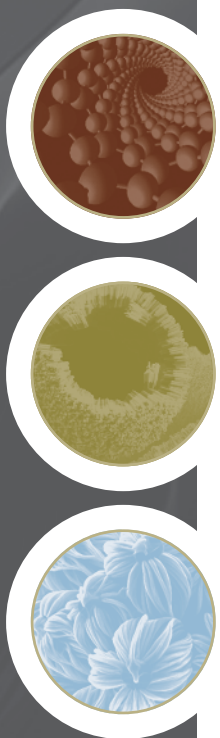
Woodrow Wilson International Center for Scholars
Project on Emerging Nanotechnologies

THINKING BIG ABOUT THINGS SMALL:

Creating an Effective Oversight System for Nanotechnology

Mark Greenwood



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Foreword

Hundreds of nanotechnology-enabled products have already entered the market in areas ranging from cosmetics to foods to sporting goods. The rate of commercialization is poised to accelerate, with products increasing in both number and diversity across multiple industrial sectors. However, the oversight system for nanotechnologies is immature. Given the novel behavior and properties of nanoscale materials, it is not obvious whether, or to what extent, existing regulations might apply. To date, discussions about nanotechnology oversight have focused on the adequacy of specific statutes, such as the Toxic Substances Control Act (TSCA) administered by the Environmental Protection Agency (EPA). There has been far less discussion about the adequacy of the analytical assumptions and approaches underlying our environmental statutes in general. For instance, will core assumptions about risk assessment and risk management translate from a macro to a nano world? Because nanotechnology is already here, and both workers and consumers may already be exposed to risks, we cannot afford to "wait and see."

This report looks broadly at a variety of regulatory approaches for products and facilities and examines the analytic methodologies—such as emissions monitoring or the use of analogies and structure activity relationships to predict risks—that underpin these regulations. In most cases, the report uses EPA and its regulations as a basis for discussion. In every case, nanoscale materials will likely challenge the existing approaches, potentially rendering them inoperative or, at best, sub-optimal.

As an alternative, the report suggests that a number of statute-independent questions need to be addressed and answered by government, industry, non-governmental organizations (NGOs), and other key stakeholders. These questions involve:

- Risk criteria (what is and is not a problem?);
- Information needs (what do we need to know to support decision-making?); and
- Risk management measures (what tools should be used to manage risk?).

Solving issues in these areas, rather than relying strictly on specific statutes, will be key to effective nanotechnology oversight. In addition, a serious discussion of these core elements of an oversight system is likely to increase industry engagement and provide better guidance to technology developers that operate on the cutting edge of the science.

There is much at stake. How the oversight system evolves at this early stage will have significant impacts on industry structure, the competitive strategies of firms, and approaches to intellectual property. It can ultimately define who can "play" or not, especially if the costs of testing and data submissions are high. These impacts have not received the attention they deserve but need to be addressed as soon as possible.

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Executive Summary

As nanotechnology becomes more and more a commercial reality, concerns about the adequacy of current oversight tools have increased and discussions of possible new oversight methods have begun. This report looks at oversight as encompassing a wide range of mechanisms and institutions that will be involved in protecting human health and the environment. The purpose of this report is to focus greater public attention on three sets of issues that will necessarily define the framework of an effective oversight system for nanoscale materials, regardless of the agency or regulatory statute:

- Risk criteria (what is and is not a problem?);
- Information needs (what do we need to know to support decision-making?); and
- Risk management measures (what tools should be used to manage risk?).

Current public discussions about the emerging oversight system have not given adequate attention to these topics but, instead, have tended to focus on specific laws and statutes. Essentially, we have let the laws set the boundaries of our discussion, rather than exploring a wider set of questions that need to be answered if society is to adequately address any potential risks from nanotechnologies.

The report begins by examining the issues that arise when present approaches to risk characterization, including the use of analogies and structure activity models, are applied to nanotechnology. These approaches assume that our existing knowledge of chemical behavior is a fairly good predictor of the future, an assumption that may be undermined by the emergence of novel properties at the nanoscale. Determining the nature and extent of exposure will also be problematic, especially across the entire life cycle of nanotechnology-based products.

Attempts to characterize risks will lead to the development of information needs. These are likely to be the subject of some of the first major debates around the appropriate levels of oversight. The amount of information needed to understand the risks and exposure routes of nanomaterials is likely to be more extensive, and expensive, than what is currently expected for conventional chemicals. New testing may be needed. This will raise real issues about who can support testing obligations and whether these obligations will become barriers to innovation or significant hurdles for small businesses. In the end, information requirements and associated testing may ultimately determine what products will be viable and what businesses will succeed.

As companies and government approach the larger issues around risk management, the limitations of existing laws become more apparent. Existing product-based regulations have difficulty addressing issues related to environmental releases of materials during use and waste management scenarios that will arise with products at the end of their life cycles. An oversight system is needed that will function across the entire life cycle, managing risks where the need is greatest. One part of this system may include the use of labels for

nanoscale materials—an issue that is likely to be contentious—as will other measures designed to increase transparency through the public disclosure of information.

Given the flow of new nanotechnology-based products into the marketplace, we cannot defer discussions about risk criteria, information needs and risk management measures. Oversight decisions are being made today, and companies are already having discussions about guidelines to protect workers from potential exposures. The evolving requirements of any oversight system will have long-term impacts on business models that can be successful in the development of nanotechnology. The purpose of this report is to force the discussion of nanotechnology oversight outside of the confines of existing laws and statutes in the hope that more innovative solutions can be found that both foster innovation and protect humans and the environment.

Introduction

Nanotechnology is no longer the stuff of dreams. It has become an important technological driver of innovation in today's economy. With this emerging role, nanotechnology poses an inevitable question: How can we make sure that it will be used safely?

The public discussion of this question has already begun. A wide spectrum of interests in the United States seems to agree that some form of oversight system is needed to assure that nanotechnology develops without adverse effects on health, safety and the environment. Many groups recognize the potential societal benefits of nanotechnology, from a variety of perspectives. At the same time, there also seems to be a common understanding that some nanoscale materials will have hazardous properties that need to be identified and managed. While the specifics of how to manage these risks has spawned many debates and the political process for improving the oversight system has begun, much of the rhetorical excess that has haunted the development of biotechnology has so far been avoided.

This support for some form of oversight system anticipates that a set of institutions will need to assure that common terms, best practices, testing obligations and public accountability will be established. Certainly government regulation will play a key role in the oversight system, but it is both unnecessary and impractical to leave the oversight role entirely to a limited set of already overburdened federal agencies. Nanotechnology is moving too quickly for such a strategy. Instead, a variety of consensus standards, codes and understandings, both domestic and international, are likely to play key roles in the oversight system for nanotechnology.

Thus, when using the term "oversight system," this report intends to include the full range of institutions and mechanisms that could be involved in the protection of health, safety and the environment. While examples will be drawn primarily from the experience of government, the intent of this report is to identify the issues that need attention, rather than to address questions about what institutions should set policy.

The purpose of this report is to focus greater public attention on three sets of issues that will necessarily define the framework of an oversight system for nanoscale materials:

- Risk criteria (what is and is not a problem?);
- Information needs (what do we need to know to support decision-making?); and
- Risk management measures (what tools should be used to manage risk?).

Current public discussions about the emerging oversight system have not given adequate attention to these topics.

A variety of well-intentioned, cooperative efforts are currently addressing questions that are important, but somewhat narrow. For example, the U.S. Environmental Protection Agency (EPA) has been grappling with questions about the jurisdiction of the Toxic Substances Control Act (TSCA) over nanotechnology, and the agency has begun exploring a voluntary program to obtain information on existing nanotechnology substances in the

marketplace. Clearly, EPA is trying to determine how to "get started" on what will be a long, complex endeavor and thus is undertaking what appear to be manageable steps. While such an approach is understandable, is it a strategy that meets the challenges of nanotechnology?

Commercialization of nanotechnology is moving very quickly. A recent inventory of nanotechnology-enabled consumer products has identified over 380 products already in commerce from 17 countries.[1] Another study has indicated that the number of nanotechnology-enabled drugs and biomedical devices in the pipeline for regulation has increased by almost 70 percent in just one year.[2,3] A new inventory just released in Japan has identified over 260 products in the marketplace, including over 90 cosmetics and over 15 food products.[4]

Under these circumstances, an incremental approach to creating a reasonable oversight system is not a prudent strategy. It is time for government, industry, the scientific community, non-governmental organizations (NGOs) and other interested parties to begin a more systematic discussion about the core elements of an oversight framework for nanoscale materials, both those already on the market and those that are likely to follow in the near future. This should include substantive debate about the three topics—risk criteria, information needs and risk management measures—addressed by this report. Greater understanding—and, hopefully, consensus—about the general design of an improve oversight system will provide a context and a sense of direction for all parties who are working toward common goals, while recognizing that there may be several paths to the same endpoint.

1. See Inventory of Nanotechnology Consumer Products, Washington, DC: Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, 2006, available at http://www.nanotechproject.org/consumerproducts, accessed January 3, 2007.
2. *2006 Nanomedicine, Device & Diagnostics Report.* Atlanta, GA: NanoBiotech News, National Health Information, LLC, 2006.
3. A list of nano-based medical products already available on the market, including drugs, drug delivery devices and diagnostic tests, can be found at Nanotechnology and Medicine Inventory, Washington, DC: Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, October 2006, available at http://www.nanotechproject.org/86, accessed January 3, 2007.
4. This online inventory can by found at http://staff.aist.go.jp/kishimoto-atsuo/nano/index.htm and in a translated version at http://translate.google.com/translate?u=http%3A%2F%2Fstaff.aist.go.jp%2Fkishimoto-atsuo%2Fnano%2Findex.htm&langpair=ja%7Cen&hl=en&safe=off&ie=UTF-8&oe=UTF-8&prev=%2Flanguage_tools, accessed January 3, 2007.

The Need for Effective Oversight

Why Now?

Certainly some will argue that the core issues identified in this report are complex and will benefit from more information and experience. In a slower-moving context, such a strategy would make sense. It is a mistake, however, to defer discussion about the risk criteria, information needs and risk management measures that will underpin an effective oversight system for nanotechnology for the following reasons:

- Oversight decisions are being made today. Government agencies are already conducting reviews of new nanoscale materials. In doing so, they are taking positions in all three of the key areas. What is missing is a public discussion of these positions.

- In industry, groups of leading companies are beginning to discuss guidelines about how to protect workers potentially exposed to nanoscale materials. As they do so, they will inevitably be reaching conclusions in each of the three areas.

- A better understanding of the risk criteria and information needs that will initially guide nanotechnology oversight would facilitate consensus on a roadmap for research priorities. In 2005, EPA solicited comment on its *Nanotechnology White Paper*, which discusses the agency's research needs related to nanotechnology.[5] While the document is a serious look at the range of issues that can arise with nanotechnology, it is less successful as a practical statement of priorities about nanotechnology research, given EPA's limited budget for such work.[6]

- A serious discussion of the core elements of an oversight system is likely to increase industry engagement. Many of the innovators in this field are small companies that often lack the human and financial resources to participate in pilot programs or other initiatives that seem preliminary. Some of these firms do not have highly developed product stewardship systems for addressing the health and environmental implications of their products. Such firms are much more likely to step forward to participate in a discussion that addresses core requirements about the risk criteria, information requirements and risk management

5. *External Review Draft Nanotechnology White Paper.* Washington, DC: Environmental Protection Agency, December 2, 2005, available at www.epa.gov/osa/pdfs/EPA_nanotechnology_white_paper_external_review_draft_12-02-2005.pdf, accessed January 3, 2007 ("EPA White Paper").
6. In September 2006, the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the Committee on Technology, National Science and Technology Council issued a similar strategy document, entitled *Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials*. This document is more successful as a summary of research that has, and could be, conducted than as a pragmatic action plan. Both the EPA and NSET documents serve as a reminder that the United States Government is under-funding its overall research program on the health and safety aspects of nanotechnology. As indicated in a recent report by Dr. Andrew Maynard of the Woodrow Wilson International Center for Scholars, *Nanotechnology: A Research Strategy for Addressing Risk*, the U.S. Government's investment in such research is quite small. In the long run it is critical to increase the scope and pace of health and environmental research on nanomaterials so the results are available to inform oversight decisions as well as help in communicating to the public.

measures that will define what actions they should take to manage nanotechnology safely if they are engaged early in the oversight process.

- A substantive discussion about the core policies of an oversight system would also provide important guidance to technology developers that operate at the cutting edge of the science. In fast-moving industries, where technologists are exploring many options in short time frames, innovators will respond to even weak signals from governments and other standard setters about potential problem areas. They will look for options that appear to minimize potential concerns about health and safety while maintaining performance at reasonable costs. It is time to start the discussions of the core policies of an oversight system so that clear signals can be sent to these technology innovators.

- The requirements of an oversight system, especially those related to information generation, will have long-term effects on the evolution of the business models that can be successful in the development of nanotechnology.

Designing a Product Oversight System

Current discussions in the United States about health and safety protections related to nanotechnology tend to assume that oversight should focus on *products* containing nanoscale materials.[7] Such a perspective is notable because the most developed environmental regulatory programs in the United States focus not on products but on *facility* emissions and management.[8]

While there is a need for a broader dialogue about how the full range of environmental statutes should address developments in nanotechnology, it is reasonable to focus initially on products containing nanoscale materials, while keeping in mind that facilities and related production processes must also be addressed as the establishment of the regulatory system progresses.[9] In focusing on product oversight, however, it will be important to address *occupational* risks, both in commercial-scale operations and in the laboratory, where human exposure to nanoscale materials is likely to be greatest. As will be discussed below, product oversight systems have historically been well-suited to addressing workplace risks.

In considering what form of oversight system makes sense for products containing nanoscale materials, it is useful to recognize

7. See J. Clarence Davies, *Managing the Effects of Nanotechnology*, Washington, DC: Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, January 2006, available at http://www.nanotechproject.org/file_download/30, accessed January 3, 2007, p. 14; EPA White Paper, *supra* note 5, p. 24.
8. The EPA's budget is dominated by programs established under the Clean Air Act, Clean Water Act, Safe Drinking Water Act, Resource Conservation and Recovery Act and Comprehensive Environmental Response, Compensation and Liability Act to prevent and clean up pollution at specific facilities or sites.
9. There are several reasons to look at a broader range of programs as part of an oversight system for nanotechnology, but two factors are particularly important. Product regulatory programs have inherent difficulties setting management practices for downstream activities, such as disposal operations. It is difficult for a product oversight system to predict how such residuals will arise and be managed and to employ typical product management tools (e.g., product labels) to set clear standards. In addition, at least in the United States, the federal programs for product oversight tend to operate with much smaller resource bases than the more extensive environmental regulatory programs that oversee facility management.

that regulatory systems for products in the United States have historically followed one of three general patterns:

1. Product-specific Approvals

Under this approach, manufacturers or marketers of products submit information about their products to an oversight agency and receive licenses to introduce, distribute and market their products in commerce. Typically the advocate for the license carries a burden to demonstrate the safety—and, in some cases, the efficacy—of the product for the claimed benefits used in advertising and labeling. The informational requirements faced by applicants for a license under this type of program are often rather substantial, making the license difficult to obtain and highly valuable in the marketplace once granted.

This model is followed most directly by the U.S. Food and Drug Administration (FDA) in its regulation of drugs and certain medical devices. At EPA, this model reflects the design of the pesticide program under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). EPA's program under the Clean Air Act (CAA) for the registration and regulation of fuels and fuel additives also resembles this model.

2. Product-specific Screening

In this model, the manufacturer or marketer of a product provides basic information about a product to an oversight agency, usually within some fixed time frame, before the product is intended to enter commerce. During this "review period," the agency must decide whether it has any concerns about the product, based on its intended use, the information supplied by the product manufacturer and other information available to the agency.

If the agency raises no objection in the fixed time period, the product may proceed to commerce. The agency may provide a written recognition that the product can proceed with its intended use, although this recognition is sometimes characterized as an "acceptance," rather than an "approval," of the product. Alternatively, the agency may raise objections to the product, which typically leads to some form of restriction or to additional data submission requirements. When an agency raises objections to a product during the screening stage, it may take formal action (e.g., administrative order) to impose requirements or direct a submitter to seek a more formal approval, as described above.

The federal regulatory program that perhaps best characterizes this model is the pre-manufacture review program for new chemicals under TSCA. FDA also employs a similar approach in its "510(k)" reviews of medical devices claimed to be similar to existing products and for drugs manufactured consistent with U.S. Pharmacopeia monographs.

3. Regulation by Government Initiative

For other classes of materials, agencies screen available information about products and initiate investigations or more formal regulatory action if they become aware of an issue of significant concern. In this model, manufacturers do not provide product-specific information to agencies unless asked. Generally, agencies carry the burden of proof to demonstrate that a product presents an unreasonable risk. Agencies typically use general rulemaking authority to impose controls in this situation.

This model defines the authority and approach of the federal government in a wide range of areas. EPA's TSCA authority over

existing chemicals in commerce follows this model, as does the Consumer Product Safety Commission (CPSC). Likewise, FDA employs this approach for food additives and food packaging "generally recognized as safe" (GRAS), as well as for cosmetics.

At least at this time, the "Regulation by Government Initiative" model described above is probably the prevailing model for oversight of nanoscale materials now in commerce, although this profile may change in the future.[10] While some have suggested that Congress should consider the development of a new statute to regulate nanotechnology, such legislation does not seem imminent.[11] Assuming that the current statutory and regulatory system remains in place, we must assume that the evolving oversight system for nanoscale materials will reflect a mix of the three approaches described above. A series of definitional issues (e.g., is a material a new or existing chemical?) and use patterns (e.g., is a material a drug or a cosmetic?) will determine agency jurisdiction and the degree of oversight that a product faces.

To be certain, the applicability of existing regulatory programs will dictate many of the risk criteria, information requirements and management practices that will apply to specific products. Agencies will want to adhere to their current policies and practices to the extent possible. At the same time, nanoscale materials present challenges for all the current regulatory programs, raising new issues that reveal gaps in existing policies, data and assessment methodologies. Moreover, these regulatory programs are likely to be influenced by the other non-regulatory elements (e.g., voluntary standards) of the emerging oversight system for nanotechnology.

Therefore, it is important in all these contexts that interested parties begin discussing in a more systematic way the risk criteria, information needs and risk management practices that should be guiding the oversight system for products containing nanoscale materials.

10. For a compendium of consumer products containing nanoscale materials, see Inventory of Nanotechnology Consumer Products, *supra* note 1.
11. See Davies, *supra* note 7, p. 18.

The Building Blocks of a Product Oversight System

As indicated above, an effective and transparent product oversight system will necessarily be built upon three sets of policies:

- *Risk Criteria*—What health, safety and environmental effects of a material constitute a problem, including the identification of appropriate surrogates for gauging such effects? How much risk from the material does the system view as acceptable, perhaps considering the benefits of the product?

- *Information Needs*—What information is needed to determine whether a product is acceptable under the risk criteria guiding decisions? What further data is needed to confirm or rebut assumptions being made about the product's effects?

- *Risk Management Measures*—What set of product specifications, handling practices, disclosures and use limits are necessary to assure that risks from the product remain in an acceptable range? Or, should risk management be addressed by a general exposure standard accompanied by a monitoring program based on approved protocols?

While this report will examine each of these policy areas separately in the next three sections, these policy areas will not be fully distinct in an effective oversight system. They are intertwined: one set of policies is often nested within the policies in one of the other areas. The risk criteria, for example, define the areas where information will be needed. Data submissions may also trigger additional risk criteria, which will then trigger additional data needs. Risk management measures obviously follow directly from risk criteria. At the same time, the willingness to adopt certain risk management measures may eliminate the need to explore certain risk issues or to collect certain data. Often, certain risk management measures are seen as alternatives to data collection obligations.

Those who are familiar with the workings of the new chemical program under TSCA will recognize that EPA's policies under that program reflect these three building blocks. Yet this observation does not suggest that the TSCA statutory framework is necessarily the preferred framework for product oversight. In fact, the TSCA statute did not address any of these topics in a systematic way.[12] Instead, EPA has set the core TSCA policies on risk criteria, information needs and risk management measures on an incremental basis over several decades. The issues EPA addressed in developing that program were universal questions that all product oversight programs must face.

12. The TSCA statute, which was passed in 1976 and has remained essentially unchanged, defined the jurisdiction of the program (i.e., pre-manufacture review of new chemicals), created a few exemptions, put limits on the data EPA could require in an initial pre-manufacture notice and specified the time frame in which EPA had to make a judgment on individual new chemicals. EPA was left with the task of defining the substantive policies that would guide the program.

The oversight system's approach to risk criteria, information needs and risk management measures will shape the overall social and economic trajectory of nanotechnology. What categories of nanoscale materials represent the most promising commercial products? What kinds of companies can face the rigors of commercial development? What research is most needed? The time to begin public discussion of these broader questions and guiding policies is now.

In the following sections, challenges associated with addressing risk criteria, information needs and risk management practices issues in the development of an effective oversight system for nanoscale materials will be identified and analyzed.

Risk Criteria

Oversight systems for nanoscale materials will try, to the extent possible, to build upon the policies that have guided the review of conventional chemical substances. This reflects a natural tendency to stay with the familiar way of doing business. Such an approach for nanotechnology, however, is a rational starting point and is the one taken by governments in both the United States and Europe.

In the sweep of hype and euphoria about nanotechnology, it is important to recognize that many of today's nanomaterials are variations on existing materials. The basic chemistry of a nanoscale material usually remains the same as that of its "macroscale" predecessor, though its physical structure may vary significantly, thereby changing its risk characteristics. The existing toxicity profile of the bulk material is a logical starting point in any review of a nanoscale material, but it is only a starting point.

Nanotechnology is unlikely to require a whole new framework for basic toxicology. Several regulatory agencies and scientific groups that have begun to look at the scientific challenges presented by nanotechnology have concluded that the range of currently available toxicity tests provides a logical place to begin to assess the potential risks of nanoscale materials.[13]

This assumption will be challenged over time as nanotechnology matures. As companies move from use of first-generation nanoscale materials (e.g., simple "passive" nanoparticles) to more complex structures, such as active nanostructures capable of changing their properties during use, and systems of nanostructures, the approaches to toxicological testing will need to evolve. Similarly, the likely convergence of nanotechnology and biology will pose special challenges.

While pre-existing toxicity information on the "macroscale" version of a chemical is relevant to evaluating a nanoscale version of the same chemical, the challenge is that such information is probably *not sufficient* for effective oversight. Much of the appeal of nanoscience is that it allows materials scientists to create novel properties and functions at the nanoscale level that are not achievable outside the nanometer domain. A nanotechnology oversight system must develop a perspective on whether these novel properties and functions are associated with adverse health and environmental effects. Once developed, that perspective necessarily establishes the default assumptions that define the contours of the oversight system's risk criteria.

It will be argued that this challenge is less critical for the formal "product approval" programs identified earlier, such as the FDA drug approval and EPA pesticide registration programs. This viewpoint reflects the fact that products covered by these programs tend to require significant amounts of toxicity testing and product characterization prior to their approval and introduction into the marketplace. There is some merit to this argument. The broad batteries of tests used

13. See *Developing Experimental Approaches for the Evaluation of Toxicological Interactions of Nanoscale Materials,* Gainesville, FL: National Toxicology Program, November 3-4, 2004, p. 6; Nakissa Sadrieh, Ph.D. "Considerations for Regulation of Nanomaterial Containing Products," January 2006, slide 33, available at http://www.fda.gov/nanotechnology/NIST_meeting_houston_01-06.ppt, accessed January 4, 2007.

in these programs may well identify differences in toxicity associated with nanoscale versions of existing chemical substances.

Yet, even in the product approval oversight model, there will be some gaps in the scope of needed testing that can be addressed only after the oversight system defines the linkages between novel nanoscale attributes and adverse health or environmental effects. Moreover, oversight bodies will struggle, under any of the three models described above, to understand how nanomaterials migrate in the environment and how exposure might vary over their life cycles.

Living with "Regulation by Analogy"

All product oversight systems rely, to a greater or lesser extent, on analogies to other materials. Under the current version of the TSCA program, for example, EPA relies on what it calls "structure activity relationships" (SAR) to evaluate the health and environmental effects of new substances. In essence, EPA has built up a body of data and insights about the likely toxicity associated with certain chemical structures that are commonly found in many materials. On the basis of this SAR analysis, EPA reviews a set of basic information about the chemical and physical characteristics of a new chemical and reaches a judgment about its likely toxicity. This judgment then guides the agency's approach to testing and risk management.[14]

EPA has developed the SAR approach over several decades. It is a starting point for evaluating any substance, including nanoscale materials. It is not, however, currently capable of addressing toxicity that may be associated with the novel properties and behaviors of a nanoscale material. Given the dynamic nature of nanotechnology development, it is unlikely that the technology will remain "stable" long enough for the iterative, and painstaking, process that led to the SAR framework for conventional chemicals to generate a comparable framework for nanoscale materials. By the time EPA might be able to develop a SAR approach for the more prevalent nanostructures of today (e.g., carbon nanotubes), the cutting edge of new products may have switched to nanostructures integrated with biological materials, guided assemblies and other innovations for which the SAR model becomes obsolete.

While a routinized approach such as SAR may not be viable for nanotechnology, the basic premise of SAR—using analogies to assess the risks of nanomaterials—is inevitable. As will be discussed in the next section, the developing oversight system is likely to expect greater levels of data for nanoscale materials than has been expected for existing chemicals. At the same time, it is neither reasonable nor politically realistic to expect that industry will develop an exhaustive set of toxicity and exposure testing data for every material for every application. Some form of "tiered" testing is more likely to emerge, and that tiered system will be guided by risk criteria that are based on what is known about existing nanomaterials and related chemicals.

14. On the basis of this analytic framework, EPA has developed and made publicly available a manual defining "Categories of Concern," which explains in some detail the agency's general approach to certain classes of chemicals, particularly in regard to testing obligations. See generally, Miriam Wiggins-Lewis, J. Vincent Nabholz, and Rebecca Jones, *TSCA New Chemicals Program (NCP) Chemical Categories*, Washington, DC: Environmental Protection Agency, October 2002, available at www.epa.gov/opptintr/newchems/pubs/cat02.pdf, accessed January 3, 2007 ("Categories of Concern").

Accordingly, oversight bodies will build their policies concerning particular products around analogies that they draw between new nanoscale materials and other materials about which more is known.

An important, and very timely, example of this issue concerns the analogies that government agencies will use to review nanoparticles. Suppose, for example, EPA were to define the risks of nanoparticles by drawing an analogy to the agency's approach to particulates under the CAA. In that context, EPA has defined particulates smaller than 2.5 microns as per se pollutants and has developed elaborate air pollution control strategies to eliminate emissions of such particles. Under that definition, all nanoscale particles (presumed to be below 100 nanometers) would be deemed detrimental to public health. It seems unlikely that nanotechnology would prosper under such a policy.

While such a policy is probably too draconian to consider as a guide to oversight of engineered nanomaterials, there are other versions of this same question that would have significant impact. For example, in evaluating many inorganic materials submitted under the TSCA new chemical program, EPA evaluates whether the substance will generate respirable particles. If so, EPA then determines whether the material is analogous to one of several substances, including crystalline silica, talc, titanium dioxide or carbon black. If the analogy is drawn to crystalline silica, the substance is assumed to be quite toxic and is presumed to be a human carcinogen. If the analogy is drawn to titanium oxide, the substance faces a much more benign presumption and the data on cancer is presumed to be "inadequate" to classify the material as a human carcinogen.[15]

How EPA might apply those analogies, or similar analogies it constructs for nanoscale materials, will have profound effects on innovation, products and businesses. Such analogies may determine whether the product is allowed in certain uses and will certainly determine occupational controls, labeling and other notification requirements at a manufacturing site. Significantly, the analogy also defines the testing that a product developer must meet if it wants to overcome a presumption that a product will cause an effect of concern.

The Role of Exposure

A particularly important aspect of the risk criteria for nanoscale materials, regardless of the oversight mechanism used, is how those risk criteria address questions of exposure. There certainly will be situations where a combination of factors greatly reduces the potential for exposure. Thus, a set of risk criteria that focused only on the potential hazard of a chemical structure would not be reflective of reality.

A critical issue to define in considering exposure is whether the oversight system will focus on the nanoscale material itself, on the larger product in which it is commercialized or on the fate of the product after its use. Existing regulatory systems tend to look at all these questions to some degree, but the nature of nanoscale materials probably warrants a closer look at the commercial product throughout its life cycle.

Many nanoscale materials are components of a larger matrix of materials. This occurs because nanoscale materials are often being used in small amounts to add a particular characteristic (e.g., the ability to conduct electricity) to an existing material.

15. Ibid., p. 118.

In addition, some nanoscale materials may have characteristics (e.g., the potential to agglomerate and lose performance) that dictate the use of coatings that are essential parts of the product as used. In other situations, such coatings may be used to address directly a particular characteristic that might raise health concerns (e.g., a physical shape analogous to that of asbestos fibers).

This question of what form of the nanoscale material to evaluate will probably generate some debate. Some people will argue that the "matrixed" nature of many nanoscale materials at the use stage of their life cycles should reduce the potential exposure and risk of the material.[16] Others will argue that the breakdown of coating materials during the latter stages of a product's life cycle or through metabolism in the body necessitates a focus on the nanoscale material itself.

Balancing Product Risks and Benefits

Another critical issue that needs to be discussed in defining the risk criteria for nanoscale materials is social trade-offs. For product oversight systems, the need to weigh the basic advantages and disadvantages of a product is a well-established principle. This stands somewhat in contrast to regulatory debates over environmental standards for facilities, where the appropriate use of cost-benefit analysis remains controversial.

In the context of product regulation, oversight systems consider a range of positive and negative attributes about a product and then reach an overall conclusion. This is certainly the case in oversight systems such as the FDA drug approval program, which looks at efficacy (e.g., assuring that approved medicines perform as claimed) as well as safety concerns (e.g., determining whether the side effects of a medicine undermine its value as a cure).

Additionally, the same logic operates, perhaps less obviously, in product oversight systems that do not explicitly evaluate product claims from a consumer protection perspective. EPA's pesticide and TSCA oversight programs evaluate products against an "unreasonable risk" standard that allows for consideration of the economic, social and environmental costs—as well as the benefits—of a product.

Assuming that the risk criteria for nanoscale materials will inevitably involve some balancing of the advantages and disadvantages of individual products, public consideration of this issue is warranted. This discussion need not devolve into a replay of old debates about the merits of cost-benefit analysis. Part of the discussion should certainly involve consideration of scenarios where the risks of a technology cannot be overcome by any putative benefits. At the same time, it would be useful to define some categories of benefits (e.g., pollution prevention, enhancements of public health, environmental cleanup, energy and resource conservation) that draw broad public support and that justify development of products that carry real, but manageable, risk.

The need to consider social trade-offs underscores a broader point about all aspects of

16. This perspective can lead to a focus on oversight of "free" nanoparticles that are separate from nanomaterials contained in a larger matrix. A recent proposal for a voluntary reporting program in the United Kingdom asks participants to report only on "free" nanomaterials. See *Consultation on a Proposed Voluntary Reporting Scheme for Engineered Nanoscale Materials*, London, UK: Department for Environment, Food and Rural Affairs, March 2006, available at http://www.defra.gov.uk/corporate/consult/nanotech-vrs/consultation.pdf, accessed January 3, 2007, p. 16.

the risk criteria. Even though the operational aspects of these criteria may appear highly technical and scientific, they are ultimately value statements. Risk criteria will define how we value the benefits of nanotechnology and what social risks we are willing to take in order to see it prosper. When values are involved, there always will, and should, be some debate. Hopefully, regulatory agencies will take advantage of the apparent opportunity to have a more thoughtful, less polarized discussion of these issues.

Information Needs

While risk criteria constitute the soul of a product oversight system, information requirements that the system imposes define its initial profile. Accordingly, the information requirements are likely to be the subject for some of the first major debates about the appropriate level of oversight.

The Reality of Significant Testing Obligations

For several reasons, the information requirements for nanoscale materials are likely to be more extensive than those currently expected for conventional forms of the same materials. Due to their size and novel properties, nanomaterials have much greater potential to move throughout the body than larger particles do. This potential understandably leads to greater concern about a range of health effects. For example, with respect to inhalation of larger particles, regulatory agencies have tended to focus on potential toxic effects in the respiratory system. Emerging data on nanomaterials, however, suggest that they are able to cross cellular barriers and migrate to multiple organ systems, including the brain.[17] This potential, therefore, indicates the need for toxicity testing that examines multiple organ systems and disease endpoints.

Scientists also recommend that testing regimes for nanoscale materials should include a thorough characterization of the materials' physical and chemical characteristics.[18] Knowing the unique characteristics of a nanoscale version of a chemical or material will help scientists understand the properties that are most likely to be associated with toxic effects. Such information facilitates the development of control strategies for that particular substance. In addition, such information increases the overall body of information about the relationship between the characteristics of nanoscale materials and toxicity. Over time, these insights may allow the oversight system to develop more targeted information needs.

Collecting needed information is likely to be costly, particularly in the early years of an oversight system. As indicated above, the range of needed information will probably be extensive. In addition, material testing will be more difficult to perform at the nanoscale. For example, generating pure samples of nanoscale materials and administering doses to test animals in a manner that simulates realistic conditions is likely to require special care and skills in the laboratory. It will take some time before a wide range of laboratories, including the contract laboratories upon which smaller companies must rely, have that capability.

Until testing at the nanoscale becomes more routine, product developers will face premium prices for toxicity tests on nanoscale materials. These costs will be particularly onerous for small- and medium-size enterprises. Thought needs to be given to

17. Gunter Oberdörster, et al., "Principles for Characterizing the Potential Human Health Effects from Exposure to Nanomaterials: Elements of A Screening Strategy," *Particle and Fibre Toxicology*, October 6, 2005, 2:8, available at http://www.particleandfibretoxicology.com/content/pdf/1743-8977-2-8.pdf, accessed January 3, 2007 (ILSI Report); Gunter Oberdörster, et al., "Translocation of Inhaled Ultrafine Particles to the Brain," *Inhalation Toxicology*, June 2004, 16: 6-7, p. 437.
18. ILSI Report, p. 33.

provide incentives for such companies interested in proactive testing of their products. Government can also play an important role in the development of new, faster toxicity testing and screening methods that firms could use during product development to identify potential problems.

When Is New Testing Needed?

Two of the trends described above may appear inconsistent. As just discussed, it is likely that effective oversight of nanoscale materials will require more information than is typically required for the review of traditional chemicals. At the same time, it has been argued that oversight agencies will often depend on analogies to other materials in evaluating the risks of nanoscale materials.

In a sense, there *is* an inconsistency in how these trends are proceeding at the current time. Some nanoscale materials are moving into commerce without specific evaluation of their health and environmental implications, reflecting an assumption that the potential effects of nanoscale materials are similar to those of the macroscale version of the same material. In other cases, very similar nanoscale materials are receiving more intensive evaluation, either by governments or by individual companies with robust product stewardship programs, before they proceed to market.

Why is this occurring? The current oversight system for nanotechnology is immature. The various actors who are expected to conduct oversight do not have a common view of risk criteria and information needs. In addition, the institutional roles concerning oversight, running the gamut from the jurisdiction of regulatory programs to contractual obligations in customer-supplier relationships, need further clarification. While this report does not attempt to address these topics, they are important questions that will need attention.

Nonetheless, even in a mature oversight system, the need for more information about nanoscale materials and a reliance on "regulation by analogy" will co-exist. These trends are ultimately compatible. The need for more information about nanoscale materials derives from certain challenges that are inherent in oversight, such as translocation of nanomaterials in the body and understanding of their surface characteristics. Thus, the starting point for the oversight system is that the information needs will be robust.

Over time, as science and oversight mature, a series of factors will warrant calibration of those information needs. Use patterns for products containing nanoscale material will certainly influence information needs. For example, oversight of a nanoscale material in a consumer product that is broadly dispersed will require more information than evaluation of a site-limited intermediate in a contained industrial process. Similarly, some product manufacturers and users may adopt risk management measures that mitigate certain concerns, reducing the need for certain data. For example, a manufacturer may prevent discharges to surface water and thereby avoid the need to conduct aquatic ecotoxicity testing.

In this same manner, oversight of a particular nanoscale material may rely on analogies to other materials, either at the nano or macro scale, to define the potential risk of the material. Such analogies can reduce or increase the scope of potential testing. In some cases, an oversight body evaluating a particular material will base its risk

assessment on the toxicity database for an analogous material and waive the need for further testing. In other cases, risk-based analogies will spur additional testing. For example, an oversight body could draw an analogy that creates a "worst-case" presumption about a particular material. This approach creates an incentive for manufacturers to generate additional toxicity testing and to demonstrate that such a worst-case presumption is not warranted.

Another factor that can influence the scope of needed testing is the production volume for a product. It is fairly common in current regulatory programs to establish "testing triggers" for particular substances that ratchet up testing obligations on the basis of higher production volumes. This approach has the advantage of creating a nexus between testing rigor and potential risk, while also addressing the affordability of testing for the manufacturer.

A reliance on production volume to guide information needs is likely to be controversial for nanoscale materials. As an example, some stakeholders have maintained that certain volume-based exclusions from the standard review policies of the TSCA new chemical program are not appropriate for nanoscale materials, arguing that these materials could have significant health or environmental effects at relatively low production volumes.[19] Thus, an important question that the oversight system will need to address at an early stage is what information needs should be met *before* a nanoscale material enters commerce and what types of information can be addressed *later*, as the market for the material develops.

Who Can Support Testing Obligations?

The debate on testing needs will center primarily on scientific and policy questions about what is needed to understand potential risk. Beneath the surface, however, will be an important economic implication: what kinds of companies can participate in the commercialization of products containing nanoscale materials? Eventually, the high cost of information collection for nanoscale materials creates a tipping point at which it is no longer feasible for small companies to bear the costs of the oversight system. This is important because much of the innovation in nanotechnology is emerging from small companies around the world.

Some may characterize such a regulatory hurdle as a barrier to innovation. While there is some merit to this argument, the more practical implication is that it changes the economic model for commercialization. In many areas of current technology, small companies are at the cutting edge of innovation. Once these companies develop new ideas, they take steps to perfect their intellectual property (i.e., obtain appropriate patents) and establish, often with support from external investors, the economic viability of their technology.

These companies then face a crossroads: should they commercialize the product themselves, or sell or license the technology to others? If the costs of needed regulatory clearances are low, they may obtain the clearances themselves because, at a minimum, the clearances can increase the value of the product to potential business partners. If the cost of regulatory clearance becomes

19. Letter from Richard Denison and Karen Florini, Environmental Defense, to Susan Hazen, Acting Assistant Administrator, Office of Prevention, Pesticides and Toxic Substances, U.S. Environmental Protection Agency, September 2, 2004, p. 4.

too high, they will sell or license the technology to larger companies that have the capital and expertise to manage the regulatory process.

At this stage in the development of nanotechnology, it is not yet clear whether the commercialization of nanoscale materials will become primarily the business of large, highly capitalized companies, relying on their own research and the ideas of small innovator companies, or be a pathway that turns small innovator companies into the large companies of tomorrow. Many economic factors influence that trend, but the costs of the informational requirements of the oversight system generally play a significant role. For example, few small companies can take a new drug to market, in part because they do not have resources and expertise to navigate the FDA regulatory process.

What Products Are Viable?

The information needs of a nanotechnology oversight system may also affect the range of applications for which nanotechnology is used. This depends on whether the information requirements will differ significantly depending on the product application.

By analogy, EPA and the U.S. Department of Agriculture (USDA) have been concerned for many years about how to protect "minor uses" of pesticides. The EPA pesticide regulatory program calls on pesticide manufacturers to provide extensive information on pesticide use and food residues for each of the agricultural crops on pesticide product labels. However, for many vegetable and fruit crops that are grown in much smaller quantities than commodity crops such as corn, soybeans and wheat, the pesticide companies do not receive enough return on pesticide sales to justify the data collection obligations they must meet to support some minor uses. Thus, many minor uses of pesticides have been dropped from pesticide labels, even though more effective and environmentally protective use of those pesticides could probably have been developed.

At this time, it is still too early to tell whether situations analogous to the minor use pesticide problem will develop in niches of the nanotechnology world. The possibility of such an issue is not necessarily a reason to avoid defining information needs that differ by use patterns. At the same time, companies and government agencies may need to consider whether legitimate information requirements are creating disincentives that conflict with larger social goals. Corrective measures can be taken. For example, Congress has created programs supporting "orphan drugs"—drugs used to treat rare diseases affecting only a small portion of the population—recognizing that the economic dynamics of pharmaceutical development, including the costs of the oversight system, do not favor development of such drugs.[20]

A Starting Point for Discussion

The needed debate on the information needs for effective oversight of nanoscale materials has a useful starting point. In October 2005, the International Life Sciences Institute (ILSI) released a report describing the views of an expert working group on the elements of a screening strategy for nanoscale products.[21] This document, which reflects the views of a cross-section of academic, government and industry scientists, sets a framework for the

20. For description of FDA's program under the Orphan Drug Act, see http://www.fda.gov/orphan/.
21. ILSI Report, *supra* note 17.

kinds of testing that should be considered for screening nanoscale materials.

The ILSI document reinforces the assumption, held by many scientists, that testing programs for nanoscale materials are likely to include significant analytic work on the physical and chemical properties of the materials themselves, both in their pure "nano" form and in their form in a commercial product. Beyond that, the ILSI paper describes a range of in vitro and in vivo tests that should be considered for various substances, influenced by the initial route of exposure to the substance (the "portal of entry") and the potential translocation of the substance in the body.

The document does not attempt to define particular testing protocols. It also does not attempt to recommend policies on minimum testing requirements or specify what conditions should trigger specific tests. The range of testing outlined in the ILSI paper, however, serves as a reminder that the potential scope, and thus expense, of needed testing could be significant. It underscores the need for a serious discussion of what the testing obligations should be in a nanotechnology oversight system.

Risk Management

As indicated earlier, this report focuses on the design elements of a *product* oversight system for nanotechnology. This is an important context when looking at risk management measures because product oversight systems are inherently better at addressing some kinds of issues than others.

Aligning Risk Management with Product Life Cycle

A product oversight system is well-suited to address product design measures that can help reduce risk. For example, such a system can mandate certain coatings or other product formulations and delivery measures that minimize exposures to nanoscale materials. Also, product oversight systems are usually effective in addressing concerns about worker exposure or product quality at the point of manufacture. The entities involved in the manufacturing stage of the material's life cycle are typically involved in the process of obtaining clearance for the product.

Product oversight systems are also well-suited to risk reduction strategies based on labeling and other forms of communication to customers. These strategies may include directions for use, warnings and general information about the product's content.

Reliance on these strategies, however, can become less effective as the chain of distribution gets longer and multiple parties are using, formulating or modifying a manufactured product. Similarly, a product oversight program is challenged when the range of applications for a regulated material expands. It becomes increasingly difficult for the oversight system to anticipate all the exposure scenarios and translate them into specific risk management approaches that can be articulated on labels.

Product oversight systems have difficulty addressing issues related to environmental releases of materials during use and the waste management scenarios that arise with products at the end of their life cycle. The conditions under which these environmental releases occur are rarely understood at any level of precision when a product is first being introduced into commerce, the typical point at which product oversight systems consider risk management.

For example, carbon nanotubes are presently being used in sporting goods, conductive composites, batteries, fuel cells, solar cells, biomedical devices, fibers, fabrics and sensors. Since this array of uses presents a range of exposure scenarios, it is hard to imagine how to design a single label for the base product that would address the potential health, safety and environmental risks in any great depth.

Product oversight systems usually rely on label requirements as the means to define management practices at points where a product is processed or used. These systems do not usually employ permits, emission-monitoring protocols and record-keeping requirements to tailor requirements to particular points of use. Thus, a product oversight system can have difficulty determining whether appropriate risk management measures have been put in place.

Given these strengths and weaknesses of product oversight systems, the question to consider for nanotechnology is where, in the product life cycle, risk management measures are most needed. Several current

efforts would suggest that an important priority is to develop appropriate occupational controls for the manufacture of nanoscale materials because workers will be the most exposed population.[22] Given that focus, a product oversight system is likely to lead to an effective risk management strategy. Measures related to occupational controls and hazard communication are well-established elements of existing product oversight programs.[23]

If, however, concerns develop about the release of nanoscale materials into aquatic environments at points of processing or use, existing programs for product oversight may not be as effective. FDA, for example, would not have great expertise about water pollution control strategies. Even within EPA, the TSCA new chemical program tends to address water pollution concerns for new chemicals with fairly rudimentary control measures, such as a prohibition of "intentional" discharges to water, but not specific wastewater discharge limits.

Interplay Between Risk Management and Information Collection

Risk management strategies must necessarily be aligned with information collection expectations. As suggested earlier in this report, the oversight system must decide whether to focus just on the nanoscale material itself or on the whole product in which the nanoscale material is contained and marketed. This is important for developing a risk management, as well as an information collection, strategy. For example, establishing controls on the design and manufacture of end products using a nanoscale material may be a critical strategy for risk management, which may generate end-product performance testing requirements.

Risk management strategies will have to be aligned with testing strategies in other ways as well. A particularly important set of policies relates to how risk management approaches can be used as alternatives to testing requirements. If a company is prepared to accept certain controls in the design of its product, in its manufacturing process or in its product labeling, can it avoid the expense of undertaking certain kinds of testing? Such trade-offs are routinely employed in existing regulatory programs. How will this concept apply to nanoscale materials?

The role of monitoring in risk management strategies for nanoscale materials is an extremely important consideration. It is broadly understood that monitoring for nanoscale materials in products, workplaces and the environment is going to be a difficult and potentially expensive task. Proven methods are not readily available. While methods will probably be developed at some point, it is not at all clear that the cost of routine monitoring using those methods will be reasonable.

If low-cost monitoring methods are not available, the range of effective risk management measures narrows. Reliable and credible monitoring protocols are essential for the development of "performance standards" that give companies flexibility to develop cost-effective measures to meet a risk reduction goal. For example, workplace exposure concentrations and environmental emissions

22. The voluntary standards group ASTM International formed a committee in 2005 to, among other topics, develop good management practices for worker protection. See ASTM E56, *at* http://www.astm.org.
23. For example, the TSCA new chemical program often relies on mechanisms established under the Occupational Safety and Health Administration's hazard communication program to assure that appropriate information about chemical management is delivered to workers.

standards are typically linked to monitoring requirements. Without practical monitoring protocols, risk management strategies will be limited to design requirements or management practices that are expected to reduce exposure. At a facility level, effective end-of-pipe and fence-line monitoring can be used to provide companies with greater flexibility for process changes, but cost-effective monitoring methods for nanoscale materials do not yet exist.

The Role of Labeling

Finally, the nature of labeling for nanoscale materials is likely to be a key policy concern. In particular, there will be substantial debate about whether a product containing nanoscale materials should have a label that explicitly notifies the public that a nanomaterial is in the product.

In discussing this issue, it will be important that stakeholders consider why such labeling would make sense.[24] If, for example, the government has an interest in tracking where nanomaterials are being used in the economy, there are several mechanisms, other than labeling, that can be used to obtain that information.

Labeling is generally intended to help the consumer use a product in a manner that is effective for its intended purpose and that is safe. Contextual information, such as the ingredients of the product and hazard warnings, also provides reinforcement of those primary objectives. Assuming these are the appropriate objectives for labeling, policymakers will need to define what objectives are served by a "nano" label, particularly if labeling is broadly required.

To the extent that a "nano" label is meant to carry an implied hazard warning, there will be significant opposition to this idea. Many supporters of nanotechnology believe that most nanotechnology materials, particularly as used in the commercial products offered to consumers, will not represent substantial public risks.

Other stakeholders will start from a differing set of assumptions. For example, some will argue that the potential for translocation of nanoparticles within the body represents an exposure that should be identified to consumers. In the experience with genetically modified organisms (GMO) in food, the issue of "GMO labeling" was one of the most divisive issues discussed in public policy debates about the technology.

Some parties may argue as a general matter that there is a "right to know" about the presence of nanoscale materials in a product. Yet that assertion begs the question of how the information should be used. The Toxic Release Inventory (TRI) program's premise that communities should know about chemical releases in their neighborhoods was certainly valid. Yet that program required notification only for a list of chemicals that Congress or EPA had identified as "toxic chemicals." How the TRI analogy might apply to nanoscale materials, particularly those that have not yet been linked to a negative health or environmental impact, will be quite controversial.

Questions about the potential use of "nano" labeling will be divisive because they are about values. There is no scientific answer to these questions. For this reason alone, it is a subject that deserves attention soon.

24. Given the popularity of nanotechnology at this time, some companies are advertising the presence of nanoscale materials in their products. In this situation, the only apparent role of an oversight system is to assure that the product's claims are factually correct.

Conclusion: The Issue of Transparency

The matter of how "public" the elements of the nanotechnology oversight system should be is an essential question that must be answered. Several groups have already made it quite clear that transparency of the process and the basis for risk decisions is essential if the oversight system is to be credible.[25] In addition, recent focus groups that explored public attitudes and perceptions of nanotechnology found that disclosure and transparency were critical to building public confidence in the ability of government and industry to manage risks associated with nanotechnology.[26] Few could argue with the general reasonableness of transparency for these purposes.

At the same time, product oversight systems are usually accompanied by understandable sensitivity about public disclosure of information in the following areas:

- When a new material is first being evaluated by government agencies, the sponsor of the product will not want the identity of the product disclosed because this information discloses business strategy to competitors. This sensitivity usually declines once the product has been commercialized and is available for evaluation, and reverse engineering, by those competitors.
- A company's planned production volume for a material is routinely viewed as confidential.
- The process used to manufacture a particular substance is almost always treated as confidential information by the manufacturer.
- Similarly, companies will view information about their customers and downstream distribution networks as the essence of their business and, thus, highly confidential.
- Statutory protections of trade secrets do not generally extend to health and safety studies, which are typically viewed as public information. In some cases, companies will contend that information about the specific identity of a chemical substance should be treated as confidential.
- Finally, companies often look for ways to assure that other companies cannot use their health and safety data, particularly in obtaining clearances with regulatory authorities, without some form of compensation. This can sometimes lead to rules about who may have access to certain health and safety studies.[27]

25. John Balbus, et al., "Getting Nanotechnology Right the First Time," *Issues in Science and Technology*, Summer 2005, p. 70; National Resource Defense Council, "Nanotechnologies: Tiny Particles Promise Much, But Could Pose Big Risk," March 20, 2005, available at http://www.nrdc.org/health/science/nano.asp, accessed January 3, 2007.
26. Jane Macoubrie, *Informed Public Perceptions of Nanotechnology and Trust in Government,* Washington, DC: Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, September 2005.
27. Section 10(g) of the Federal Insecticide, Fungicide and Rodenticide Act provides an example of how this issue is addressed in EPA's pesticide program.

Stakeholders will need to decide for themselves whether aspects of this pattern raise concerns. Those who believe that more information should be available in one of these areas should be prepared to explain what is needed and why. At that point, the real discussion about transparency can begin, hopefully in the context of a realistic view of risk communication.

In its report *Improving Risk Communication*, the National Research Council of The National Academies offers a helpful, pragmatic guide to what the goal should be in discussing transparency:

> "Risk communication is successful only to the extent that it raises the level of understanding of relevant issues or actions and satisfies those involved that they are adequately informed within the limits of available knowledge."[28]

Good risk communication does not mean that all participants agree on questions of values and appropriate decisions about risk, either as a public policy matter or at the level of personal choice. It simply means that they are receiving sufficient information to reach their own conclusions.

To the extent there are significant debates about regulatory transparency concerning nanoscale materials, it will be important that stakeholders identify the kinds of decisions they want to be able to make. From that grounding, options can be explored about assembling information in differing ways that do not threaten or compromise core business confidentiality concerns. Hopefully, all parties can feel adequately informed within the limits of the information that can be made available.

A Final Note

In the end, there are many reasons to be optimistic that nanotechnology will prosper and expand exponentially over the next several years. One reason for that optimism is that a broad spectrum of interests is now looking for opportunities to collaborate on strategies to manage the health, safety and environmental issues that might arise with nanoscale materials.

The window of opportunity to make real progress on this front, however, will not be open forever. For this reason, it is essential that all stakeholders interested in responsible management of this technology begin to focus their energy on defining the core building blocks that define a product oversight system: (1) risk criteria; (2) information needs; and (3) risk management measures. In addition to focusing on these building blocks, stakeholders must engage in pragmatic discussions about the ground rules for transparency.

The need for this discussion is no more distant than nanotechnology itself. And this means that the time for it is now.

28. The National Academies, *Improving Risk Communication*, Washington: DC: National Academy Press, 1989.

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Reports

PEN 1: Jane Macoubrie, *Informed Public Perceptions of Nanotechnology and Trust in Government*, September 2005.

PEN 2: J. Clarence Davies, *Managing the Effects of Nanotechnology*, January 2006.

PEN 3: Andrew D. Maynard, *Nanotechnology: A Research Strategy for Addressing Risk*, July 2006.

PEN 4: Jennifer Kuzma and Peter VerHage, *Nanotechnology in Agriculture and Food Production: Anticipated Applications*, September 2006.

PEN 5: Michael R. Taylor, *Regulating the Products of Nanotechnology: Does FDA Have the Tools It Needs?*, October 2006.

PEN 6: Karen F. Schmidt, *NanoFrontiers: Visions for the Future of Nanotechnology*, March 2007.

Congressional Testimonies

David Rejeski, "Environmental and Safety Impacts of Nanotechnology: What Research Is Needed," United States House of Representatives, Committee on Science, November 17, 2005.

J. Clarence Davies, "Developments in Nanotechnology," United States Senate, Committee on Commerce, Science and Transportation, February 15, 2006.

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Andrew D. Maynard, "Research on Environmental and Safety Impacts of Nanotechnology: What Are the Federal Agencies Doing?," United States House of Representatives, Committee on Science, September 21, 2006.

Inventories

Nanotechnology Environment, Health and Safety Risk Research, released November 2005.

Nanotechnology Consumer Products, released March 2006.

Agrifood Nanotechnology Research and Development, released March 2006.

Nanotechnology and Medicine, released October 2006.

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