Status and Future of Research on Environmental, Health, and Safety Issues of Nanotechnology

Testimony before the
U.S. Senate Committee on Commerce, Science, and Transportation
Subcommittee on Science, Technology and Innovation
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Oral Testimony

Good afternoon. I wish to thank Senator Kerry and the other members of the Subcommittee for inviting me to testify today. I am Lee Ferguson, an assistant professor at the University of South Carolina. Since 2003, I have led a team of researchers investigating the fate and effects of nanomaterials in the environment. I feel strongly about the need to continue and expand this research, and I'm happy to talk with you about it.

Primary point: Development and commercialization of nanotechnology may present unforeseen hazards to environmental and human health – it is essential that scientific research be continued to address this issue.

Since the initial authorization of the National Nanotechnology Initiative in 2003, the Federal Government has supported scientific research into the environmental and health impacts of nanotechnology[1]. There exists now a growing body of work addressing the risks associated with nanomaterials; however, it is clear that we still have much to learn.

What we know: The current state of the science with respect to environmental, health, and safety issues of nanotechnology can be summarized briefly.

[1] For example, since 2003 the U.S. EPA National Center for Environmental Research has coordinated extramural funding efforts among EPA, NSF, DOE, NIOSH, and NIEHS to address environmental and health effects of nanomaterials (http://es.epa.gov/ncer/nano/index.html).

- We have learned that nanomaterials are very difficult to measure accurately in environmental and biological systems. It has become clear that existing analytical methods are simply inappropriate or insufficient to make these measurements.
- We also have learned that nanomaterials may be transported in the environment in ways that are not necessarily predictable from existing scientific models and that nanomaterials may interact directly with pollutants-of-concern such as PCBs and heavy metals.
- Finally, there are indications of risks associated with exposure of humans and ecosystems to nanomaterials. These risks include direct toxicity and uptake of nanomaterials into biological tissues.

Federal prioritization: Through the NNI, the Federal Government has developed a roadmap aimed at prioritizing research needs with respect to environmental, health, and safety issues of nanotechnology[2]. This prioritization is essential so that an organized effort can be made to address environmental and health impacts of nanotechnology *as this technology is developed*. This last point is critical – we cannot afford to wait until nanotechnology is fully developed to begin assessing its risks and hazards to human health and the environment.

Future research needs: I wish to highlight specific areas of research that I believe deserve particular attention:

- Without methods for detecting and characterizing nanomaterials in the environment and in human tissues, nanomaterial exposure assessment is impossible. Research into analytical methods and metrology of nanomaterials is a top priority and support for this work should be accelerated within the NNI.
- With respect to research on environmental and human health effects of nanomaterials, I stress the need to develop standardized testing methods that are appropriate to assessing toxicity and biological uptake of nanomaterials and their manufacturing byproducts.
- There is a critical need to assess routes of human and ecological exposure after release of nanomaterials into the ambient environment. We still have very limited knowledge of the treatability of nanotechnology wastes as well as the routes by which nanomaterials may enter and move within our air and water.
- Finally, our ability to assess and predict risk of emerging nanotechnologies to human and environmental health depends on understanding the mechanisms by which nanomaterials act

[2] The five primary research categories identified for priority research consideration are (1) Instrumentation, Metrology, and Analytical Methods; (2) Nanomaterials and Human Health; (3) Nanomaterials and the Environment; (4) Human and Environmental Exposure Assessment; and (5) Risk Management Methods. These categories and the associated research strategies are outlined in three documents: National Science and Technology Council 2006, *The National Nanotechnology Initiative: Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials*, http://www.nano.gov/NNI_EHS_research_needs.pdf; National Science and Technology Council 2007, *Prioritization of Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials*, http://www.nano.gov/Prioritization_EHS_Research_Needs_Engineered_Nanoscale_Materials.pdf; and National Science and Technology Council 2008, *The National Nanotechnology Initiative: Strategy for Nanotechnology-Related Environmental, Health, and Safety Research*, http://www.nano.gov/NNI_EHS_Research_Strategy.pdf.

on biological systems. This understanding represents a grand scientific challenge and will require significant and well-supported effort.

During reauthorization of the NNI, I ask you to consider the resources that are needed now and in the future for addressing these concerns. Between 2005 and 2009, expenditures within the NNI on EHS research have increased from 3% to approximately 5% of the total NNI budget. A significant increase in our scientific understanding of the environmental and health impacts of nanotechnology will require a more substantial investment. A realistic target in the very near term should be to increase the level of funding for EHS research on nanotechnology to exceed 10% of the NNI budget.

I wish to close by saying that we have a unique opportunity now – through the NNI we have begun to address the EHS risks of nanotechnology ***simultaneously*** with the development of this technology. We have only to look at the lessons learned from PCBs and other legacy chemical contaminants to realize the dangers of waiting until new technologies are mature to assess their environmental and health risks. I urge this Committee to consider these concerns during the reauthorization of the NNI. Thank you for considering my testimony.

Written Testimony

I wish to thank Senator Kerry and the other members of the Subcommittee for inviting me to testify about the current status and future needs of research into the environmental, health, and safety issues of nanotechnology. I am Lee Ferguson, an assistant professor of chemistry and biochemistry at the University of South Carolina. Since 2003, I have led a team of researchers at USC, funded by the U.S. EPA Science to Achieve Results (STAR) program[3] and organized within the USC NanoCenter investigating the fate and health effects of nanomaterials in the environment. Our overall goal is to elucidate the potential for manufactured nanomaterials to be transported within the aquatic environment and the associated hazards of such transport to both aquatic and human life. I feel strongly about the need to continue and expand this research, and I'm happy to talk with you about it.

Primary point: Development and commercialization of nanotechnology may present unforeseen hazards to environmental and human health – it is therefore essential that scientific research be conducted to address this issue.

Since the initial authorization of the National Nanotechnology Initiative in 2003, the Federal Government has continuously supported intramural and extramural scientific research into the environmental and health impacts of nanotechnology[4]. As a consequence, there exists now a

[3] U.S. EPA STAR Program: Chemical and biological behavior of carbon nanotubes in estuarine sedimentary systems. Award # RD-83171601 P. Lee Ferguson, PI.; G. Thomas Chandler; and Walter A. Scrivens, University of South Carolina, Columbia, SC

[4] For example, since 2003 the U.S. EPA National Center for Environmental Research has coordinated extramural funding efforts among EPA, NSF, DOE, NIOSH, and NIEHS to address environmental and health effects of nanomaterials (http://es.epa.gov/ncer/nano/index.html).

growing body of work addressing the risks associated with nanomaterials; however, it is clear that we still have much to learn.

What we know: The emergence of nanotechnology is an exciting opportunity that could result in significant contributions to the treatment of disease, development of more effective polymer composites, fuel cells and capacitors, and clean-up of polluted groundwater. Although the use of nanoparticles may allow for significant advances in science and technology, assessment of potential negative health and environmental impacts on humans, non-human biota, and ecosystems is imperative before their widespread production and use. The same properties that make these particles desirable, may also contribute to their toxic potential and extensive studies to address both the acute and chronic effects of nanoparticles are necessary to determine if negative health and environmental impacts outweigh the potential benefits. In humans, a concerning route of exposure is via direct inhalation, both in the workplace where these particles are manufactured and used, and from the innate environment contaminated with particles released from anthropogenic and natural sources[5,6]. Other routes of exposure that are currently a concern include dermal and dietary**.** The current state of the science with respect to environmental, health, and safety issues of nanotechnology can be summarized briefly.

- We have learned that nanomaterials are very difficult to measure accurately in environmental and biological systems – this greatly complicates assessment of occupational and environmental exposure as well as occurrence and fate of these materials in the environment. It has become clear that existing analytical methods (e.g. those designed for detecting and quantifying chemical contaminants) are simply inappropriate or insufficient to make these measurements[7].
- We also have learned that nanomaterials may be transported in the environment in ways that are not necessarily predictable from existing models for more conventional contaminants, and that nanomaterials may interact directly with pollutants-of-concern such as PCBs and heavy metals, potentially leading to mobilization and enhanced toxicity[8].
- Finally, there are clear indications of risks associated with exposure of humans and ecosystems to nanomaterials. These risks include direct toxicity and uptake of nanomaterials into biological tissues[9,10]. However, the mechanisms by which nanomaterials exert biological effects are poorly known and there is a clear need for basic research directed at new methods for assessing "nanotoxicology".

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[5] Maynard AD, Baron PA, Foley M, Shvedova AA, Kisin ER, Castranova V. Exposure to carbon nanotube material: aerosol release during the handling of unrefined single-walled carbon nanotube material. *J Toxicol Environ Health A* 2004; 67: 87-107.
[6] Nel A, Xia T, Madler L, Li N. Toxic potential of materials at the nanolevel. *Science* 2006; 311: 622-627.
[7] U.S. Environmental Protection Agency. 2007. Nanotechnology White Paper. Washington, D.C. EPA/100/B-07/001. p. 40-41.
[8] Ferguson PL, Chandler GT, Templeton RC, DeMarco A, Scrivens, WA, Englehart, B. Influence of sediment-amendment with single-walled carbon nanotubes and diesel soot on bioaccumulation of hydrophobic organic contaminants by benthic invertebrates. *Environ. Sci. Technol.* 2008; in press.
[9] Lam CW, James JT, McCluskey R, Hunter RL. Pulmonary toxicity of single-wall carbon nanotubes in mice 7 and 90 days after intratracheal instillation. *Toxicol Sci* 2004; 77: 126-134.
[10] Templeton RC, Ferguson, PL, Washburn, KM, Scrivens, WA, Chandler, GT. Life-cycle effects of single-walled carbon nanotubes (SWNTs) on an estuarine meiobenthic copepod. Environ. Sci. Technol. 2006; 40: 7387-7393.

Federal prioritization: Through the NNI, the Federal Government has developed and refined a roadmap aimed at identifying and prioritizing research needs with respect to environmental, health, and safety issues of nanotechnology[11]. The five primary research categories identified are (1) Instrumentation, Metrology, and Analytical Methods; (2) Nanomaterials and Human Health; (3) Nanomaterials and the Environment; (4) Human and Environmental Exposure Assessment; and (5) Risk Management Methods.

The Nanoscale Science, Engineering, and Technology (NSET) subcommittee of the National Science and Technology Council (NSTC) has done a commendable job of focusing the disparate interests of the Federal agencies party to the NNI such that an organized effort can be made to address environmental and health impacts of nanotechnology <u>*as this technology is developed*</u>. This last point is critical – we cannot afford to wait until nanotechnology is fully integrated within our commercial enterprises to begin assessing its risks and hazards to human health and the environment.

Future research needs and challenges: Nanomaterials have not been well characterized in terms of their environmental occurrence, behavior, and toxic potential even though they may contribute to occupational and general air/water pollution through manufacturing and waste disposal as well as through inclusion in drug delivery and therapeutic applications. Large data gaps exist with regard to our basic understanding of the potential for manufactured nanoparticles to cause deleterious effects on human as well as ecological systems.

In assessing possible health and environmental effects of manufactured nanomaterials, it is important to study their impact in relevant model systems and in chemical forms reflective of occupational/environmental exposures. There are many different types of nanoparticles/nanomaterials and each of these will have a behavior (for example toxicity or transport) dictated by chemical and physical factors unique to the material. Below, I comment on specific areas of research within the framework outlined by the NSET subcommittee that I believe deserve particular attention:

- Without methods for detecting and characterizing nanomaterials in the environment and in human tissues, exposure assessment and environmental occurrence and fate studies are impossible. I wholeheartedly agree with the NSET subcommittee that research into analytical methods and metrology of nanomaterials is a top priority and support for this work should be accelerated within the NNI.
- With respect to research on environmental and human health effects of nanomaterials, I stress the need to develop standardized testing methods that are appropriate to assessing toxicity and biological uptake of nanomaterials.

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[11] This strategy is outlined in three documents: National Science and Technology Council 2006, *The National Nanotechnology Initiative: Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials*, http://www.nano.gov/NNI_EHS_research_needs.pdf; National Science and Technology Council 2007, *Prioritization of Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials*, http://www.nano.gov/Prioritization_EHS_Research_Needs_Engineered_Nanoscale_Materials.pdf; and National Science and Technology Council 2008, *The National Nanotechnology Initiative: Strategy for Nanotechnology-Related Environmental, Health, and Safety Research*, http://www.nano.gov/NNI_EHS_Research_Strategy.pdf.

- It is clear from my own work as well as that of others that we must consider not only the health and environmental risks of manufactured nanomaterials but also that of byproducts generated during manufacturing. This is a relatively unexplored area of research and should be considered.
- There is a critical need to assess routes of human and ecological exposure after release of nanomaterials into the ambient environment. We still have a very limited knowledge base regarding the treatability of nanotechnology wastes as well as the routes by which nanomaterials may enter and move within our air and water. This should be a top priority for EHS research within the NNI.
- Finally, our ability to accurately assess and predict risk of emerging nanotechnologies to human and environmental health is critically dependent on our understanding of the mechanisms by which nanomaterials act on biological systems at the cellular and molecular level. This understanding represents a grand scientific challenge and will require significant and well-supported effort.

As you look to reauthorization of the NNI, I ask you to consider the resources that are critically needed now and in the future for addressing these emerging concerns. In 2005, expenditures through the NNI budget on nanotechnology-related EHS research totaled approximately $35 million or 3% of the total NNI budget. As of today, the NNI budget request for 2009 allocates $76 million or approximately 5% of the total request to research on EHS issues of nanotechnology. It is very clear that a significant increase in our collective scientific understanding of the environmental and health impacts of nanotechnology will require a more substantial investment. A realistic target in the very near term should be to increase the level of funding for EHS research on nanotechnology to meet or exceed 10% of the NNI budget.

I wish to close by saying that we have a unique opportunity now – through the efforts of the NNI we have begun the process of addressing EHS risks of nanotechnology ***simultaneously*** with the development of this technology. We have only to look back at the lessons learned from PCBs and other legacy chemical contaminants to realize the dangers of waiting until new technologies are mature to assess their environmental and health risks. I urge this Committee to consider these concerns during the reauthorization of the NNI. Thank you for considering my testimony. In the appendix below I have included a summary of the research currently being conducted at the University of South Carolina on environmental and human health issues in nanotechnology.

Appendix: Ongoing Research at the University of South Carolina on the Environmental Fate and Health Effects of Manufactured Nanomaterials

Research Team: Dr. Lee Ferguson, Dr. Tara Sabo-Attwood, Dr. G. Thomas Chandler, Dr. John Ferry, Dr. Tom Vogt, Dr. Gene Feigley, Dr. Alan Decho, Dr. Sean Norman, Dr. Lee Newman, and Dr. Shosaku Kashiwada

Although the use of nanomaterials may allow for significant advances in science and technology, assessment of potential negative health and environmental impacts on humans, non-human biota, and ecosystems is imperative. The same properties that make these particles desirable, may also contribute to their toxic potential. Our research team at USC is studying the potential toxic effects that various nanoparticles have on humans, microbial communities, and aquatic ecosystems. This is an interdisciplinary effort which involves cooperation among chemists, physicists, biologists, toxicologists, and microbial ecologists, among others. The focus of our research efforts are described below. For more information, please visit http://www.nano.sc.edu/thrust_nanoenvir.asp.

Subproject #1: Pulmonary toxicity of nanomaterials
Project leaders: Tara Sabo-Attwood and Gene Feigley

In humans, the dominant route of exposure is suspected to occur via direct inhalation, both in the workplace where these particles are manufactured and used, and from the environment contaminated with particles released from anthropogenic and natural sources. Health-effects studies of air exposure to nanomaterials will require design of novel inhalation toxicology facilities and filtration technologies not available presently in the United States. Our group is uniquely qualified to design, build and test a small-scale prototype facility to assess aerosol generation, fate and transport. Construction of this prototype will lead to the development of inhalation exposure protocols for relevant animal models to assess the toxicological impacts of nanoparticles. In addition, we have already establishd complimentary in vitro studies that reveal toxic effects of single-walled carbon nanotube (SWNT) in human lung cells, and are currently exploring the molecular mechanisms responsible for this toxicity.

Subproject #2: Environmental fate, transport and toxicity of carbon nanomaterials in aqueous systems
Project leaders: Tom Chandler, Lee Ferguson, Shosaku Kashiwada

Project Focus:
Synthesis of unique radioisotope-labeled nanomaterials for toxicological, fate and environmental transformation studies
Single-walled carbon nanotube (SWNT) fate in aquatic/sedimentary systems is still largely under-explored. The USEPA has supported research by our team at USC aimed at elucidating the

toxic effects and environmental fate and transport behavior of SWNT in estuarine environments. Our results have shown that manufacturing byproducts of SWNT are toxic to estuarine meiobenthic copepods and that copepods ingest but do not bioaccumulate SWNT from sediments. In addition, we have shown that SWNT are highly sorptive to hydrophobic organic contaminants such as PCBs and PAHs, and that organisms ingesting SWNTs with associated organic contaminants can bioaccumulate the associated organics in their tissues. Studies on environmental fate of SWNT under simulated estuarine conditions reveal that SWNT materials aggregate strongly and agglomerate to natural particles (e.g. clay and sand) in the presence of high ionic strength solutions (e.g. seawater), but that this behavior is inhibited by the presence of high concentrations of dissolved organic matter.

As part of our EPA-funded research, we have been developing a repository of pure, radio-labeled carbonaceous nanomaterials for national environmental toxicology and chemistry uses. With our collaborator Research Triangle Institute, Inc. we have custom synthesized single- walled carbon nanotubes. We are using these materials to perform experiments aimed at uptake/bioaccumulation and linked acute/chronic toxicity of SWNTs in at least two model invertebrate systems, fish and marine invertebrates (copepods). The ^{14}C-SWNT materials are also being used to study particulate sorption, aggregation, transport in porous media, and bio/phototransformation in a laboratory setting.

Subproject #3: Microbial applications and degradation of nanomaterials
Project leaders: Alan Decho, Sean Norman, John Ferry

Biofilms consist of bacteria cells attached to a surface that produce a large network of extracellular polymeric secretions (EPS). In doing so, bacterial cells are able to protect themselves against antimicrobial agents, and manipulate their local environment. Biofilms commonly occur in natural and engineered environments. However, their presence often incurs multibilllion dollar costs for hospitals (e.g. most hospital-acquired infections are biofilms), industry (e.g. cause metal corrosion and biofouling, reduce heat transfer efficiency), potable water system maintenance (i.e. protect pathogenic bacteria against chlorination), as well as being important in natural environments. Our research focuses on using nannoparticles to detect and monitor biofilms, study how the nanoparticles are captured and sequestered, and determine if the bacteria degrade these particles in various settings.

- **Biofilm Nanosensors**: Understanding biofilm processes, and controlling their costly effects is important has important economic, health, and environmental implications. The development of specific Nanosensors for monitoring bacterial processes within biofilms is an important step in the in-situ detection and monitoring of biofilm processes. Our studies aim to develop specific sensors that can be 'captured' by a biofilm, then provide important physical/chemical/metabolic information regarding processes occurring within the biofilm.
- **Capture and Sequestration of NanoParticles by Biofilms**. Bacterial biofilm are an efficient filter for particulates, colloids and dissolved molecules. They are likely important in the capture and concentration of nanoparticles under different Environmental conditions. We strive to: 1) understand how biofilms sequester nanoparticulates, and 2) manipulate biofilms to enhance capture efficiency.

- **Biofilm Test Systems:** This phase involves the development of biofilm culture systems that accurately mimic natural biofilm populations. Such systems will be coupled to CSLM, Raman/CSLM, and other analysis instrumentation for precise testing of antimicrobial approaches on living and engineered nanosurfaces.

Microbial interactions and degradation
This project is directed at determining the influence of nanomaterials on environmental microbial activity. Nanomaterials have unique antimicrobial properties that may be exploited in environmental disinfection and/or infection control. There are also therapeutic applications for this research relative to artificial implants, prostheses, etc.

Specific Goals: Particular attention will be paid to questions such as: Do the materials in question support or inhibit the formation of biofilm communities? Are microbial communities capable of affecting the structure of associated nanomaterials (i.e., metabolically transforming them)? Do nanomaterials exert selective population pressure on microbial communities (i.e. selectively targeting one particular type of microbe vs another in mixtures)?

We will develop 'nanoprobes' (fluor-, SERS-based) for biofilm investigations in environmental studies. We will also develop/build biofilm flow-through cells and bioreactors for live culturing, and observation, of biofilms in the presence/absence of nanomaterials using our new confocal (CSLM) and Raman-confocal systems in ENHS.

Subproject #4
Photocatalysis of reactions mediated by nanomaterials
Project leaders: John Ferry, Tom Vogt

Project Focus:
Development of nanostructured materials with applications for environmental modification or remediation is the focus of this project. We are primarily interested in developing mixed metal oxide visible light activated photocatalysts for effecting sunlight activated oxidation in the aqueous phase. The materials focus will be active catalysts (nanoparticulate metal oxides) that engage in direct electron transfer with substrates and passive materials that may exhibit catalytic properties by promoting close association (such as various nanocarbons). We will monitor the degradation of catalytically active nanomaterials in environmental matrices, using microscopic and molecular techniques. We will assay the catalytic activity of the material during degradation, which is an exploratory evaluation of the structure activity relationship. We will assay the physico-chemical behavior of the material upon exposure to environmental conditions (e.g. aggregation, adsorption of "poisons" that affect catalyst activity, etc). We will explore application venues for materials that are effective photoactivated oxidants (drinking water and surface disinfection, biomedical applications, etc).

Subproject #5
Plant Interactions with Nanoparticles
Project leaders; Lee Newman, Tara Sabo-Attwood, Jason Unrine, Cathy Murphy

Project focus
Plant uptake and response to nanoparticles will have significance on many levels. First and foremost is to understand the parameters of plant uptake of the particles; what types (i.e., chemical composition) of particles are taken up, is there a size limit or shape preference, do the chemicals used to cap the particles impact uptake? Could plant compounds affect the bioavailability of particles in a natural system? In independent studies, we have already exposed the model plant, Nictoianna xanthi, to several different sized gold nanosphere, gold nanosheres with different capping chemicals, and silver nanospheres. Through simple light microscopy we have identified spheres of 3-5nm within the vascular tissue of the roots of the plants, and aggregation of larger spheres on the outside of the roots. We have observed enhanced precipitation of the particles when exposed to root exudates. We have also had a plants analyzed by one the using the beam lines at Brookhaven National Laboratory’s Synchrotron Light Source, and had XANES collected for selected areas of the plants analyzed. We found that the particles were retained as gold, and not gold salts within the plant, and that the pattern of accumulation differed within the plant tissues.