The Nanotechnology-Biology Interface: Exploring Models for Oversight

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Workshop Report

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Introduction

Nanotechnology, or really any technology, does not exist in a vacuum. It is derived from human efforts and affected by social, cultural, and political climates. Yet, few technologies emerge with the societal consequences in mind. Social and economic issues often gain most attention after technologies enter the marketplace and are widely used. Within the U.S. National Nanotechnology Initiative (NNI), resources have been directed towards the investigation of the societal issues that might accompany the applications of nanotechnology on their road to development and use. Approximately 4% of NNI funding has been used to study the social, educational, and ethical implications of nanotechnology.[1] Many experts in this area have cited negative experiences with past technologies, such as stem cell research and genetic engineering, as the impetus for dealing with the contextual issues for nanotechnology early and often.

Society drives and regulates technology, attempting to minimize the downsides and maximize the benefits. Appropriate oversight of new technologies is important for ensuring the health and environmental safety of products and instilling public confidence. Most people agree that ultimately the success of any technology is dependent on proper governance within a societal context. Mishaps or accidents can preclude future use and development, and there is a delicate balance between allowing technology to flourish and putting regulatory or non-regulatory oversight systems in place.

Discussions of oversight frameworks for nanotechnology have largely focused on occupational health issues associated with engineered nanoparticles, such as buckyballs and carbon nanotubes.[2] Less attention has been paid to widespread applications in medicine, food and agriculture, and the environment, for which consumers, patients, ecosystems, farmers, or the general public may bear the risks and benefits. Several of these "nano-bio" applications are already entering the marketplace, while others are emerging in development and clinical trial phases. However, there have not been many focused public conversations on appropriate oversight frameworks for them. It is in this context, that the Center for Science, Technology, and Public Policy hosted the workshop "The Nanotechnology-Biology Interface: Exploring Models for Oversight" on September 15, 2005.[3]

Kenneth H. Keller, moderator of the workshop and Charles M. Denny, Jr. Professor of Science, Technology, and Public Policy at the University of Minnesota, opened the workshop by describing our recent paradigm shift as a society from a reductionist approach in science, in which a phenomenon is largely considered on its own in the laboratory, to a systems approach, in which there is recognition that every part of one phenomenon interacts with another. This systems approach can be extended to connect technology with its context in society. In other words, how we govern social, economic and political systems affects what happens to technology. He framed the workshop along two general themes:

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[1] Roco, M.C. "The emergence and policy implications of converging new technologies integrated from the nanoscale." *Journal of Nanoparticle Research* 7:129-143 (2005).

[2] 2nd International Symposium on Nanotechnology and Occupational Health, University of Minnesota, October 3-6, 2005.

[3] In a public workshop, over 160 people from academe, industry, state and federal government, trade organizations, law and venture capital firms, and the general public convened to discuss governance issues for the nano-bio interface. The day following the public workshop, approximately 35 speakers and other experts continued the discussions. The workshop was funded by the Consortium on Law and Values in Health, Environment, and the Life Sciences. http://www.lifesci.consortium.umn.edu/.

1) anticipating consequences and understanding interconnections, as people feel more confident about new technologies when we are proactively and openly thinking about their possible effects; and 2) evaluating whether existing governance systems fit the features, many of them novel, of emerging technologies. More specifically, the workshop addressed the following questions:

- Is there or will there be a mis-match between the ability to generate nanoparticles and the ability to detect or determine the effects of these particles? Should the two be linked in any regulations developed with respect to nanoparticle use?

- Are there procedures developed for other technologies that could or should be adopted or adapted to assure the safety of nanoparticles and materials developed from them? What is the appropriate balance between government regulation and investigator or industry voluntary guidelines?

- What is the relationship between claims made for the potential of nanotechnology and the challenge of building public confidence in the safety of it? What is the appropriate strategy for balancing these two factors to preserve momentum in the development of the technology?

- If new governance models are designed, or existing ones revised, what is the appropriate process? What scientific, economic, social, and other factors should be considered? Who should be involved in developing the models?

This report highlights key points of discussion from the workshop and the opportunities and challenges associated with oversight at the nano-bio interface. It is organized around the themes of the workshop sessions: science and applications at the nano-bio interface, health and environmental safety concerns, regulatory and non-regulatory approaches to governance, striking an appropriate balance for governance in a societal context, and far-future applications and how governance systems can account for them. The report summarizes each presentation and reflects on the larger ideas in each session. It concludes with a summary of the general themes that emerged from the workshop. We hope that the workshop and this report are the beginning of closer examinations of nano-bio governance.

Science and Applications

Some question how nanotechnology came to be and whether it is really new. Materials science, biochemistry, chemical engineering, aerosol science, and particle technology have been around for several decades, yet only recently have been included in the forefront of nanotechnology research and development. To better understand the field of nanotechnology, the first session of the workshop reviewed specific applications of nanotechnology to biology (Table 1) and tackled the question of what makes nanotechnology special.

Nanotechnology is defined by the NNI as "the understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications."[4] Nanomaterials can arise from a "top-down" approach, in which macroscopic material is broken down to the nanoscale, or from a "bottom-up" approach, in which individual atoms or molecules are coaxed or self-assemble into nanoparticles.

Skeptics believe that as a society we have hijacked many different fields and applications and now call it "nanotechnology" as a way to create "hype" and get funding. However, others would argue that in last ten years, we have had better abilities to control, understand, and analyze materials at the nano-scale (Box 1) and that nanomaterials have special properties; and therefore, a new area is justified. There is disagreement as to whether a precise definition of nanotechnology is necessary for oversight and framing of other contextual issues. Regardless, nanotechnology reflects a multidisciplinary conglomerate of ideas and methods. In this sense, it is an umbrella that brings people together to solve problems. Secondary effects of bundling various basic research questions, fields, disciplines, and applications together include increased collaboration and understanding among the actors and scientists involved.

[4] National Nanotechnology Initiative. "What is Nanotechnology?" http://www.nano.gov/html/facts/whatIsNano.html. Accessed November 30, 2005.

Box 1. Tools of nanotechnology

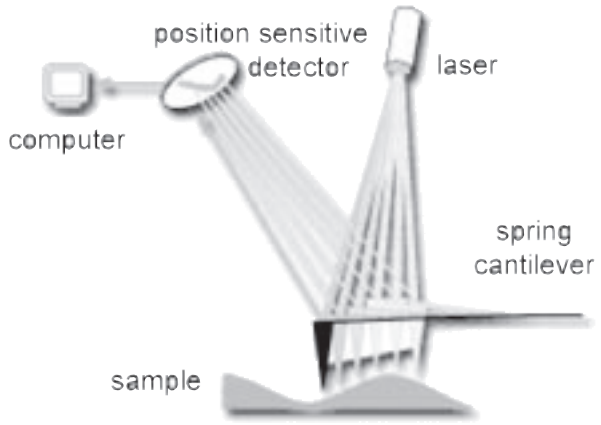
Source: http://www.che.utoledo.edu/nadarajah/webpages/whatsafm.html

"The scanning tunneling microscope (STM) and atomic force microscope (AFM) provide pictures of atoms on or in surfaces. A system that uses variations of the principles used by an STM or AFM to image surfaces is often called a scanning probe microscope (SPM).

The AFM works by scanning a fine ceramic or semiconductor tip over a surface much the same way as a phonograph needle scans a record. The tip is positioned at the end of a cantilever beam shaped much like a diving board. As the tip is repelled by or attracted to the surface, the cantilever beam deflects. The magnitude of the deflection is captured by a laser that reflects at an oblique angle from the very end of the cantilever. A plot of the laser deflection versus tip position on the sample surface provides the resolution of the hills and valleys that constitute the topography of the surface. The AFM can work with the tip touching the sample (contact mode), or the tip can tap across the surface (tapping mode) much like the cane of a blind person.

Other measurements can be made using modifications of the SPM. These include variations in surface microfriction with a lateral force microscope (LFM), orientation of magnetic domains with a magnetic force microscope (MFM), and differences in elastic modulii on the micro-scale with a force modulation microscope (FMM). A very recent adaptation of the SPM has been developed to probe differences in chemical forces across a surface at the molecular scale. This technique has been called the chemical force microscope (CFM). The AFM and STM can also be used to do electrochemistry on the microscale.

AFM is being used to solve processing and materials problems in a wide range of technologies affecting the electronics, telecommunications, biological, chemical, automotive, aerospace, and energy industries. The materials being investigated include thin and thick film coatings, ceramics, composites, glasses, synthetic and biological membranes, metals, polymers, and semiconductors. The AFM is being applied to studies of phenomena such as abrasion, adhesion, cleaning, corrosion, etching, friction, lubrication, plating, and polishing."



The first session of the workshop overviewed applications and implications of nanotechnology for biology, including the use of nanotechnology in basic biological research, medicine, agriculture, and the environment. The first speaker, Andrew Taton, Professor of Chemistry at the University of Minnesota, noted that nanomolecules and particles, such as viruses, molecular motors, and membrane vesicles, exist naturally in biology, but the new nano-bio interface explores the interactions of the natural with the man-made. He provided numerous examples of work at this interface (e.g., some of those in Table 1) and argued that the nano-scale is unique from a physical standpoint, in that properties change when you whittle size down. He stated that one of the great technological challenges right now is to meld inorganic or man-made particles with biological molecules and make them more compatible. Dr. Taton's group works on coating nanoparticles to make them more "biofriendly." He argued that the nano-bio interface is here, and that the pace of applying nanotechnology to health is moving very quickly.

This rapid emergence creates a host of technical challenges and opportunities. For example, workshop participants discussed whether quantum dots interact with molecules in cells and interfere with typical cellular reactions. There are studies that indicate that quantum dots bind cellular components and can be toxic. Dr. Taton's lab is developing biocompatible coatings to prevent such interactions. Dr. Taton stressed the importance of getting together in a forum like the workshop to discuss safety and toxicity issues before the widespread use of nanoparticles.

Darrell Untereker, Vice President of Corporate Research and Technology at Medtronic, Inc., argued that nanotechnology is not "a technology" per se, but a collection of things that happen at a certain scale. He stated that nanotechnology is not entirely new, and when we discuss public policy, it is important that we do not forget that the basic scientific principles are the same. For him and others in industry, the primary question is what can be done with nanotechnology to benefit society. Dr. Untereker described ways in which the medical device industry uses nanotechnology, such as for corrosion-resistant device coatings, or will use it in the future, such as for nanodevices to detect physiological states of patients. He emphasized that there is the possibility of moving faster than wise. However, on the other hand, he stressed that we should not put impediments to moving forward, because future gains to be made from knowledge and applications of nanotechnology go beyond what we can conceive today.

Larry Walker, Professor of Biological and Environmental Engineering at Cornell University, reviewed applications of nanotechnology in industrial biotechnology and agriculture. He described the many global challenges that we face—the high cost of energy, providing food to feed increasing populations, and securing safe water—and stressed the increased need for agriculture to provide raw materials and energy needed for our transition towards a sustainable world. Dr. Walker spoke about the use of nanotechnology to better understand how cellulases work to produce ethanol and identify and quantify naturally-occurring microorganisms for generating products and energy from waste (Table 1). He stressed the importance of working in multidisciplinary teams for the sustainable deployment of nanotechnology and for American land grant institutions to act as independent sources of information about the benefits and pitfalls of nanotechnology.

Table 1. A few examples of research and applications at the nano-bio interface

(Note: this table does not include all possible categories of applications)

Source: compiled by J. Kuzma.

Sector	Application	Method or Material	Details
Agriculture	Basic Research on Energy Production	Nanodetection	Single molecule detection to determine enzyme/substrate interactions (e.g., cellulases in production of ethanol).
	Agrochemical Delivery	Nanoparticles, nano-capsules	Delivery of pesticides, fertilizers, and other agrichemicals more efficiently (e.g., only when needed or for better absorption).
	Animal Production	Nanoparticles Nanomaterials in chips (nanochips)	Delivery of growth hormone in a controlled fashion. Identity preservation and tracking.
	Animal or Plant Health	Nanosensors	Detect animal pathogens, such as foot and mouth disease virus. Detect plant pathogens early.
	Animal Medicine	Nanoparticles, nanodevices	Deliver animal vaccines.
	Plant Production	Nanoparticles	Delivery of DNA to plants towards certain tissues (i.e., targeted genetic engineering).
Food	Sensing	Nanosensors	Detect chemicals or foodborne pathogens; biodegradable sensors for temperature, moisture history, etc.
	Safety	Nanoparticles	Selectively bind and remove chemicals or pathogens.
	Packaging	Nanoclays, nanofilms	Prevent or respond to spoilage. Sensing features for contaminants or pathogens.
	Healthy Food	Nanoemulsions, nanoparticles	Better availability and dispersion of nutrients, nutraceuticals, or additives.

Environment	Microbial Ecology and Characterization	Microfluidics, micro-nano arrays	Identify and quantify microbial populations for biocontrol, composting, bioremediation, etc. (e.g., nano-single strand conformation profiling of DNA for counting single molecules).
	Sensing	Nanosensors	Detect environmental contaminants early; assess states of populations or ecosystems.
	Remediation	Nanoparticles	Bind contaminants and remove them.
Medicine	Ex vivo Diagnostics	Nanoparticle labeled DNA	Microarray analysis for medical genomics (e.g., detecting patient genetic response to pathogens, or tailoring treatments to individuals).
	In vivo Diagnostics	Nanoparticles	Magnetic particles for imaging (e.g., MRI of tumors).
	Drug Delivery or Gene Therapy	Nanoparticles	Tag particles and target drugs or genes to specific tissues. Increase bioavailability or solubility. Make drugs more bioactive. Liposomes, dendrimers, and other inorganic or organic particles.
	Tissue Scaffold	Surface nanomaterials, nanocoatings	Promote cell growth, providing a matrix (e.g., neuron growth on nanofabricated silicon).
	Medical Devices	Nanocoatings	Coatings to make devices, such as pacemakers, corrosion resistant and biocompatible.
		Nanosensors	Sense chemicals in the body and adjust device function accordingly.
Biology—Basic research	Sensing, Detecting, and Characterizing	Cantilevers	Bend in response to molecular interactions.
		Nanowires	Use nano-conductivity for characterizing interactions (e.g., between viruses and proteins).
		Quantum dots	Label different cells, proteins, or cellular components with colored tags. Track movement, relationships, etc. at the subcellular level. Long lifetime is a positive feature of these tags.

Health and Environmental Safety

The ability to assess the health and environmental impacts of nanoparticles and other nanomaterials is a cornerstone for governance. It is not sufficient, but seems necessary for a good oversight framework. Standard models of chemical, ecological, or microbial risk assessment likely apply to nano-bio products, but within the models, data needs and technical questions might be very different given the special biological, chemical, and physical properties that arise at the nanoscale. In general, we are lacking fundamental knowledge and data for assessing the potential risks of nanoproducts used in or derived from biological systems. Yet, nanotechnology is now here. At the workshop, current activities and studies in environmental health and safety (EHS) research were presented, along with mechanisms and institutions for funding and conducting such work.

Nora Savage, Environmental Engineer at the Office of Research Development at the Environmental Protection Agency (EPA), discussed EPA's activities at the nano-bio interface. EPA works through the NNI's Nanoscale Science, Engineering, and Technology committee (NSET), which is responsible for coordinating federal research and development at the nanoscale (Figure 1). The National Nanotechnology Coordinating Office (NNCO) is the point of contact for NSET. Several federal agencies fund EHS research under NNI (Box 2). According to Dr. Savage, for fiscal year (FY) 2006, the total NNI budget request was approximately $1 billion and NNI EHS research totaled $38.5 million.

There is general difficulty in classifying EHS research as "implications" or "applications," and this is a point of contention in the health and environmental safety community. For example, the general development of sensors could be placed in either category. Also, applications research can provide information for implications and vice versa. Dr. Savage indicated that to date, EPA has funded approximately $15.6 million of applications research to address existing environmental problems or prevent future problems, and it has funded $10.2 million in implications research to address the interactions of nanomaterials with the environment and potential risks. Environmental applications of nanotechnology include improved monitoring and detection capabilities, ultra-green manufacturing and chemical processing, waste minimization, reduced energy usage, clean energy sources, remediation and treatment technologies, and sustainability applications. Implications research for nanomaterials includes studies on toxicity and its mechanisms; effects of manufacturing on ecosystems; transportation and fate of nanomaterials; bioaccumulation, transformation, and availability; and dose-response assessment.

Dr. Savage pointed out that many health and environmental applications of nanotechnology have a dual nature. For example, the ability of nanoparticles to cross the blood-brain barrier has advantages for delivering drugs to the brain, which is an organ that is otherwise difficult to reach, but that same feature amplifies toxicity concerns. In environmental applications, nanomaterials may be used to penetrate and remediate subsurface areas, but their penetration abilities could also lead to ecosystem damage. More generally, the novel properties and uses of nanotechnology which provide benefits also cause regulatory concern.

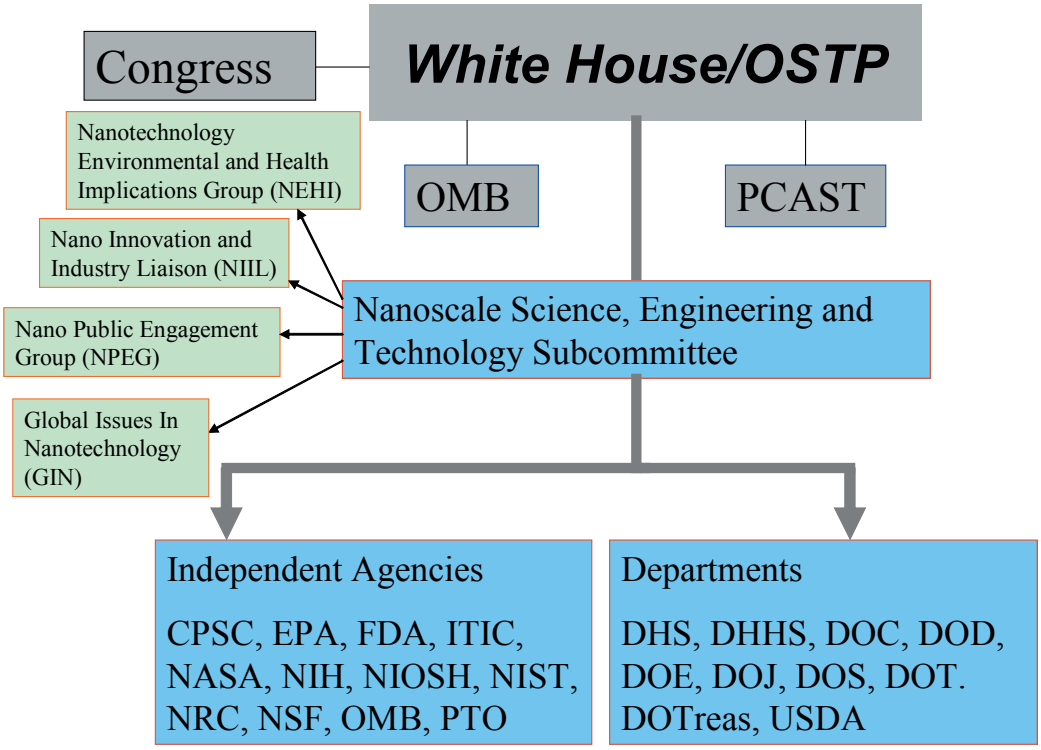
EPA governs nanotechnology with its mission to protect human health and the environment in mind. EPA's nanotechnology framework includes facilitating nanotechnology's promise for environmental protection, understanding problems that might arise for health or the environment, and considering environmental benefits and impacts from the beginning. Dr. Savage mentioned the UK Royal Society report,[5] which recommended that nanomaterials not be used in the environment until we have better understanding of their fate, transport, and effects. The U.S. is not currently taking that approach.

[5] Royal Society of the UK. *Nanoscience and Nanotechnologies: Opportunities and Uncertainties:* (2004). http://www.nanotec.org.uk/finalReport.htm Precise recommendation is:
"Specifically, in relation to two main sources of current and potential releases of free nanoparticles and nanotubes to the environment, we recommend: (i) that factories and research laboratories treat manufactured nanoparticles and nanotubes as if they were hazardous, and seek to reduce or remove them from waste streams; (ii) that the use of free (that is, not fixed in a matrix) manufactured nanoparticles in environmental applications such as remediation be prohibited until appropriate research has been undertaken and it can be demonstrated that the potential benefits outweigh the potential risks."

Figure 1. Federal organizations involved in nanotechnology

OMB, Office of Management and Budget; PCAST, President's Council of Advisors in Science and Technology; OSTP, Office of Science and Technology Policy; CSPC, Consumer Product Safety Commission; EPA, Environmental Protection Agency; FDA, Food and Drug Administration; ITIC, Information Technology Industry Council; NASA, National Aeronautics and Space Administration; NIH, National Institutes of Health; NIOSH, National Institute of Occupational Safety and Health; NIST, National Institute of Standards and Technology; NRC, National Research Council; NSF, National Science Foundation; PTO, Patent and Trademark Organization; DHS, Department of Homeland Security; DHHS, Department of Health and Human Services; DOC, Department of Commerce; DOD, Department of Defense; DOE, Department of Energy; DOJ, Department of Justice; DOS, Department of State; DOT, Department of Transportation; DOTreas, Department of the Treasury; USDA, US Department of Agriculture.

Source: N. Savage, presentation, September 15, 2005.



Box 2. NNI environmental health and safety research

NTP, National Toxicology Program; see Figure 1 for other abbreviations

Source: N. Savage, presentation, September 15, 2005.

NSF Basic research: environmental effects of nanoparticles; nanoparticles in air pollution; water purification; nanoscale processes in the environment.

NTP Potential toxicity of nanomaterials, such as titanium dioxide, several types of quantum dots, and fullerenes.

DOD Physiochemical characteristics and toxicological properties of nanomaterials; computational model that will predict toxic, salutary and biocompatible effects based on nanostructured features.

EPA Toxicology of manufactured nanomaterials; fate, transport, and transformation; human exposure and bioavailability.

DOE Transport and transformation of nanoparticles in the environment; exposure and risk analysis; health effects.

NIH Nanomaterials in the body and cell cultures; laboratory use for diagnostic and research tools.

NIST Measurement tools, tests, and analytical methods.

Jacob Finkelstein, Professor of Pediatrics, Environmental Medicine, and Radiation Oncology at the University of Rochester, stressed that we currently do not have enough information to characterize the risks of nanomaterials and devices. We know that there are risks, but we are just reaching the point now where we can begin to ask the right questions about their nature and magnitude. His group develops approaches for risk assessment, not to stifle the technology, but rather with the ultimate goal of appropriately using it.

He described the importance of using risk assessment paradigms (Box 3) for evaluating the risks of nanotechnology in a way that is meaningful to regulators. The fundamental use of paradigms will likely be the same for products of nanotechnology, but data needs may not be. For example, at the nano-scale, cellular uptake mechanisms are different, as particles below 20 nm can be taken up by the endothelium skin layers and those below 10-50 nm can enter cells through receptor mechanisms. Nanoparticles have been found to cross the blood-brain barrier (Figure 2, page 14). They also have higher surface areas and greater numbers of particles at concentrations similar to larger particles. Surface properties are different at the nanoscale, and quantum properties dominate. Therefore, Dr. Finkelstein argued that the special properties and effects of nanoparticles should be considered and new strategies in toxicology are needed.

Some factors complicating risk assessments include differences in the exposure medium (e.g., air, water, or food), routes of exposure (e.g., inhaled, consumed, or contacted), and dose-response relationships. In certain media, it is not known whether nanomaterials exist as single particles or agglomerates. Also, there are differences in dose-response curves depending on whether the curves are expressed by mass, number of particles, or surface area. Furthermore, most tests are short-term, and long-term toxicity and effects remain unknown. Dr. Finkelstein outlined some key questions for toxicology research on nanomaterials:

- Which physicochemical characteristics of nanoparticles are associated with adverse effects? (e.g., size, chemistry, crystallinity, biopersistence, surface coating, porosity, or charge)

- Is cellular uptake involved? If so, what are the uptake and translocation mechanisms?

- What should be considered when designing biocompatible nano-sized materials? What would make a toxic nanoparticle biocompatible?

Dr. Finkelstein hopes we can define a systematic approach that will help us address the special toxicological issues associated with nanotechnology. He proposed a tiered and combined approach, involving first, detailed physico-chemical characterizations of particles or other materials, then acellular and cellular assays comparing dose by mass, number, and surface area, and finally, *in vivo* assays. He noted that appropriate endpoints for *in vitro* assays can be difficult to determine, as single cell types are often not relevant, given that various types of tissues are exposed in the body.

Ideally, adequate information for each step in risk assessment would be available, but for many nano-products, researchers and regulators are currently relying on qualitative judgments for nearly every step. Dr. Finkelstein stressed that we need data on what type of human exposure to expect, dose-response relationships, kinetics and cellular interactions, and correlations of properties of materials to their toxicity. His group is developing a relational database to determine organizing principles for assessing toxicity. Group members are systematically looking at a number of different materials and properties to correlate those with biological effects. In addition to the work of Dr. Finkelstein, an expert group of the International Life Sciences Institute (ILSI) Research Foundation recently published a report on a screening strategy for hazard identification of nanomaterials based on their characteristics.[6]

Dr. Finkelstein also pointed out that nanomaterials will not only lead to human exposure, but can be dispersed in the environment and could be toxic to ecosystems (Figure 3). He agreed that nanoparticles have been around in nature for a long time, but with our current ability to engineer them for specific purposes, he stressed that measuring and assessing their environmental distribution become even more important.

Box 3. Standard human-health risk assessment paradigm for chemicals

Source: National Research Council. *Risk Assessment in the Federal Government: Managing the Process* (1983).

Step 1: Hazard Identification

Step 2: Dose-Response Assessment

Step 3: Exposure Assessment

Step 4: Risk Characterization

[6] Oberdörster, G. et al. "Principles for characterizing the potential human health effects from exposure to nanomaterials: elements of a screening strategy." *Particle and Fibre Toxicology* 2:8 (2005).

Figure 2. Uptake and distribution of nanoparticles in an organism

Source: Oberdörster et al. *Environmental Health Perspectives* 113:823-839 (2005); J. Finkelstein, presentation, September 15, 2005.

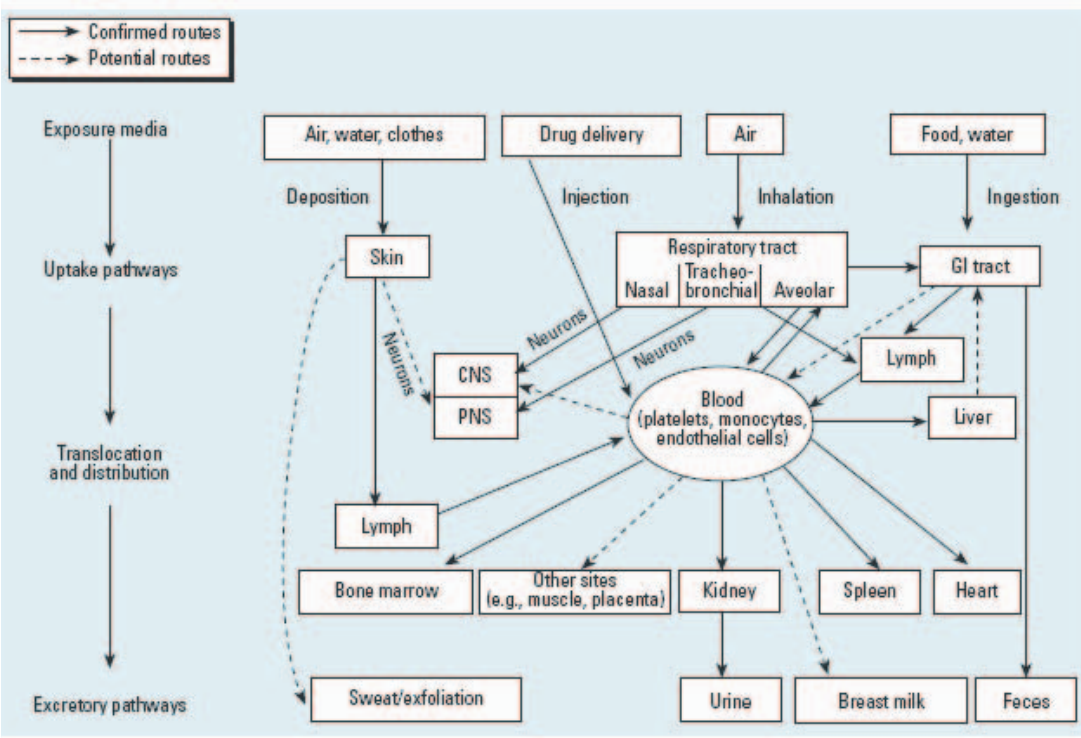
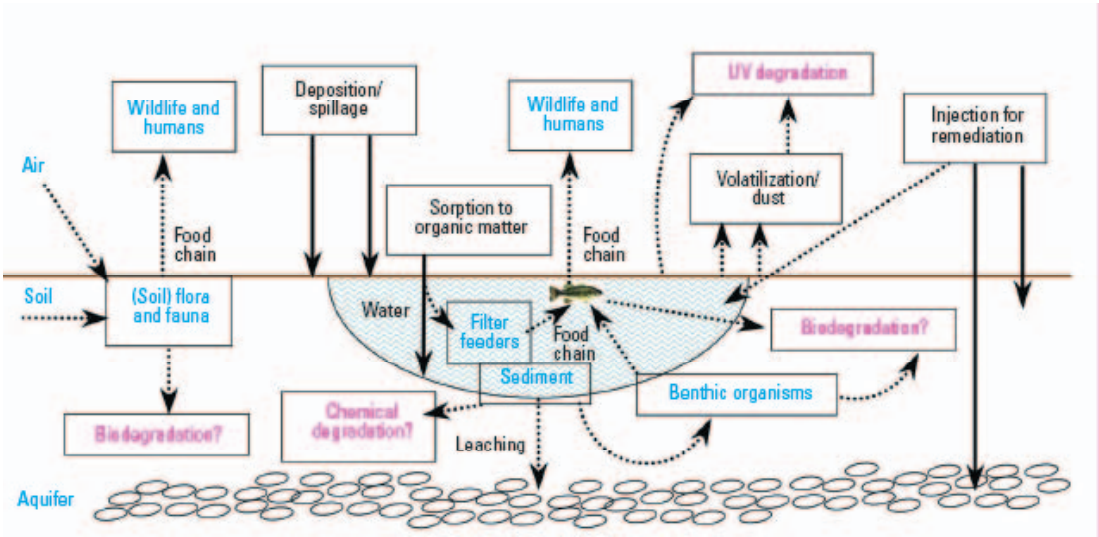


Figure 3. Environmental pathways and potential exposure routes

Source: Oberdörster et al. *Environmental Health Perspectives* 113:823-839 (2005). J. Finkelstein, presentation, Sept 15, 2005.



Governance Frameworks

Governance systems are currently in place for a variety of products associated with new technologies. For the design of oversight models for nanotechnology, there are opportunities to learn from past experiences with other technologies and products, and it is important not to recreate what already exists. Some argue that nanotechnology is already suitably covered by existing regulatory and non-regulatory oversight activities, whereas others disagree, arguing that many products on the market are falling through the cracks of a system that has not been formalized or coordinated. As a society, we have choices of creating new laws and/or regulations, revising existing ones, interpreting existing ones to cover nanoproducts, designing non-regulatory approaches, or modifying existing non-regulatory approaches. The diversity of the products at the nano-bio interface might preclude a single approach or framework, as one size might not fit all (Table 2).

One particular example of oversight from which lessons could be learned is the Coordinated Framework for the Regulation of Biotechnology.[7] In this case, a governance approach was developed for the products of biotechnology by using a patchwork of existing laws. EPA, the Food and Drug Administration (FDA), and the US Department of Agriculture were identified as lead agencies for specific products (Table 3). Underlying principles of the framework were that the products, not the process of biotechnology, should be the focus of regulation and that genetically engineered organisms (GEOs) are not fundamentally different from non-engineered organisms. Therefore, existing laws were determined to be sufficient. After the framework was published, the agencies chose paths to develop regulations under existing laws or provide guidance and policies under them. This approach and others should be closely examined for their relevance to the products of nanotechnology.

This session of the workshop examined oversight systems for the nano-bio interface. It also considered appropriate features of governance systems for ensuring public confidence and safety.

[7] Office of Science and Technology Policy. Coordinated Framework for the Regulation of Biotechnology. 51 Fed Reg 23302 (1986).

Table 2. A few examples of products of nanotechnology applied to health, food, or the environment

(Note: this is not a complete list)

Source: J. Kuzma, compiled from company web searches; many examples from the list were initially provided by N. Savage, EPA.

Company	Product	Purpose/Method	Stage
Health/Medicine			
American Bioscience, Inc. (ABI)	Abraxane®	Nanoparticulate formulation of the widely used anticancer drug paclitaxel for metastatic breast cancer. First approval of protein albumin nanoparticles as a "natural solvent."	Received final FDA approval in Jan. 2005.
BioSante Pharmaceuticals	BioVant™, BioOral™, BioAir™	Calcium phosphate-based (CAP) nanotechnology for oral, nasal, and trans cutaneous routes of delivery of vaccines and proteins.	CAP is in preclinical safety trials, as indicated by the company website.
GP Surgical	TiMESH	Hernia mesh made with titanium nano-coating.	FDA approved, implanted device; commercially available.
Health Plus International, Inc.	Spray For Life®, Vitamin B12 Energy Booster	Nanoceutical™ Delivery System (NDS), disperses active molecules into nanodroplets, increases bioavailability of nutrients or drugs.	Commerically available, but not FDA approved.
StarPharma	VivaGel™	Polyvalent, polylysine dendrimer as the active ingredient. Intended to prevent transmission of sexually transmitted diseases (STDs).	Determined to be safe and well-tolerated in Phase 1 clinical trials as an Investigational New Drug (IND) under FDA (2004), according to the company website.
Environment/Health			
EnviroSystems	EcoTru®	Nanoemulsion technology to disinfect surfaces for bacteria and viruses.	Commercially available.
Severn Trent Services & Bayer AG	SORB 33® Bayoxide® E33	Nano-sized surface structures that are able to absorb arsenic; composed of ferric oxide.	Certified for drinking water systems by American National Standards Institute/NSF Standard 61. FDA pre-market review would be required under the Federal Food Drug and Cosmetic Act (FFDCA) if used in bottled water.

Food/Health			
bioMerieux	FoodExpert-ID®	High-throughput gene chip for testing food and animal feed for traceability and safety.	In trials in some European countries (2004).
Nanocor	Variety of products under the Nanomer® trademark	Nanoclays and composites providing barriers to oxygen and carbon dioxide flow used in food packaging to keep freshness and block out smells.	Nanomer® nanoclays are available for commercial use. Infrastructure in place to produce more than 100 million pounds annually.
Nanoplex Technologies	Nanobarcodes® Particles	Encodeable, machine-readable, durable, metallic rods. Particles are intrinsically encoded by virtue of the difference in reflectivity of adjacent metal stripes. Used for supply-chain tracking for food.	Product expected on market in 2006.
NutraLease Shemen Industries Ltd	Canola Active	Nanocapsules in cooking oil to improve bioavailability of nutraceuticals, for example, plant sterols to reduce the body's absorption of cholesterol in the blood.	On market in Israel; FDA has not reviewed this product. Sponsor website indicates "Canola Active - complies with FDA requirements."
OilFresh	OilFresh™	Vertical insert, made of an advanced nanoceramic material. For use in cooking oil for better quality.	Sponsor website indicates "OilFresh is authorized by the FDA." However, as material is not expected to migrate into food, FDA pre-market review was not required.
Samsung	Nano SilverSeal™	Nano-silver compound in the product design to suppress the spread of bacteria and other microbes in refrigerators.	Commercially available.

Lynn L. Bergeson, Managing Director of Bergeson & Campbell, P.C., Washington, DC, spoke about EPA activities pertinent to nanotechnology and the challenges facing the agency. EPA is a large organization committed to protecting human health and the environment, and it has many important responsibilities and priorities. However, its budget has been flat or decreasing in recent years, and its diminished resources pose difficult challenges for prioritizing activities. Ms. Bergeson posed the question of how EPA can use its statutory authority and develop capacity to review scientific and technical information about nanotechnology under such resource constraints. There already are products in commerce (Table 2), so the problem is particularly important now. Despite the challenges, EPA is harnessing its abilities to provide guidance on the scope of its regulatory authority and devoting its limited resources to considering how best to reap the benefits and identify and control the risks of nanotechnology. Ms. Bergeson provided examples of EPA activities in these areas.

EPA convened its Science Advisory Board (SAB) in December 2004 to consider nanotechnology and other emerging technologies. The SAB is the main external expert body that provides advice to the EPA on scientific and science policy matters. It concluded that nanotechnology can provide great benefits, but nanomaterials require additional investigations of environmental, health, and social impacts. SAB members noted that advancements in new technologies are occurring at unprecedented rates, making it difficult for government agencies to keep abreast of emerging developments. The SAB suggested that additional skill sets may be needed at the agency in order to develop new approaches (e.g., toxicological) for nanomaterials. Ms. Bergeson stated that the good news is that there is broad recognition at the very highest levels of EPA that nanotechnology needs attention; but the bad news is that since the SAB meeting, EPA has not been able to progress in resolving many of the difficult issues the SAB identified in 2004.

In another example, Ms. Bergeson described EPA's consideration of a voluntary reporting program under the Toxic Substances Control Act (TSCA) for the review of existing nanomaterials. Chemical substances are currently regulated under TSCA, which was enacted in 1976. However, Congress did not necessarily envision that this statute would be used to manage the risks and benefits from nanomaterials. Ms. Bergeson indicated that amending TSCA is unlikely in the short term, and perhaps even in the long term. Therefore, creative ways are needed to ensure that nanoscale materials are addressed appropriately under existing legal authorities. EPA believes that TSCA is sufficiently elastic to address nanoscale materials and has requested on several occasions, comment on the feasibility of a voluntary program. The agency has also urged stakeholders to come together to discuss the features of such a program. Ms. Bergeson noted that in general, there is broad support for a voluntary reporting program as a starting point, but that the difficulty lies in developing the details of this type of program.

The National Pollution Prevention and Toxics Advisory Committee (NPPTAC) was formed under the auspices of the Federal Advisory Committee Act to provide guidance to EPA on TSCA implementation and related EPA toxics programs. The NPPTAC recently agreed to form an ad hoc interim work group on nanoscale materials to provide guidance on

the prudence and scope of a voluntary reporting program on nanoscale materials. The Nanoscale Materials Voluntary Program (NVP) was agreed upon in concept during the NPPTAC ad hoc interim work group discussions convened through the summer of 2005, which progressed and concluded in the fall of 2005. The work group was charged with taking public input and issues into consideration and assessing the possible review of nanoscale materials under TSCA. The recent NPPTAC work group report describes the NVP as follows: [8]

> The NVP is intended to encompass engineered nanoscale materials now in or soon to enter commerce and the approaches under the NVP are intended to be available to both "new" and "existing" chemical nanoscale materials, regardless of whether they would otherwise qualify for various exemptions, or fall below reporting or notification thresholds, now applicable under TSCA provisions. This scope would apply without prejudice as to whether such distinctions, exemptions, or thresholds do or should apply in other contexts beyond the duration of a voluntary program. Participation in the NVP does not supersede, rather it complements, the new chemical notification requirements for new chemical nanoscale materials.
>
> In this context "soon to enter commerce" is defined as applying to pre-commercial new and existing chemical engineered nanoscale materials for which there is clear commercial intent on the part of the developer, excluding such materials that are only at the research stage, or for which commercial application is more speculative or uncertain.

Details of the NVP for which agreement will be difficult include, among others, defining the scope (e.g., should it review emerging chemicals, or only those now in commerce), deciding whether data generation should be part of the program, balancing transparency with protecting confidential business information, and including a diverse number of small and medium sized enterprises. The NPPTAC transmitted to EPA Administrator Stephen L. Johnson its "Overview of Issues for Consideration by NPPTAC" on November 22, 2005.[8] The document offers the NPPTAC's analysis and views of a framework for a voluntary program for engineered nanoscale materials, a complementary approach to new chemicals nanoscale requirements under TSCA, and other relevant issues.

In addition to the above activities, EPA's Science Policy Council (SPC) developed a white paper on nanotechnology that will have cross-program implications for the agency. The paper reviews science deficits and data needs for the agency and guides programmatic elements for both applications and implications of nanotechnology. The draft of the white paper was released to the public for comment in December 2005.[9]

[8] EPA. Overview of Issues for Consideration by NPPTAC. Available at http://www.epa.gov/oppt/npptac/pubs/nanowgoverviewdocument20051109.pdf (2005).
[9] EPA. External Review Draft Nanotechnology White Paper Prepared for the U.S. Environmental Protection Agency by members of the Nanotechnology Workgroup, a group of EPA's Science Policy Council. Available at http://www.epa.gov/osa/nanotech.htm (2005).

Ms. Bergeson concluded that there is currently little interface between nanotechnology, biotechnology, information technology, and other emerging and converging technologies within EPA, because the agency lacks adequate time and resources to consider these matters. This interface is critically important, and EPA recognizes the need in this area. Ms. Bergeson expressed her belief that EPA lacks the resources necessary to progress expeditiously with the regulation of products of nanotechnology in a way that will ensure public confidence and that voluntary, collaborative efforts are essential to fill this void. The challenges for EPA are to stay on top of program priorities set years in advance, while responding to crises (e.g., Hurricane Katrina and other natural disasters affecting human health and the environment) and anticipating and managing emerging technologies, including nanotechnology. Training, recruitment, and infrastructure development were identified by the SAB as key priorities for EPA to meet these challenges.

Table 3. Coordinated framework for the regulation of biotechnology

Source: National Research Council. *Genetically Engineered Pest-Protected Plants: Science and Regulation* (2000).

Agency	Jurisdiction	Laws
US Dept. of Agriculture (USDA)	Plant pests, plants, veterinary biologics	Federal Plant Pest Act (FPPA)
Food and Drug Administration (FDA)	Food, feed, food additives, vet drugs, human drugs, human biologicals, medical devices	Federal Food, Drug and Cosmetic Act (FFDCA)
Environmental Protection Agency (EPA)	Microbial and plant pesticides; novel microbes	Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA); FFDCA; Toxic Substances Control Act (TSCA)

Norris Alderson, Associate Commissioner of Science at FDA, described FDA activities at the nano-bio interface. He stated that FDA's approach to nanotechnology is no different than its approach to any other technology, as the agency regulates on a product by product basis. It does not regulate technologies, but regulates several kinds of products (Box 4) in basically three ways. Drugs are regulated via a pre-market approval process, and they have to pass safety, efficacy, and manufacturing standards. Devices that are of low risk are regulated on the basis of "acceptance of the product." They are expected to meet pre-approved standards (category 510ks), and if these are met, marketing can begin. Cosmetic products can be marketed without any type of evaluation or review. Dr. Alderson stressed that FDA processes are not static, and as the agency learns more, it evolves its review methods. FDA also provides assistance to industry to bring products to the marketplace. In addition to its regulatory activities, FDA oversees research on the products it regulates.

Safety considerations for FDA include access of nanomaterials to cells and tissues, time in the cells and tissues, clearance of the materials in cells and tissues, and effects on cell and tissue function. Absorption, distribution, metabolism and excretion (ADME) are key issues. Extensive preclinical tests, involving pharmacology, toxicology, geno-toxicity, developmental toxicity, immunotoxicity, and carcinogenicity, are required for safety evaluations. Features of tests include the use of high dose multiples, at least two animal species, histopathology on most organs, and extended dosing periods. However, FDA does not conduct these safety tests themselves, but rather the drug sponsor develops them. The agency provides guidance and direction for the tests and evaluates them after they are conducted. It considers not only safety, but also pre-clinical medical utility for products and manufacturing standards for a consistent and quality product.

Another important issue for FDA is nanomaterial release into and impacts on the environment following human and animal excretion. Dr. Alderson questioned whether the agency has the information and correct methodology to determine the nature of release and quantify nanoparticles in the environment. The agency also needs more information on the forms of nanoparticles that are presented to cells, standardized procedures to detect particles in cells, stability and critical and physical properties of nanomaterials, and the effects of scale-up and manufacturing on the characteristics of nanomaterials. Dr. Alderson stated that in general, the FDA believes that existing toxicological tests are adequate for most nano-products. The agency will continue to proceed in that manner until it sees a need for a change.

Dr. Alderson described several regulatory issues for the agency. One is the regulation of "combination products." These typically span different centers at FDA, each having a separate review process. Many more combination products are coming down the pipeline, and challenges in coordinating their review will need to be met. Another issue is the fact that FDA can only regulate products based on the claims of the sponsor. Ultimately, FDA may be unaware that nanotechnology is being used in a particular product. Furthermore, FDA has only limited authority for potentially high risk nano-products, such as cosmetics. He cited key challenges: preparing for "unknown" risks, dealing with them, and adopting new procedures for doing so; communicating with manufacturers of new medical products; involving stakeholders; communicating risks to the public; and reporting relevant scientific findings in a timely fashion.

Box 4. FDA regulated products

Source: N. Alderson, presentation, September 15, 2005.

- Foods
  - All interstate domestic and imported, including produce, fish, shellfish, shell eggs, milk (not meat or poultry)
  - Bottled water
  - Wine (<7% alcohol)
  - Infant formula
- Food additives
  - Colors
  - Food containers
- Cosmetics
- Dietary supplements
- Animal feeds
- Pharmaceuticals
  - Human
  - Animal
  - Tamper resistant packaging
- Medical devices
- Radiation emitting electronic products
- Vaccines
- Blood products
- Tissues
- Sterilants
- Counter-terrorism products

Evan Michelson, Research Associate from the Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, described other types of issues in governance systems, including risk perception (e.g., what the public sees with regard to nanotechnology and how it responds) and structural risks (e.g., how nanotechnology affects the structure of industry). He stated that there is not enough work being done in these areas or on ecological risks. For example, he noted that globally, there are at least 27 firms producing carbon nanotubes, with 108 metric tons produced in 2004 and 1000 metric tons projected for 2009. However, there has been little attention paid to end-of-life issues such as incineration, land-filling, and recycling.

Mr. Michelson stressed that both the public and industry are concerned about controlling nanotechnology, managing the risks, and considering potential gaps in regulation. Workers in industry and students in academic labs are primarily the ones who are exposed to nanoparticles right now, especially in developing countries where infrastructure and training for health and environmental safety are lacking. In the case of carbon nanotubes, he indicated that production is shifting to Korea and China, yet both in the U.S. and abroad, there is no agreed upon guidance in terms of worker safety practices for nanomaterials. He noted that regulatory guidance is particularly important for small businesses which often do not have the resources to devote to environmental health and safety.

Risks will change and shift as nanotechnology does. For example, we are currently moving from passive nanostructures to active nanostructures, such as those at the nano-bio interface (Figure 4). Mr. Michelson argued that our state of understanding about risk is in the past and as the technology moves forward, people will only accept risks if big benefits occur. However, many are worried that the big benefits, such as cancer treatment or cheap and clean energy, will not materialize if regulations are not in-step with advances and a mishap occurs as a result. He stated that with a growing number of nano-based products out on the market, the federal oversight process will increasingly have trouble keeping up with the pace of product development and market entry, as it can take several years to fund and conduct research on the health and environmental risks, and even longer to amend or formulate regulations.

Figure 4. Projected movement of nanotechnology.
Source: E. Michelson presentation, September 15, 2005; timeline adapted from M. Roco, NSF.

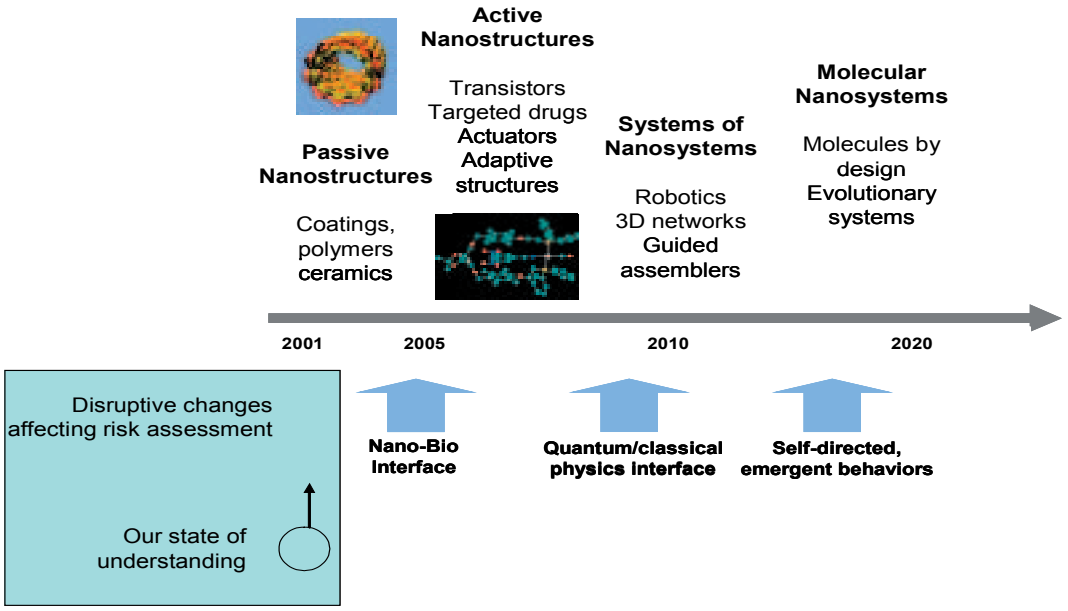
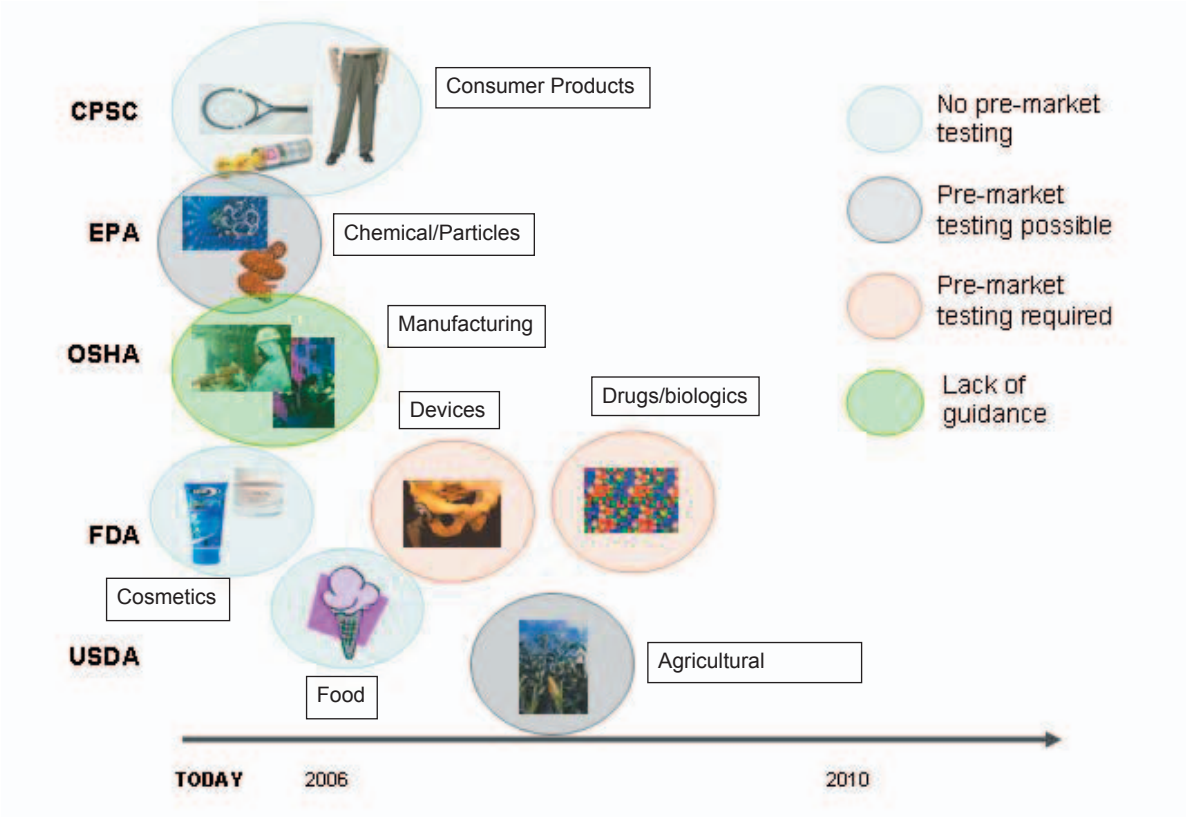
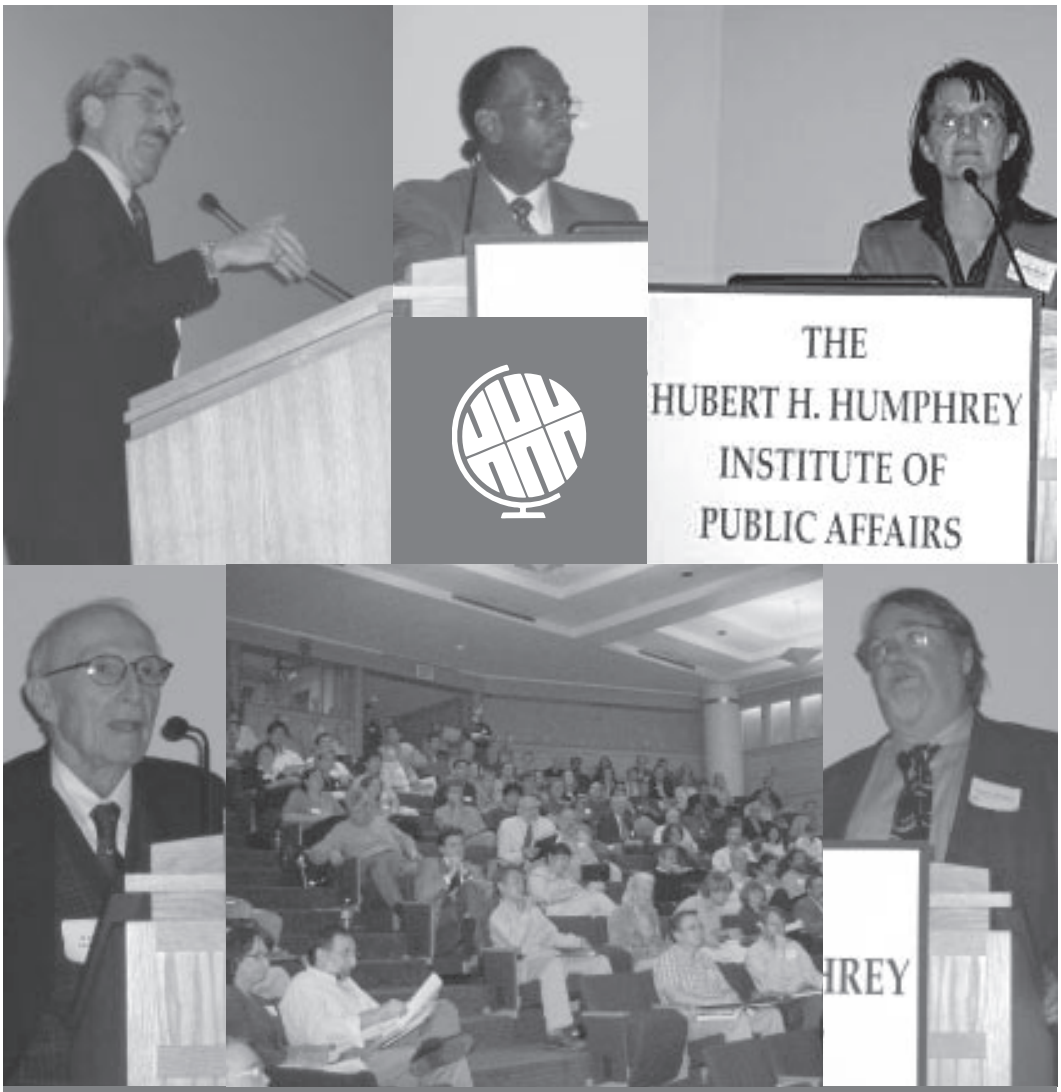


Figure 5. Current regulatory system in the U.S. in the context of nanoproducts
Source: E. Michelson presentation, September 15, 2005.





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Mr. Michelson stressed that it is important to consider both the current and potential cracks in the regulatory system, as well as the general approach that we, as a society, want to take towards regulation. He indicated that some products, such as cosmetics, make it through the system today without any required safety review (Figure 5, page 24). For some substances, like drugs, there is comprehensive safety review, and other products fall in between these two extremes. He also identified a range of potential approaches to the regulation of nanomaterials, from more restrictive, like a moratorium on use or the treatment of nanomaterials as new substances, to more permissive, like voluntary standards and guidelines or no special state of regulation. Mr. Michelson discussed an example where proactive regulation, in the form of a city ordinance for use of recombinant DNA in Cambridge MA in 1976, was one of the factors that led Biogen to move its headquarters to that area. Public aspects of transparency, good governance, and a mature understanding of the field made the location attractive for business.

He concluded with several important questions about oversight at the nano-bio interface (Box 5), including whether the federal agencies have the authority to appropriately regulate nanotechnology, whether the political will exists to do so, and whether the agencies have the resources to do so, even with the authority and will.

Box 5. Key questions about nano-bio governance

Source: E. Michelson, presentation, September 15, 2005.

- Whom does the public trust to manage the risks posed by nanotechnology?
- Has risk information been communicated and made available to the public?
- Are public perceptions being included and used to inform debates about proposed and pending regulation? What mechanisms work best to regulate nanotechnology-based products?
- Have potential long-term risks, issues, and consequences been analyzed? If so, by whom and how?
- How have uncertainties and "domains of ignorance" been taken into account during the decision-making, policy-making, and standard-setting process?
- Who will be responsible, and who will be held accountable, for any unforeseen harm, ill-use, or dangerous applications of nanotechnology?
- Do EPA, OSHA, USDA, etc. have the authority to regulate nanotechnology?
- Does the political will exist to implement that authority?
- Do the agencies have the resources (e.g., money, people, expertise, etc.), even if authority and will exist?

Alan Ziegler, Member of the Board of Directors of the Converging Technologies Bar Association (CTBA), discussed a non-regulatory scheme for governance that combines tort law and insurance to reduce social costs and harm, and how this scheme could be used for the products of nanotechnology. The primary function of tort law is to remedy harm or compensate victims, while that of insurance is to spread risk. However, both also create incentives to reduce accidents in business operations and affect the pace of change and innovation in society.

Specifically, he discussed the concept of enterprise liability and two theories under it. One theory is that it is fair to put the burden of action on those who have ability to pay and spread the risk (i.e., fairness rationale). The other theory is based on the notion that if potential injurers know they will be held liable for harm, they will take appropriate actions to reduce harm (i.e., economic rationale). In some cases, a defect in manufacturing, design, or warning is necessary for product liability. However, in other cases, an injury traceable to the product used in its normal way may be enough for liability. Recently, there has been a tidal wave of litigation for medical products. In some cases, this stifles innovation in development of useful products. For example, a drug that works great 99.8% of the time and leads to serious harm 0.2% of the time could potentially cost developers billions of dollars in lawsuits, much more than profits from the sale of it. Nano-bio products face this climate of liability and litigation.

Insurance can provide some protection to developers, but there are issues that reduce its effectiveness. Moral hazard is a theory in which developers that have insurance may change their behavior and engage in more risky actions. Also, as uncertainty in risk increases, premium costs rise to the level where coverage effectively is not available for valuable societal activities. Mr. Ziegler gave the example of insurance for vaccine developers. In the 1970s, costs of the insurance on the DTP vaccine for children rose 2000%, and 96% of that rise was due to product litigation. Due to cost, insurance essentially was not available to developers. Insurers have the ability to set safety standards for those they insure, and lower premiums if standards are met. In this sense, they are helping to manage risks in industry. If the developer does not comply, the insurance policy costs could increase or the policy could be cancelled.

Many believe that the greatest benefits of the nano-bio interface will come in medicine and pharmaceuticals, but Mr. Ziegler raised concerns that current insurance practices will not be able to cope with coming changes in nanoproducts, as they will be too revolutionary, widespread, and rapid. High litigation and lack of affordable insurance could deter research and development, or if development occurs, products may only be affordable for very few. He described ways of dealing with this issue. For example, government could absorb the costs as the defendant, statutory caps could be placed on compensation for harm, government could indemnify victims, or statutory restrictions could be placed on lawsuits. He proposes that we need statutory change if we are to reap the benefits of nanotechnology: we need to tighten regulations so mishaps do not occur; insulate manufacturers if they follow tight regulations; and create selected compensation funds. These actions would remove substantial obstacles to realizing the promise of nanotechnology.

Striking a Balance

Society is both a supporter and watchdog of new technologies, and it strikes a balance between allowing technology to flourish and limiting it to acceptable use. Organizations play multiple roles, sometimes both promoting technology while ensuring its safety. The societal context for the nano-bio interface includes social, economic, institutional, political, and ethical issues and is not limited to technical risk or regulatory authority. In the past, there have been tendencies in scientific communities to argue for governance based solely on "sound science." Yet, science alone cannot determine what level of risk is acceptable, and factors involved in risk analysis vary among regulatory agencies. Risk managers consider other factors, including social ones, before making decisions. Decisions are seldom based solely on science, especially when significant scientific uncertainty exists. Societal contexts come into play in setting the scope of technical risk assessments and interpreting their relevance for communities.[10] In this model, the public is not just the recipient of risk communication, but actively involved in all facets of risk analysis and decision making. In the third session of the workshop, questions of oversight were expanded from technical risks and benefits of nanoparticles and regulatory frameworks and authorities, to societal contexts that interpret and affect nano-bio applications.

First and foremost, there is a need to understand public viewpoints on nanotechnology and learn more about its context from the perspective of non-experts. Jane Macoubrie, Senior Visiting Scholar at the Woodrow Wilson International Center for Scholars, spoke about her work on public perception of nanotechnology and trust in government. In two separate surveys in 2004, she found that 95% of respondents did not trust government or industry to effectively manage the risks associated with nanotechnology.[11] In experimental issue groups where people were given information on nanotechnology, she found that medical and general industrial applications for nanotechnology generated lower trust and that higher education levels of participants predicted lower trust. People's basis of concern was generally experience, or a "history of failed precautions." However, at the same time, her studies found that people are excited about the benefits and the knowledge to be gained through nanotechnology.

In 2005, Dr. Macoubrie conducted another study to address why there is such low trust in government and industry, what people want that would increase trust, and where people are presently getting information about nanotechnology.[12] The work also addressed whether trust was relative to specific regulatory agencies or parts of government, why there was such low trust in medical and industrial applications, and whether new information on nano-bio convergence would have influence on trust. In this study, she found that people generally do not have knowledge of nanotechnology, but once given information, they have

[10] National Research Council. *Understanding Risk* (1996).
[11] Cobb, M. and Macoubrie, J. Public perceptions about nanotechnology: risks, benefits and trust. *Journal of Nanoparticle Research* 6: 395-405 (2004).
[12] Macoubrie, J. Pew Charitable Trusts Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, *Informed Public Perceptions of Nanotechnology and Trust in Government*, September (2005).

neutral or positive attitudes about it. She also found that people tend to get information about nanotechnology primarily from public television and radio, word of mouth, or magazines. In her study, there was increased trust in some agencies after learning about nanotechnology, but less in others. Before and after learning, participants trusted Congress and the White House the least, and after learning, participants lost trust in FDA and USDA. Top categories of concern among the participants were "true unknowns"(13%), regulation (13%), human health risks (13%), testing and research for safety (12%), and effect on the environment (10%).

The study groups recommended the following for restoring public trust: better and more testing to discover risks; engaging the public and providing information; and adopting mandatory standards. Group participants generally thought that voluntary standards are not enough. However, 76% said that a ban on nanotechnology would be over reacting. Dr. Macoubrie emphasized that the public has a particular perspective, one that industry and regulators should consider. She argued that for nanotechnology, we do not want to spend billions of dollars and end up with an industry that lacks the confidence of consumers and is not viable.

Robert Hoerr, Cofounder, Chairman, and CEO of Nanocopoeia, Inc., presented the small company perspective. His company is very much aware of the importance of public perception and the value of proceding with caution. It developed the ElectroNanoSpray™ nanoparticle generator for use in creating suspensions of particles for gene delivery, drug formulation, device coating, and other applications. Researchers at his company are positioned amidst the convergence of drugs, devices, and nanotechnology, and Dr. Hoerr raised the concern that what they are doing might not fit nicely into the classic regulatory paradigm.

He pointed out that the same things that make nano-drugs attractive also present special concerns (Table 4). These concerns need to be kept in mind when a process is developed, and each compound and opportunity should be carefully reviewed. He also stated that nanotechnology presents unique risk characteristics, which are often unknown when work with the materials begins. Additionally, there is almost no one to turn to for help with risk information. For example, it is not clear what gloves or masks do to limit exposure to nanoparticles. Yet to reduce risk to workers, industry needs to control exposure. His company follows that principle in its laboratories. They use common sense, adherence to good manufacturing principles, and safe material handling procedures. Dr. Hoerr agreed that all stakeholders need to be involved in risk assessment and that future regulation should be data-driven and cost manageable. However, he argued that fear should not drive the process, as heavy regulatory burdens could have profound effects on small companies.

Paul Thompson, Professor of Philosophy and W.K. Kellogg Chair in Agricultural, Food, and Community Ethics at Michigan State University, discussed two topics related to nanotechnology used in agriculture and food: power relationships and changes in rural communities. He made the point that mobilization of groups will occur due to continued failure to address social and ethical issues surrounding technology. One social issue involves

power relations in the food system, which extends from suppliers to farmers; to processing, distribution and marketing in industries; and finally to consumers. Retailers and consumers haven't typically been engaged in what is happening in early stages. Important factors for them have been price and quality, as they are visible and testable. However, recently, there have been changes in this paradigm. For example, retailers are increasingly interested in upstream processes for inventory control and product standards (e.g., grocery chains refusing to sell genetically modified foods), and consumers are starting to show interest in upstream processing (e.g., organic farming, animal treatment).

Dr. Thompson noted that these broad changes are in a sense technology-driven, but they are also affected by regulatory processes. Currently, regulation is based on the end-product and health and safety standards. He questioned what role regulation will take as we see a shift in consumer interest towards the supply chain. There will be a need to balance market power with protecting consumer rights to know and choose. He posed the question of whether consumers should have legal rights with respect to the food system. Early in the supply chain, process standards might not be wanted. For example, farmers might not want consumers telling them to not use genetically modified seed. Dr. Thompson suggested that questions of power and rights are too deep for scientists to handle alone.

There is evidence that technology has changed the structure of agriculture.[13] There are fewer and larger farms, and there is evidence for decline in rural communities as a result. Dr. Thompson noted that agricultural biotechnology was debated in this context, and as a result, there is dissatisfaction with it. Non-governmental organizations (NGOs) and community groups have pushed to influence directions for agricultural research that more directly serve the public. However, they have largely been unheard, and therefore, such groups have shifted focus to where they can challenge what is occurring, for example, through litigation and regulatory challenges. He asked whether concerns about the structure of industry, consumer choice, and ultimately, what is in the best interest of the public, are on the trade-off agenda for agrifood nanotechnology.

Karen Florini, Senior Attorney at Environmental Defense (ED), evaluated current regulatory activities for nanotechnology that affect public perception of safety. ED is optimistic about nanotechnology's promise for the environment--for cleaner or renewable energy, more efficient lighting, water filtration, and lightweighting of materials. However, the organization is concerned about the toxicity of engineered nanomaterials. In 1998, ED worked in collaboration with the American Chemistry Council and EPA to create a program under which chemical producers agreed to generate screening-level toxicity data for high production volume (HPV) chemicals. This program illustrated that voluntary initiatives can play a useful role under certain circumstances in addressing environmental concerns. The HPV challenge was prompted in part by an ED study showing that 71% of a pilot group of HPV chemicals lacked basic screening for toxicity, at least from what could be determined from the public record. Ms. Florini argued that more extensive information should be available for nanomaterials in light of the novel properties that they may exhibit.

[13] National Research Council. *Publicly Funded Agricultural Research and the Changing Structure of U.S. Agriculture* (2002).

With other chemicals, ED has seen significant problems arise with government oversight, liability, and public perception. Ms. Florini posed the question of how we can get nanotechnology right this time. She summarized four key steps: increase risk research funding by government and industry, develop effective regulations, introduce voluntary interim standards, and conduct meaningful stakeholder engagement. She noted that it is difficult to tease out exactly how much money is spent on risk implications research, as current statistics often mix those funds with those for applications of nanotechnology. Her group believes that much more should be spent on research to assess the risk of nanomaterials.

Ms. Florini listed potential regulatory avenues, or statutes that could apply to the products of nanotechnology. However, she said that there is skepticism in the environmental law community about whether those statutes, with the exception of FFDCA and TSCA, will be used for nanomaterials in the near to medium term. With respect to TSCA, there are a number of critical issues as to whether the statute will be able to accomplish anything. For example, there are important questions about which nanoparticles are new chemicals under TSCA, and thus triggered for the Pre-Market Notification (PMN) program; what data are needed for PMN reviews; and whether current PMN exemptions make sense. NNI defines nanotechnology as creating and using structures that have novel properties, yet under TSCA, some nanomaterials might not be considered new, as the molecular structure or formula might be the same. Her proposal is that an engineered nanomaterial should be considered new regardless of whether its molecular structure of formula is new, unless its chemical and physical properties are demonstrably the same as its conventional analog.

Ms. Florini also noted that there are currently no baseline data requirements under PMN. Developers are required to submit the chemical's identity and modest additional information. If developers have toxicity data, they must submit it, but they are not required to generate it unless EPA asks them specifically to do so. She and others at ED believe that EPA should provide nanomaterial producers with guidance on data that should be included with a PMN, such as basic information on chemical characteristics, environmental fate and transport, and toxicity. Finally, she emphasized the importance of stakeholder involvement in the design of oversight systems, including people from civil society, labor, industry, and academe.

Davis Baird, Professor of Philosophy at the University of South Carolina, spoke about his work on the societal, epistemological, and ethical dimensions of nanotechnology. He indicated that as a society, we need to understand nanotechnology from the inside. Nanotechnology should not be put in a "black box" and thought of as having "impacts" on society. Instead, we should open up the box and study the "interactions" between social and ethical practices and creating knowledge at the nanoscale. He stressed that understanding and directing these interactions will require understanding the practices of knowledge production and dissemination. This understanding can only be achieved by bringing multiple disciplines into fruitful exchange. However, Dr. Baird pointed out that there are barriers in universities to multidisciplinary research, such as reward and tenure systems.

Communication about nanotechnology will impact how the public views nanotechnology and affects the governance of it. As one example, Dr. Baird's group is working on how nanotechnology is portrayed visually to the public. In some instances, visual images of nanotechnology look very familiar (e.g., IBM logo written at the nanoscale). However, the real "nanoworld" might look very different (e.g., filled with motion and collision). Images are very important, and his group is investigating what it takes to better understand and use images of the nanoscale.

Table 4. An example of balance: the promise and pitfalls of drug nanoparticles

Source: R. Hoerr, presentation, September 15, 2005.

Promise	Pitfalls
Increased surface area	Increased reactivity?
Increased bioavailability	Increased toxicity?
Lower doses effective	Lower doses toxic?
Skin and membrane penetration may speed onset of action	Toxicity through nontraditional routes of administration?

The Future

The final session of the workshop addressed the need to look toward and consider far-future applications of nanotechnology in the design of oversight systems. For example, some are now concerned that the 1986 Coordinated Framework for the Regulation of Biotechnology was not designed for the present diversity of biotechnology products and that existing laws are being twisted in strange ways (e.g., genetically engineered animals are proposed to be regulated as new animal drugs under FDA). The developers of the coordinated framework did not necessarily envision the types of products now in development.

Christine Peterson, Vice President of the Foresight Nanotech Institute, described mid- and longer-term time frames for the future. In the mid-term, five years and beyond, more active nanostructures will be developed, such as sensors, actuators, and targeted drugs. She argued that it is difficult to get information in this time frame, as it is beyond most business time frames, and academics do not like to speculate. The military is paying attention to it, and important economic and strategic changes accompany its evolution.

In the longer term, molecular nanosystems, not just materials or single devices, will emerge. The boundaries for this era will be limited only by what is physically or chemically possible. Longer term goals for the use of nanotechnology might also include more complete control of the structure of matter, making materials atomically precise, and designing molecular machines to do work. With these future applications, additional governance issues arise. Health and environmental safety issues will still be around, however, concerns about privacy and surveillance will increase, as well as the use of nanotechnology for terrorism.

Applications to human enhancement will present society with fundamental social and ethical issues. Nanotechnology could someday be used to improve senses, memory, strength, and beauty; delay or even stop aging; or control emotion and personality. Ms. Peterson posed the question of whether these applications should be illegal and raised the point that in an international context, they are unlikely to be illegal everywhere. Differences in international governance could create inequalities, as only people who can afford to travel and pay for such enhancements will benefit. Furthermore, there will be cultural differences in acceptance of these applications, and values of various societies need to be respected.

Her organization is developing guidelines for safer development of nanotechnology,[14] which are designed to address the potential positive and negative consequences in an open and scientifically accurate matter. The objective of the guidelines is to provide a basis for informed policy decisions by citizens and governments. Specific guidelines for the responsible development of nanotechnology-based productive nanosystems are included.[15] Ms. Peterson views voluntary guidelines as the first step, although they are not enough. She challenges those who say certain applications are impossible, remembering when many said that about the internet and mammalian cloning, and argued that we need to stretch our minds in thinking about the future.

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[14] Foresight Nanotech Institute. *Foresight Guidelines Version 4.0: Self Assessment Scorecards for Safer Development of Nanotechnology* by N. Jacobstein and G. H. Reynolds Version 4.0: http://www.foresight.org/guidelines/current.html (2004).

[15] http://www.foresight.org/guidelines/current.html

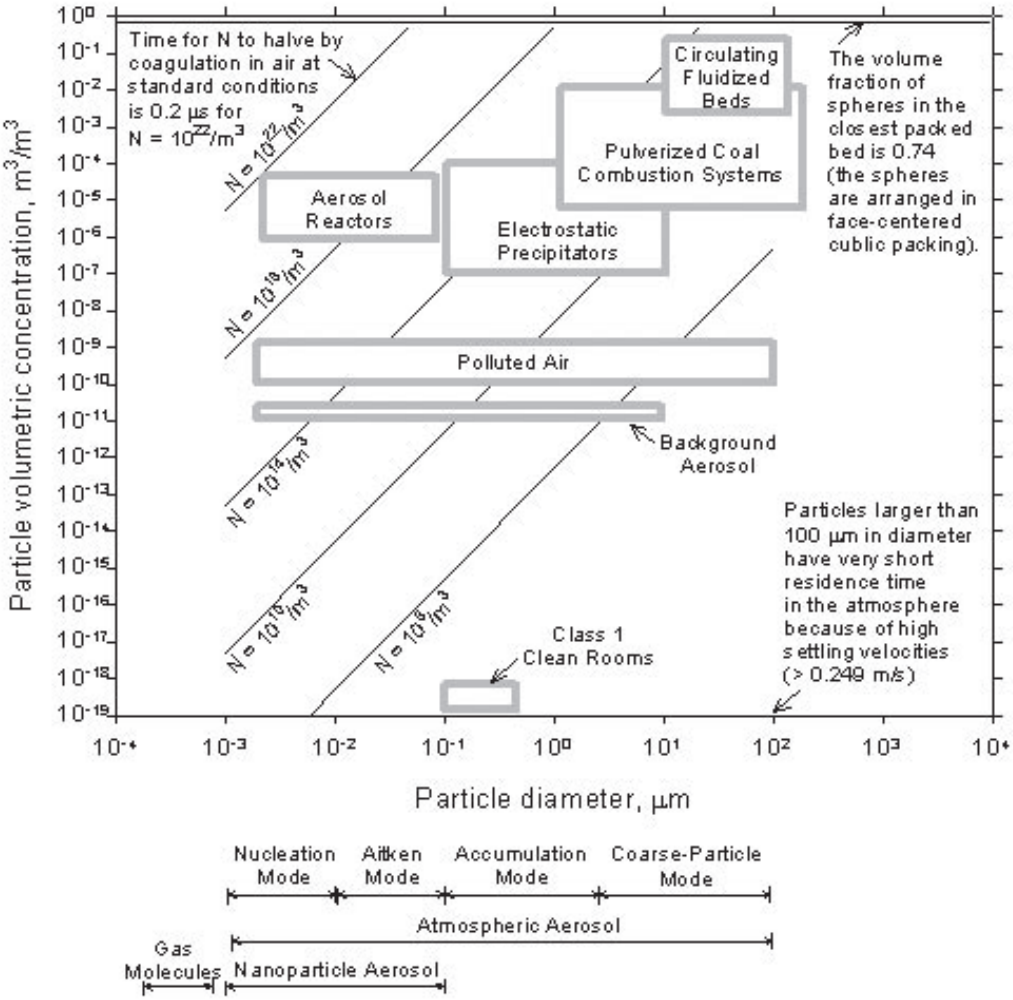
Richard H. Smith, President of the Nanotechnology Network Principal, focused on governance of nanotechnology from an investment perspective. He discussed the need for a paradigm shift from doing "normal science," in the definition of Thomas Kuhn, or "business as usual," to investing heavily in nanotechnology to solve great societal problems. He made the point that we are currently investing about $1 billion a year in nanotechnology, but we make much larger investments in science that is not as ground breaking. For example, we invest $35 billion in NIH, where projects generally need to be sure bets. He gave the example that we are spending a lot of resources to recover from Hurricane Katrina (approximately $500 M a day in September 2005), yet nanotechnology could be used to prevent disasters such as this one, or to recover from them. He argued that big investments in nanoapplications will pay off in the long run and recommended that we begin to invest in long-term, problem-focused nanoscience.

Sheldon Friedlander, Parsons Professor of Chemical Engineering at UCLA, described the parallels between aerosol science and nanoscience, and how the body of techniques and understanding from aerosol science could be used in the future for nanotechnology. Aerosol technology has a large domain, spanning particle diameters from 10^{-3} to 10^{2} μm (0.1 to 100000 nm) (Figure 6). There are aerosol and nanoparticles in the atmosphere, either naturally occurring, or from diesel emissions or industrial processes.

The aerosol system provides a useful example for developing powerful methodology. The aerosol industry has had many years of experience in data collection, including that for worker exposure. With aerosol technology, particles can be made as spherical droplets or aggregates and with specific side chains, and there is a good understanding about how aerosols form. Nanotechnology is a huge field, covering films, surfaces, liquids, and gases, and developing methodology for study of the environmental and health effects is hard to do as a result. Dr. Friedlander suggested that it would be beneficial to select focused systems that are well-established in order to better understand nanoscience and its applications.

Figure 6. Domains of aerosol technology

Source: S. Friedlander, presentation, September 15, 2005.



Conclusions

The following conclusions reflect themes that emerged from the workshop, however, given the diversity of participants (Appendix), not all of them necessarily agree with each particular one.

Defining Nanotechnology

Participants at the workshop disagreed to some extent on the importance of defining nanotechnology and its applications to biology. Some argued that definitions matter because we need to attribute benefits and pitfalls to nanotechnology, and they may be necessary with respect to governance under legal statutes and regulations. However, the nanotechnology-biology interface is broad, and many believe that we should be thinking about governance more broadly. Because there are so many diverse applications, it is important to distinguish between agricultural, industrial, and medical applications, as there are different regulatory and marketing implications, as well as different public perception and acceptance landscapes.

Participants questioned whether there will be a different set of requirements if something is defined as "nano. " FDA currently regulates according to product, not process, and in this case, the definition of nanotechnology might not be important for regulation. But many argue that there should be a different set of requirements given the public claim that nanotechnology and nanoproducts are new, have distinct properties, and allow us to do special things. Regardless, developers should not tell the public that nanotechnology is unique and thus will provide great benefits, and then turn around and tell them that a special regulatory look is not necessary. This seeming contradiction may cause a loss in public confidence in nanotechnology.

It is difficult to agree on a single definition for regulatory purposes, especially because every agency has to define nanotechnology in its own way based on the statutory authority it has. As a historical example, the Coordinated Framework for Biotechnology has operated for 20 years with different definitions of biotechnology in the federal agencies. However, many argued that definitions matter for other reasons, for example, so different disciplines have a common language for working with each other. Appreciating the way that words require meaning is important for communicating among disciplines and with the public. However, the public will perceive or define what nanotechnology is in its own way, and scientists and regulators have little control over definitions in this sphere.

The group generally agreed that we should change the use of "nanotechnology" for this field to "nanotechnologies" given the vast diversity of techniques and applications. There was also general agreement that definitions are important for particular conversations, such as those at the workshop, so participants know the focus of dialogue. However, energy and resources could be misspent coming up with a single, universal definition.

- **The use of the term "nanotechnologies" should be promoted in place of "nanotechnology."**
- **Different definitions of "nanotechnologies" may be necessary for different federal agencies due to various statutory authorities.**
- **Definitions for particular dialogues are appropriate; however, resources could be misspent coming up with a single, universal definition.**

Governance Mechanisms

Questions about governance were the focus of the workshop, and the group considered oversight paths for nanotechnologies applied to biological systems. Every new technology goes through a phase where society has choices in oversight mechanisms, and for nanoproducts, paths to governance have not been completely figured out. There is historical precedence for defaulting to systems that are already in place, and this is a choice for nanotechnologies. Other choices include rethinking current systems and redesigning them to better fit nanoproducts. Regardless, many participants stressed the need for greater interactions among policymakers, toxicologists, regulators, and developers of nanomaterials to address challenges with their oversight.

For nanoproducts, jurisdictional issues are important, as there are so many products emerging in the marketplace today. Overlaps or gaps among agency authorities need to be considered and addressed, such as the lack of required pre-market testing for cosmetics and foods.

Because of delays in new rule making at the federal level, many participants stressed the need for interim, voluntary guidelines, as it is easier to formulate than to issue regulations. The group discussed whether there should be a ban on certain types of research, ones for which there are significant unknowns about the consequences. For example, in the mid 1970s with recombinant DNA technology, scientists got together at the Asilomar conference and placed some restrictions on their work until more information could be obtained. At the workshop, the question arose about whether the same caution is needed for laboratory work given occupational health hazards associated with nanoparticles. The participants also discussed whether it is appropriate to put restrictions on research that may lead to applications that have great social consequences. Either way, interim production and use standards have a role to play, especially at the international level. In manufacturing and industry, the International Standards Organization (ISO) and American National Standard Institute are developing standards for nanotechnologies. However, in the end, solid government regulation builds trust and can be industry's friend. Many at the workshop noted that the public has more confidence in mandatory systems.

These and other specific ideas for governance from the presentations and dialogue are listed below.

- **Safety and toxicity issues should be discussed in open and multi-disciplinary settings before the widespread use of nanoparticles.**
- **New strategies in toxicology are needed to address the fact that nanomaterials have unique properties. Risk assessment paradigms may be the same, but the special properties of nanomaterials suggest that data and information needs for ensuring safety will be different.**
- **Governance frameworks for products of other technologies should be analyzed in order to learn from their lessons and assess their relevance to nanoproducts.**
- **Amending or developing new regulations and statutes is unlikely in the short, and possibly long term; therefore, creative ways to ensure that nanotechnology is used responsibly are needed. Voluntary programs and industry standards and guidelines can provide a bridge for ensuring health and environmental safety, but they should not be considered a permanent fix, as they will not ultimately foster public confidence.**
- **EPA needs additional resources to bolster its abilities to provide oversight for nanoproducts. The agency has multiple roles of funding research, risk assessment, and product safety review. Additional institutional capacity is needed to keep abreast of science and development in nanotechnology.**
- **FDA is challenged by limited statutory authority for some nanoproducts (e.g., cosmetics) and a lack of basic scientific information about nanomaterials and appropriate scientific tools to evaluate them.**
- **It is important to both consider the current and potential gaps in the regulatory system, as well as the general approach that we want to take towards regulation.**
- **The relevance of non-governmental oversight, such as liability and insurance systems, should be examined in the context of nano-bio products.**
- **Nanomaterials might not be considered new under TSCA, if the molecular structure or formula is the same as those already on the list. This could lead to gaps in oversight of health and environmental safety issues for nanomaterials. Engineered nanomaterials should be considered new regardless of whether its molecular structure of formula is "new," with the exception if their chemical and physical properties are demonstrated to be the same.**
- **EPA should provide nanomaterial producers with guidance on data that should be provided with PMNs, such as basic information on chemical characteristics, environmental fate and transport, and toxicity.**
- **The same things that make nano-drugs attractive also present special concerns. These concerns need to be kept in mind when a process is developed in industry, as workers are on the frontlines, and there is not sufficient guidance for many nanomaterials.**

Several participants stressed that public engagement in governance is needed and that there should be feedback mechanisms for public engagement early and often. The public should have input on the types of research and commercial products that are developed. Yet there are significant challenges to public engagement, including how to do it right and how to factor it into regulatory decisions (e.g., legal statutes do not allow for this). Others noted that early public engagement might not always be beneficial to industry, or even society as a whole. Some argue that this has been the case for embryonic stem cells in the United States, where the technology has been highly politicized and restricted. So, if the public is engaged in decision making, society might not get answers that are best for reaping benefits of the technology.

Public engagement in risk analysis was considered. Technical risk assessments give information on the magnitude and types of risks, but they cannot determine what "acceptable" levels of risk are. Different publics and cultures will view the same quantitative or qualitative risk differently. Risk perception leads to various interpretations, affected by whether people understand the risk, can control it, and choose to be exposed.[16] These all determine the severity of the consequences in the public eye. People care about equity, controllability, choice of exposure, time frames, intergenerational effects, and uncertainty when it comes to risk. Also, if there are greater rewards, people will likely accept greater risks (e.g., use of nanoparticles that can target cancer cells).

Traditional risk assessment paradigms have been focused on the need to be science driven, or based on "sound science." There has generally been a linear progression in that the results of risk assessments are handed to risk managers who make decisions. Then, the social context comes into play during the risk communication phase. However, there is a current wave of thinking that stakeholders and citizens should be more involved in setting the questions asked by analysts and helping to interpret them in their social context.[17] In addition, risk-based paradigms are ineffective if there is no mechanism to ensure the public availability of the data needed to evaluate risk. Currently, there are not good institutions for public engagement. Independent bodies of experts who people trust and with whom they can openly communicate are needed.

Goals of public engagement in risk analysis and governance can include either better regulation in a utilitarian sense or simply choosing the right thing to do from an ethical perspective. Although public participation in setting questions and providing knowledge for risk analysis is important, the public should not be forced to argue in the context of scientific or technical risks. There are multiple issues that concern people—the notion of what is natural and what is not, corporate control of technology and society, commercialization of science, government secrecy and impacts on trust, and how technology will affect their communities. There should be opportunities for discussion

[16] Slovic, P. "Perception of risk." *Science* 236: 280-285 (1987)
[17] National Research Council. *Understanding Risk*. (1996).

of these issues, so that they do not get confused with the technical risks and benefits to human health and the environment. Finally, there are good and bad ways of doing public participation. If the public is engaged, they should either have some ability to influence the outcome or at least know that many perspectives were considered in making decisions.

Transparency and honesty in governance is needed. Mistakes have been made with previous technologies. For example, it is difficult to get information on the regulation of biotechnology products, in part due to confidential business information (CBI). This problem might be magnified with nanoproducts, where the very chemical nature could be CBI. Currently, it is difficult to find out what is coming down the pipeline in the nanotechnology industries due to intellectual property rights and CBI. We need to consider how to balance the benefits of intellectual property protection with better transparency in governance.

In an international context, the future will be increasingly global. There are great global challenges associated with food, water, equity, the environment, and security. Nanotechnologies can play important roles in addressing these challenges. However, in the absence of institutions that can focus on societal contexts, it will be difficult to come to agreement on the appropriate use of technology. Better social institutions at the international level are needed for diplomacy, people to relate to each other, to work with others, and to understand different cultural perspectives.

Cultural differences will come into play with respect to applications for extending life, human enhancement, or privacy. Social and ethical issues not directly related to nanotechnologies will likely become associated with them. The emerging "nanoscience-biotechnology-information technology-cognitive science (NBIC)" interface and efforts to enhance human performance might fly in the face of what some people believe is an acceptable limit to science and challenge the notion of what it means to be human. Application of nanotechnologies such as these might be feared or perceived negatively by the public, and therefore, all applications might become tainted. Ethical debates should distinguish among various applications, and not only include utilitarian ethics, but also intrinsic questions about playing "god," rights to know and choose, and equitable deployment of technology.

The societal context for nanotechnologies was a focus of the workshop. Below are several conclusions and recommendations from the presentations and general workshop discussions.

- **"Risk" means not only health and environmental effects, but also has structural and perception components. It is not limited, in the public's eye, to technical risk assessments.**

- **Groups will mobilize against nanotechnology if we continue to fail to address the social and ethical issues.**

- **Conversations about nanotechnology should not be confined to science and safety. There are other important issues in nanotechnology governance, such as the structure of industry, equity of technology deployment, life-cycle of products, consumer rights, appropriate limits of technology, and power and control over the technology.**

- **Industry is generally aware of the importance of public perception and the value of proceeding with caution.**

- **Although public engagement is important, the oversight process should not be driven by fear, as unnecessary heavy regulatory burdens could have profound effects on small companies and limit nanomaterial development to large industry.**

- **To increase transparency, basic information on nature and toxicity of nanomaterials should be in the public record before entering the market.**

- **Public aspects of transparency, good governance, and a mature understanding of the field can make locations attractive for business by reducing potential uncertainty in research activities.**

- **Increased consumer attention to upstream food production processes is leading many to question whether and how to integrate process based concerns into a governance system that is largely product and safety based. Issues concerning the structure of agriculture, power distributions, rights of consumers, and ultimately, what is in the best interest of the public, are likely to emerge as nanotechnology is applied to food and agriculture. They require attention and consideration.**

- **Novel social and ethical issues will likely arise from the far-future applications of nanotechnologies, especially at the nano-bio interface. As a society, we need to begin to consider such issues, while stretching our minds about what possible applications will emerge.**

- **There are needs to reframe the interface of nanotechnology with society. Currently, the technology is seen as "having impacts" on society, but in reality, the technology "interacts" in many ways with society, and these interactions are not unidirectional.**

- **Understanding interactions between nanotechnology and society is best achieved by bringing multiple different disciplines into fruitful exchange. However, there are barriers in universities to multidisciplinary research, such as reward and tenure systems, and these barriers should be overcome.**

- **Better social institutions are needed for diplomacy; people to relate to each other; and discussing social, ethical and political issues surrounding the nano-bio interface.**

Communication and Education

In studies presented at the workshop, the public seems to want more information about nanotechnology. Participants discussed needs in communication and education, such as a "citizen school" about nanotechnology. Outreach could be done through local libraries, YMCAs, science museums, and community groups. There were suggestions to get students involved in education and thinking about social issues. Citizens generally want to learn more and have the capacity to do so, but experts and policy makers need to be willing to engage with them, listen, and educate.

Right now, there is a lot of hype about the promise of nanotechnology, and developers need to be careful about what they promise that the technology can do. Hype can ultimately lead to adverse public reaction, and the public can generally see through it, especially if they are not directly experiencing the benefits. There is a need to be cautious of overselling nanotechnology. Independent voices for education and communication are needed.

- **Communication about nanotechnology will impact how the public views nanotechnology, and ultimately it will affect the governance of it.**
- **Images of nanotechnology are important for public communication.**
- **Independent voices are needed for education and communication.**
- **Communicating hype about the promise of nanotechnologies should be avoided.**

Research Agenda

Research funding is an integral part of technology governance. In the workshop discussions, many pointed out that more funding is needed for research on the implications or impacts of nanomaterials. There is also a need for applications research to be tied to implications, and the two should be integrated in the federal research agenda. One specific implications research need is long-term toxicity tests on and testing protocols for nanoproducts. Some participants suggested that a coalition of industry, NGO, government, and academe should consult and jointly fund safety work.

Other research needs that were suggested include more projects on big, problem-focused nanotechnology and on societal implications.

- **Implications research should be distinguished, as much as possible, from applications research and given considerably more attention and funding.**
- **To solve great societal problems, structural changes in research funding are needed. Funding organizations should shift some of their focus and invest larger amounts in problem-focused nanoscience, such as clean energy, water sanitation, and disaster prevention.**

- **Funding for research on societal contexts for nanotechnology and public engagement methods should be increased.**

- **Aerosol technology should be considered as a model for better understanding nanotechnologies, their applications, and risks. It is a mature field that is rich with data and methods.**

Concluding Remarks

The conference was successful in highlighting the various oversight opportunities and challenges at the nanotechnology-biology interface. We hope it is just a step towards continuing dialogue and activity on this topic.

Appendix —Discussion Group Participants[19]

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*__Lynn L. Bergeson,__ Managing Director, Bergeson & Campbell, P.C., Washington, DC

__Dan Burk,__ Professor of Law, University of Minnesota

*__Jacob N. Finkelstein,__ Professor, Environmental Medicine and Radiation Oncology, University of Rochester School of Medicine

*__Karen Florini,__ Senior Attorney, Environmental Defense, Washington DC

*__Sheldon K. Friedlander,__ Parsons Professor of Chemical Engineering, UCLA

__Gene Goddard__, Biosciences Industry Specialist, MN Dept. of Employment and Economic Development

*__Darrel Gubrud,__ President, Gubrud Consulting, MN Nanotechnology Initiative

__Ken Hallberg,__ MN Nanotechnology Initiative

*__Robert Hoerr,__ CEO, Nanocopoeia, Inc., Minneapolis, MN

__Robbin Johnson,__ Senior Vice President, Cargill, Inc.

*__Kenneth H. Keller,__ Charles M. Denny, Jr. Professor of Science, Technology, and Public Policy, Humphrey Institute, University of Minnesota

__Steven J. Keough,__ Vice President, Surmodics, Inc.

__Jacques Koppel,__ The Koppel Group, Inc.

*__Jennifer Kuzma,__ Associate Director and Assistant Professor, Center for Science, Technology, and Public Policy, Humphrey Institute, University of Minnesota

*__Jane Macoubrie,__ Senior Visiting Scholar, Woodrow Wilson International Center for Scholars

*__Evan Michelson,__ Research Associate, Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars

Deb Newberry, Director, NanoScience Program, Dakota County Technical College, MN
Jordan Paradise, Associate Director for Research and Education, Consortium on Law and Values in Health, Environment, and the Life Sciences, University of Minnesota

*__Christine Peterson,__ Vice President for Public Policy, Foresight Institute
*__David Pui,__ Distinguished McKnight University Professor, Particle Technology Laboratory, University of Minnesota

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*__Alan S. Ziegler,__ Member of the Board of Directors of the Converging Technologies Bar Association and Attorney with Sweeney Lev LLC, Montclair, New Jersey

[19]The discussion group includes presenters and other participants who met on the day following the public workshop. Presenters are denoted with an asterisk. Views expressed in this document do not necessarily reflect the opinions of each individual listed here or the organizations with which they are affiliated.

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