.nanotechproject.org/file_download/206; and other information at www.nanotechproject.org/tags?tag=green.
[21] See ww2.samsung.co.za/silvernano/silvernano/washingmachine.html. .
[22] See letter dated January 26, 2006 to Jim Jones, Director, EPA Office of Pesticide Programs, from Chuck Weir, Chair, Tri-TAC (a technical advisory group for Publicly Owned Treatment Works (POTWs) jointly sponsored by the California Association of Sanitation Agencies, the California Water Environment Association, and the League of California Cities), at www.tritac.org/documents/letters/2006_01_27_EPA_Samsung_Silver_Wash.pdf.
[23] Sunscreens qualify as over-the-counter (OTC) drugs, and as such are required by FDA to meet more extensive requirements than are cosmetics, though considerably fewer than for prescription drugs. With respect to pre-market approval, if a new active ingredient is used in a sunscreen, some testing is required for both efficacy and dermal effects before such a product can be marketed. Use of an already reviewed active ingredient does not require such approval. One point of remaining ambiguity, however, is the extent to which FDA will consider nano versions of active ingredients they have already reviewed in their larger forms to be new active ingredients. See U.S. Food and Drug Administration, 2007, *op. cit.*
[24] Hyung H, Fortner JD, Hughes JB, Kim J. 2007. Natural organic matter stabilizes carbon nanotubes in the aqueous phase. *Environ. Sci. Technol.* 41(1): 179-184.
[25] In addition to the information and sources provided in Attachment 1, more recent reports by Federal agencies have elaborated further on the broad scope of research needed. See reference in Endnote 5.

Attachment 1

e

ENVIRONMENTAL DEFENSE

finding the ways that work

A proposal to increase federal funding of nanotechnology risk research to at least $100 million annually

Richard A. Denison, PhD, Senior Scientist[1]
Environmental Defense
April 2005

Environmental Defense has called for the federal government to dedicate at least $100 million annually, sustained for a period of at least several years, to research directly related to elucidating the health and environmental risks of nanotechnology.[2] This document summarizes our reasoning and support for calling for such an outlay.

There is, of course, no single "magic number" nor a precise means to determine the right dollar figure, given the wide-ranging set of research issues needing to be addressed and the significant associated uncertainty as to the anticipated results. Nevertheless, we believe that the amount we propose represents a reasonable, lower-bound estimate of what is needed.

Below we first provide some context appropriate to consider in assessing both the need for and costs of risk-related research on nanomaterials. We then describe the major complexities involved in assessing these risks and the broad scope of research needed to address them. Finally, we provide a number of benchmarks that we believe strongly support our proposal for spending at least $100 million annually nanotechnology risk research. These benchmarks include: experts' assessments of the expected research costs; hazard testing costs for conventional chemicals; and EPA budgets for airborne particulate matter risk research.

Context for judging risk research spending

In our view, both the public and private sectors' best interests are served by an investment to identify and manage potential nanotechnology risks now, rather than to pay later to remediate resulting harms. History demonstrates that embracing a technology without a careful assessment and control of its risks can be extremely costly from both human and financial perspectives. The failure to sufficiently consider the adverse effects of using lead

in paint, plumbing, and gasoline has resulted in widespread health problems that continue to this day, not to mention extremely high remediation costs. Asbestos is another example where enormous sums of money were spent by private companies for remediation, litigation, and compensation, even beyond that spent by the public sector to alleviate harm to human health and the environment. Standard & Poor's has estimated that the total cost of liability for asbestos-related losses could reach $200 billion.[3]

Initial research raises serious concerns that nanomaterials have the potential to pose significant health and environmental risks. The limited data now available demonstrate the potential for some nanomaterials to be both persistent and mobile in the environment and in living organisms; to cross the blood-brain barrier; and to be capable of damaging brain, lung and skin tissue.[4]

These initial studies only highlight how little is known about the health and environmental effects of engineered nanomaterials. Despite the uncertainty, the rapid development of nanomaterial applications is outpacing efforts to understand their implications – let alone ensure their safety. Thousands of tons of nanomaterials are already being produced each year,[5] and hundreds of products incorporating nanomaterials are already on the market.[6] The global market for nanotechnology products is expected to reach at least $1 trillion over the next decade.[7] Given the length of time it will take to develop an adequate understanding of the potential risks posed by a wide variety of nanomaterials, and to apply this knowledge to inform appropriate regulation, it is imperative that we dedicate substantial funding for comprehensive risk research programs now.

The National Nanotechnology Coordination Office (NNCO) estimates that fiscal year 2004 spending for environmental and health implications research stood at only $8.5 million, less than one percent of the total NNI budget.[8] Since then, such spending appears to be rising somewhat: Requested funding for FY2006 from federal agencies under the NNI for health and environmental research totals $38.5 million, just under 4% of the total FY2006 nanotechnology development budget for these agencies of $1.05 billion.[9] While an annual expenditure of $100 million represents an additional significant increase over the current level, it is still a small fraction of the more than $1 billion now being directed annually towards nanotechnology development through the National Nanotechnology Initiative (NNI). Moreover, it is a modest investment compared to the potential benefits of risk avoidance and to the $1 trillion or more that nanotechnology is projected to provide to the world economy by 2015.[10]

Complexity of defining nanomaterial risks

There is broad agreement among stakeholders that addressing the potential risks of nanotechnology will be an unusually complex task. Despite its name, nanotechnology is anything but *singular*; it is a potentially limitless collection of technologies and associated materials. The sheer diversity of potential materials and applications – which is a source

of nanotechnology's enormous promise – also poses major challenges with respect to characterizing potential risks. Nanotechnology entails:

- many fundamentally different types of materials (e.g., metal oxides, quantum dots, carbon nanotubes), and hundreds or thousands of potential variants of each;
- many novel properties potentially relevant to risk (e.g., size, structure, reactivity, surface chemistry, electrical and magnetic properties)
- many potential types of applications (e.g., fixed in a matrix vs. freely available, captive vs. dispersive use);
- many categories and types of uses (e.g., medical devices, pharmaceuticals, environmental remediation, and consumer products ranging from cosmetics to electronics);
- multiple points of potential release and exposure over the full lifecycle of a given material/application (e.g., during production, use, disposal);
- multiple potential means of release (e.g., in emissions, in wastes, from products);
- multiple potential routes of exposure (e.g., inhalation, dermal, oral);
- multiple potentially exposed populations (e.g., workers, consumers as well as public); and
- potential to cause environmental as well as human health-related impacts.

Scope of needed research

Even before the research that will allow hazards and exposures to be quantified, a number of more fundamental needs must be addressed. We currently lack a good understanding of which specific properties will determine or are otherwise relevant to nanomaterials' risk potential. Many of the methods, protocols and tools needed to *characterize* nanomaterials, or to *detect and measure* their presence in a variety of settings (e.g., workplace environment, human body, environmental media) are still in a very early stage of development.

Nor is it clear the extent to which we can rely on our existing knowledge about conventional chemicals to predict risks of nanomaterials. The defining character of nanotechnology – the emergence of wholly *novel* properties when materials are reduced to or assembled at the nano-scale – carries with it the potential for novel risks and even novel mechanisms of toxicity that cannot be predicted from the properties and behavior of their bulk counterparts. By their very nature many nanomaterials are more reactive per unit mass than their conventional counterparts. For example, aluminum in the form used in many applications, such as the ubiquitous soda can, is prized because of its lack of reactivity, but it becomes highly explosive in nano-form – hence its potential use as a rocket fuel catalyst.

Moreover, we already know that even extremely subtle manipulations of a nanomaterial can dramatically alter its properties and behavior: Tiny differences in the diameters of otherwise identical quantum dots can alter the wavelength of the light they fluoresce; slight changes in the degree of twist in a carbon nanotube can affect its electrical

transmission properties. We have yet to develop the means to sufficiently characterize or systematically describe such subtle structural changes – a clear prerequisite to being able to consistently and rigorously apply and interpret the results of toxicological testing. And only then can we begin to assess the extent to which such subtle structural changes may affect the toxicity of a material – or the extent to which such a property is stable or may be transformed in the environment or the human body.

Until these threshold questions about nanomaterials' potential risks are answered, it is unclear whether or to what extent we will be able to rely on methods widely used to reduce the amount of traditional toxicological testing needed to characterize conventional chemicals: the ability to identify "model" materials, which upon characterization could serve as a basis for extrapolation to "like" materials.

Among the types of risk research needed are the following:

- Material characterization (in manufactured form(s), during use, in emissions, in wastes, in products; in environmental media, in organisms)
- Biological fate (extent and rate of absorption, distribution, metabolism, elimination)
- Environmental fate and transport (persistence, distribution among media, transformation)
- Acute and chronic toxicity (related to both human and ecological health)

For each of these areas, existing testing and assessment methods and protocols need to be re-examined to determine the extent to which they can be modified to account for nanomaterials' novel characteristics or need to be supplemented with new methods. Similar challenges will arise with respect to methods and technologies for sampling, analysis and monitoring, all of which will be needed to detect nanomaterials and their transformation products in living systems and in various environmental media.

Benchmarks for risk research spending

Our view that significantly more needs to be spent on nanotechnology risk research is informed and supported by: a) other experts' assessments, b) our knowledge of testing costs associated with hazard characterization programs for conventional chemicals, and c) the research budgets recommended for and expended on a roughly analogous risk characterization effort, namely EPA's research on risks of airborne particulate matter. A summary of these various information sources is provided below.

<u>Experts' assessments:</u>

- Experts from a variety of fields have declared that NNI's current funding for nanotechnology risk research needs to be significantly increased. Invited experts to a workshop sponsored by the Nanoscale Science Engineering, Science and Technology Subcommittee (NSET) of the NNI, held in September 2004, called for at least a 10-

fold increase in federal spending on nanotechnology risk-related research, relative to the approximately $10 million spent in FY2004.[11]

- At that same workshop, a representative of the Nanotechnology Initiative at the National Institute for Occupational Safety and Health (NIOSH) provided an estimate of the investment needed just to begin to address workplace safety issues – which accounts for only one of the numerous settings where release and exposure to nanomaterials may occur. That estimate, which is based on an internal analysis conducted by NIOSH researchers, is that an investment of $10-20 million per year for at least 10 years will be needed – assuming the funds are able to be directed at targeted research to address specific predetermined issues. The representative further indicated that the investment necessary to identify the issues to target and to more broadly address nanotechnology implications in the workplace as the technology matures will be significantly larger.[12] (NIOSH's current funding level for this research is considerably lower, $2-3 million per year. In 2004, NIOSH initiated a five-year program to assess the toxicity of ultrafine and nanoparticles, funded at about $1.7 million in FY2004 and about $2.3 million in FY2005.[13] According to NNI, NIOSH has requested $3.1 million for FY2006 for this type of work.[14])

- At a briefing held on March 22, 2005, to preview the findings of an upcoming report by the President's Council of Advisors on Science and Technology (PCAST) that has been charged with reviewing the NNI, John H. Marburger III, Science Adviser to the President and chief of the White House Office of Science and Technology Policy, noted that the toxicity studies now underway are "a drop in the bucket compared to what needs to be done."[15]

- The chemical industry has also concluded that nanotechnology risk research should be highly prioritized and highly funded relative to other activities by the NNI. In a nanotechnology development roadmap requested by the NNI, the industry identifies an essential need to increase our "understanding of the fundamental scientific principles operating at the nanoscale, including interdependent structure-property relationships." The roadmap highlights as critical research needs the following:
    - development of characterization tools, including real-time characterization methods and tools and the associated infrastructure for their development and use; and
    - environment, health and safety, including assessment of human health and environmental impact hazards, determination of exposure potentials for nano-sized materials, and handling guidelines for operations involving nanomaterials.

  The report calls for sustained research in these areas over twenty years, and assigns its top or high priority ranking to each of the subtopics under these key elements. While actual dollar figures are not provided, the report indicates that two of these subtopics – development of real-time characterization methods and tools, and assessment of human health and environmental impact hazards – will require a level of cumulative

R&D investment that is the highest of any assigned to the priority research requirements.

- Finally, other expert comments on nanotechnology risk research needs and costs indicate that even setting up the initial infrastructure for adequate risk research will involve significant resources. The United Kingdom's Royal Society and Royal Academy of Engineering, in its seminal July 2004 report, *Nanoscience and nanotechnologies: Opportunities and uncertainties*, calls for the UK government to devote £5-6 million ($9.5-11.3 million) per annum for 10 years just to do its part to develop the methodologies and instrumentation needed to set the stage for actual testing of nanomaterials.[16]

Hazard endpoint testing costs:

There are several estimates available from chemical hazard assessment programs that can be used as context for providing at least a lower bound on the costs of testing a nanomaterial for hazardous properties. These costs are for the testing of a conventional chemical for an assortment of hazard (toxicity plus environmental fate) endpoints of concern; notably, they do *not* include costs associated with assessing exposure, which is also needed to assess risk.

It must be noted that these estimates provide only a very rough means of extrapolating to the anticipated costs of hazard testing for a given nanomaterial. A definition of what constitutes the needed set of such endpoints sufficient to characterize hazard has yet to be defined. Moreover, the number of different nanomaterials requiring testing is another major unknown, but could be very large.

Below we discuss several available hazard testing cost estimates.

- At one end of the spectrum is the so-called Screening Information Data Set (SIDS), developed by the Chemicals Program of the Organization for Economic Cooperation and Development (OECD), which consists of about 20 data elements and – as its name indicates – represents the minimum hazard information considered necessary to screen chemicals in order to set priorities for further scrutiny. SIDS focuses primarily on short-term toxicity to mammals (as models for human toxicity) and aquatic species (as a subset of indicators of potential ecological toxicity). The U.S. Environmental Protection Agency, which employs the SIDS in its High Production Volume (HPV) Challenge,[17] estimates the cost of producing a full set of SIDS data at $250,000 per chemical,[18] which is generally consistent with an industry estimate of up to $275,000 per chemical.[19] While SIDS is useful in setting priorities for further action among conventional chemicals, the information it provides is too limited to be sufficient to characterize the risks posed by nanomaterials.

- Testing cost estimates have been prepared in a Business Impact Assessment document prepared for the European Commission's Enterprise Directorate in

support of the European Union's chemical policy proposal called REACH (for Registration, Evaluation and Authorization of Chemicals). REACH proposes different levels of testing that depend primarily on the production tonnage of a chemical. At the lowest production volumes, a base set of test data – roughly equivalent to the SIDS discussed above – would be required, the generation of which is estimated to cost •151,700 (about $198,000). The most extensive test battery applicable to the highest-volume substances – and considered generally sufficient to inform a full risk assessment – is estimated to cost •1,664,260 (about $2,170,000).[20]

- An even more extensive test battery (and perhaps a more appropriate one for characterization of many nanomaterials, at least initially) is that required of pesticides under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). This hazard-only test battery consists of up to 100 individual data elements,[21] with the actual requirements varying by factors such as use and volume of use. When supplemented with detailed exposure information, EPA generally considers this dataset sufficient to conduct a risk assessment for a pesticide. An upper estimate of $10 million per chemical for testing costs has been indicated by the Agricultural Research Service for a pesticide proposed for major food crop use, with costs for most pesticides being "significantly less."[22]

Recommended and actual EPA research budgets for risks of airborne particulate matter:

As an additional benchmark for judging the appropriate level of federal expenditure for nanomaterial risk research, we considered the recommended and actual budgets for EPA research conducted over the past several years on risks posed by airborne particulate matter (PM). In 1998, at the request of EPA, a committee of the Board on Environmental Studies and Toxicology (BEST) of the National Research Council assessed the state of research in this arena and additional needs, setting out a 13-year research agenda and associated recommended budget.[23] In 2004, in the fourth report in its series, the committee looked back over the research actually conducted and the associated budget expended by EPA in the six years since its first report.[24]

We recognize, of course, the substantial differences between the nature of, state of knowledge concerning, and risk-related research needs for, airborne particulate matter (PM) and nanomaterials. Even in 1998, it was already clear that airborne PM exacts an enormous toll in terms of human morbidity and mortality – clearly not the case with nanomaterials, although we believe there is an opportunity through proactive research and action to identify and avoid such risks. Our aim here is not at all to claim any direct analogy between the two classes of materials or the magnitude of their risks, but rather to utilize the careful assessment done of the scope of research needed to assess risk.

If anything, the scope of needed research on nanomaterials is considerably broader – and hence likely to cost more – than is the case for airborne PM. Our reasoning is as follows. Airborne PM is a complex mixture of relatively well-characterized chemicals produced by

a discrete (though highly diffuse) set of sources, to which exposure occurs through a single route, inhalation. In contrast, nanomaterials:

- are comprised of many entirely novel classes of materials;
- will be applied and used in ways that will create the potential for release and exposure through many more pathways (e.g., oral, dermal; via drinking water);
- in addition to being present in air emissions, may be present in wastes, water discharges and a wide array of products;
- through incorporation into products, may result in exposure of consumers, as well as the general public and workers; and
- pose potential environmental as well as human health risks that need to be considered.

Hence – independent of the ultimate magnitude of risk identified – the *assessment* of that risk is likely to be considerably more involved and costly for nanomaterials than for airborne PM.

The research agenda and budget for airborne PM recommended by NRC in 1998 called for EPA to spend $40-60 million annually for the first six years, and declining amounts thereafter, from $31 million in year 7 to 15 million in year 13. The NRC noted explicitly that its recommended budgets should *not* be interpreted as sufficient to encompass all of the airborne PM risk research needed to be conducted by EPA or the nation as a whole.[25]

Actual EPA expenditures during the first six years of the research program (FY1998-2003) were relatively similar to the recommended amounts, as reported by NRC in its 2004 report:

TABLE S-1 EPA Funding for PM Research and Related Technical Work (in millions of dollars)[26]

	Fiscal Year Budgets					
	1998	1999	2000	2001	2002	2003
PM research	42.0	47.3	53.7	59.0	61.1	58.1
Related technical work	8.2	8.3	8.7	6.3	6.6	8.8
TOTAL	50.2	55.6	62.4	65.3	67.7	66.9

The NRC's 2004 report, which represents a "mid-course" review of EPA's airborne PM research, found that the allocated money had been well spent, noting rapid progress in some areas, slower in others, and with much work remaining to be done.

Given that addressing the potential risks of nanomaterials will very likely entail considerably greater complexity than is the case for airborne PM, we believe the NRC's assessment of research needs and associated budget needs for airborne PM risk-related research strongly supports our call for the federal government to be devoting at least $100 million annually over a number of years to address the major unknowns and uncertainties associated with the burgeoning field of nanotechnology.

Conclusion

The rapid commercialization of nanotechnology, coupled with the clear risk potential of at least certain nanomaterials demonstrated in initial studies, lends urgency to the need for the federal government to direct more of its major investment in nanotechnology development toward research aimed at identifying the potential risks and the means to address them. There is a remarkable degree of agreement among experts and stakeholders from a range of perspectives on both the need and the urgency. There is also considerable agreement that assessing these risks will be a complex task, given the range of materials and potential applications involved and the current lack of knowledge and experience with such materials. A broad scope of research will be needed, first to identify the key characteristics of nanomaterials relating to hazard and exposure; second, to adapt existing or develop new testing methods; and third, to actually assess the magnitude of hazard and exposure potential of specific nanomaterials.

We have also provided a number of benchmarks, which taken together strongly support our call for the federal government to spend at least $100 million annually on a sustained basis to fund research directly related to understanding the potential health and environmental risks of nanotechnology:

- Experts' assessments of the costs of conducting the needed research – including basic material characterization, development of the needed infrastructure (e.g., methods, tools, instrumentation) and assessment of risks in specific exposure settings (e.g., workplaces). Each of these tasks by itself is estimated to require at least a major fraction of the $100 million investment we call for.
- Actual testing costs for identifying hazard potential for conventional chemicals, which indicate the potential for testing costs *per substance* to extend into the millions of dollars.
- The recommended and actual EPA research budgets for characterizing the risks of airborne particulate matter, which have totaled at least half of the amount we have proposed be devoted to risk research on nanomaterials. As made clear by the National Research Council in recommending these amounts, they cover only a portion of EPA's and the nation's needs for research to understand the risks of airborne PM. While this task is complex, it is considerably more restricted in scope than what is expected to be needed to assess potential risks of nanomaterials.

Federal initiatives on nanotechnology to date have done a great job in accentuating and accelerating the enormous potential benefits of nanomaterials. To date, however, federal agencies have yet to come to terms with their equally critical role in identifying, managing and ideally avoiding the potential downsides. A far better balance between these two roles must be struck if nanotechnology is to deliver on its promise without delivering unintended and unforeseen adverse consequences.

###

Endnotes

[1] Environmental Defense staff members Dr. John Balbus, Scott Walsh and Karen Florini reviewed and provided substantial input into this paper.

[2] See Environmental Defense's written statement submitted to the National Academies' Committee to Review the National Nanotechnology Initiative at its March 24-25, 2005 Workshop on Standards for Responsible Development of Nanotechnology, Washington DC; and letter dated November 15, 2004 from Environmental Defense to Dr. Mihail Roco, Chair, NSTC Subcommittee on Nanoscale Science, Engineering and Technology (also attached to our written statement).

[3] Standard & Poor's, *Insurance: Property-Casualty Industry Survey*, July 15, 2004.

[4] To assist the Committee, we attached a bibliography of references and associated abstracts of risk-related research studies on nanomaterials to our written statement provided to the Committee's at its March 24-25, 2005 workshop reviewing the National Nanotechnology Initiative.

[5] See The Royal Society and the Royal Academy of Engineering, *Nanoscience and nanotechnologies: Opportunities and uncertainties*, London, July 2004, pp. 26-7, available online at www.nanotec.org.uk/finalReport.htm. This estimate is provided for the 2003-2004 timeframe, with rapidly escalating quantities projected thereafter.

[6] See, for example, an unofficial list of nanomaterial-containing products compiled by EPA as of July 2004, posted by the ETC Group online at www.etcgroup.org/documents/nanoproducts_EPA.pdf; and a description of current nanotechnology applications at www.nanotech-now.com/current-uses.htm.

[7] See, for example, Lux Research, *Sizing Nanotechnology's Value Chain*, October 2004, summary available online at www.luxresearchinc.com/press/RELEASE_SizingReport.pdf: "Sales of products incorporating emerging nanotechnology will rise from less than 0.1% of global manufacturing output today to 15% in 2014, totaling $2.6 trillion." Also see National Science Foundation, *Societal Implications of Nanoscience and Nanotechnology*, March 2001, p. 3, available online at www.wtec.org/loyola/nano/NSET.Societal.Implications/nanosi.pdf: "... projected total worldwide market size of over $1 trillion annually in 10 to 15 years..."

[8] E. Clayton Teague, *Responsible Development of Nanotechnology*, National Nanotechnology Coordination Office, April 2, 2004, available online at www.technology.gov/OTPolicy/Nano/04/0402_Teague-Infocast.pdf.

[9] National Science and Technology Council, Nanoscale Science, Engineering and Technology Subcommittee of the Committee on Technology, *The National Nanotechnology Initiative: Research and Development Leading to a Revolution in Technology and Industry: Supplement to the President's FY2006 Budget*, March 2005, p. 38.

[10] See endnote 7.

[11] Phibbs, P., *Daily Environment Report*, 9/13/04, p. A-3, "Federal Government Urged to Boost Spending on Managing Risks Posed by Nanotechnology," quoting experts invited to NSET's Research Directions II workshop held in Washington, DC on 9/8-9/04.

[12] Phibbs, P., *ibid*., quoting NIOSH scientist Andrew Maynard's statement at NSET's Research Directions II workshop held in Washington, DC on 9/8-9/04; and A. Maynard, personal communication, 4-20-05.

[13] See National Nanotechnology Initiative, "NNI Environment and Health Safety Research," available online at www.nano.gov/html/facts/EHS.htm.

[14] National Science and Technology Council, *op. cit.*.

[15] R. Weiss, "Nanotech Is Booming Biggest in U.S., Report Says," *Washington Post*, March 28, 2005, p. A6, available online at www.washingtonpost.com/wp-dyn/articles/A5221-2005Mar27.html.

[16] The Royal Society and the Royal Academy of Engineering, *op. cit.*, p. 48.

[17] See EPA's website for the U.S. HPV Challenge, www.epa.gov/chemrtk/volchall.htm.

[18] See www.epa.gov/chemrtk/hpvq&a.pdf.

[19] See the American Chemistry Council's summary of the U.S. HPV Challenge, online at memberexchange.americanchemistry.com/randt.nsf/unid/nnar-4dfn3h.

[20] Risk & Policy Analysts Ltd, Revised Business Impact Assessment for the Consultation Document, Working Paper 4, prepared for the European Commission Enterprise Directorate-General, October 2003,

Annex 1, available online at www.rpaltd.co.uk/tools/downloads/reports/reachrevisedbia.pdf. Figures cited here assume that all listed tests are required to be conducted, that none of the tests have previously been conducted, and that no estimation techniques are allowed as a substitute for testing.

[21] Requirements are summarized at www.epa.gov/pesticides/regulating/data.htm. Regulations specifying testing requirements are at 40 CFR Part 158.

[22] See "EPA and Pesticide Registration Issues," USDA Agricultural Research Service, available online at www.ars.usda.gov/is/np/mba/jan97/epa.htm.

[23] Board on Environmental Studies and Toxicology, *Research Priorities for Airborne Particulate Matter: I. Immediate Priorities and a Long-Range Research Portfolio*, Committee on Research Priorities for Airborne Particulate Matter, National Research Council, 1998, available online at books.nap.edu/catalog/6131.html.

[24] Board on Environmental Studies and Toxicology, *Research Priorities for Airborne Particulate Matter: IV. Continuing Research Progress*, Committee on Research Priorities for Airborne Particulate Matter, National Research Council, 2004, available online at books.nap.edu/catalog/10957.html.

[25] Board on Environmental Studies and Toxicology, 1998, *op. cit.*, Table 5.1, page 101. Amounts include research management, including research planning, budgeting, oversight, review, and dissemination, cumulatively estimated by the committee at 10% of project costs.

[26] Board on Environmental Studies and Toxicology, 2004, *op. cit.*, Table S-1, page 6.