STAKEHOLDER PERSPECTIVES ON PERCEPTION, ASSESSMENT, AND MANAGEMENT OF THE POTENTIAL RISKS OF NANOTECHNOLOGY

Report of the National Nanotechnology Initiative Workshop
September 10–11, 2013

About the National Nanotechnology Initiative

The National Nanotechnology Initiative (NNI) is a U.S. Government research and development (R&D) initiative involving 20 Federal departments, independent agencies, and independent commissions working together toward the shared and challenging vision of a future in which the ability to understand and control matter at the nanoscale leads to a revolution in technology and industry that benefits society. The combined, coordinated efforts of these agencies have accelerated discovery, development, and deployment of nanotechnology to benefit agency missions in service of the broader national interest.

About the Nanoscale Science, Engineering, and Technology Subcommittee

The Nanoscale Science, Engineering, and Technology (NSET) Subcommittee is the interagency body responsible for coordinating, planning, implementing, and reviewing the NNI. NSET is a subcommittee of the Committee on Technology (CoT) of the National Science and Technology Council (NSTC), which is one of the principal means by which the President coordinates science and technology policies across the Federal Government. The National Nanotechnology Coordination Office (NNCO) provides technical and administrative support to the NSET Subcommittee and supports the Subcommittee in the preparation of multiagency planning, budget, and assessment documents, including this report. More information about the NSET Subcommittee, the NNI, and the NNCO can be found at www.nano.gov.

About the Nanotechnology Environmental and Health Implications Working Group

The NSET Subcommittee and its Nanotechnology Environmental and Health Implications (NEHI) Working Group provide leadership in establishing the NNI environmental, health, and safety (EHS) research agenda and in communicating data and information related to the EHS aspects of nanotechnology between NNI agencies and the public. Through the coordinated activities of the NSET and NEHI participating agencies, the NNI actively supports the development of the new tools and methods required for research that will enable risk analysis and assist in regulatory decision making.

About This Report

This document is the report from an NNI workshop held on September 10 and 11, 2013. The workshop was designed to bring together people who are involved in Federal, regional, State, and local governmental and nongovernmental efforts to support nanotechnology-related EHS risk management in order to jointly address associated key issues. This workshop was one of a series of topical workshops sponsored by the NSET Subcommittee to inform long-range planning efforts for the NNI and its EHS Research Strategy. This report is not a consensus document but rather is intended to reflect the diverse views, expertise, and deliberations of the workshop participants.

About the Report Cover and Book Design

Book layout designed by NNCO staff. Report cover design is by Kristin Roy of NNCO staff and Kathy Tresnak of Koncept, Inc. The foreground image on the front cover (designed by NNCO staff) illustrates the three facets of nanotechnology-related risk issues that were addressed at this workshop: assessment, management, and communication.

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Stakeholder Perspectives on Perception, Assessment, and Management of the Potential Risks of Nanotechnology

REPORT OF THE NATIONAL NANOTECHNOLOGY INITIATIVE WORKSHOP

September 10–11, 2013

Washington, DC

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National Science and Technology Council
Committee on Technology
Subcommittee on Nanoscale Science, Engineering, and Technology

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Thanks are due to all workshop participants (listed in Appendix B) for taking the time to share their experiences and insights at the National Nanotechnology Initiative (NNI) Workshop on Stakeholder Perspectives on Perception, Assessment, and Management of the Potential Risks of Nanotechnology—the "R3 Workshop" for short. Particular thanks are due to the keynote and plenary speakers (listed on the workshop agenda, Appendix A), whose remarks are summarized in this report, and to the members of the Workshop Planning Team (listed below).

Workshop Planning Team

Federal Workshop Co-Chairs: Treye Thomas (Consumer Product Safety Commission), Jeffery Steevens (U.S. Army), Igor Linkov (U.S. Army)

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Special thanks are also due to the NNCO staff members and AAAS Fellows who took notes at the workshop breakout sessions and throughout the workshop, which generated much of the content of this report:

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Preface

This report on *Stakeholder Perspectives on Perception, Assessment, and Management of the Potential Risks of Nanotechnology* is the result of the National Nanotechnology Initiative (NNI) workshop held on September 10–11, 2013, in Washington, DC. The goal of the workshop was to assess the state of research progress in risk assessment, management, and communication as it aligns with the Risk Assessment and Risk Management Methods research area of the 2011 NNI Environmental, Health, and Safety (EHS) Research Strategy. The workshop was initiated and organized by the Nanotechnology Environmental and Health Implications (NEHI) Working Group of the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee under the Committee on Technology of the National Science and Technology Council, with the assistance of the National Nanotechnology Coordination Office. The workshop facilitated a vigorous stakeholder discussion of the key elements needed to assess, manage, and communicate potential risks associated with the use of nanomaterials and nanotechnology-enabled products, with a focus on practical tools that might be used by non-Federal decision makers in their consideration of potential risks. The workshop was planned by a multi-sector team, including members from academia, industry, not-for-profit entities, and the Federal Government, to ensure active participation from a broad range of stakeholders. As a result, this report provides examples of risk management, assessment, and communication approaches as described by a diverse set of workshop participants, which will assist Federal agencies in the implementation of the risk assessment and management research needs outlined in the 2011 NNI EHS Research Strategy.

On behalf of the NSET Subcommittee, we thank Treye Thomas, Jeffery Steevens, and Igor Linkov for taking the lead in organizing and co-chairing the workshop. Thanks are also due to the NEHI Working Group for leading the planning effort on behalf of the NSET Subcommittee, and to the other members of the workshop planning team (listed on the previous page). We also thank all the speakers and participants for their contributions to the workshop. We trust that you will find this report to be a valuable resource for the NNI, the nanotechnology EHS research community, and all of the other stakeholders as we work together to promote the responsible development of nanotechnology for the benefit of the United States.

Lori Henderson	Lloyd Whitman	Michael Meador
Co-Chair	Co-Chair	Director
NSET Subcommittee	NSET Subcommittee	NNCO

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Executive Summary

The goal of the National Nanotechnology Initiative (NNI) Workshop on Stakeholder Perspectives on Perception, Assessment, and Management of the Potential Risks of Nanotechnology (the "R3 Workshop") was to assess the status of nanotechnology environmental, health, and safety (EHS) risk science three years after the development of the 2011 NNI EHS Research Strategy and to identify the tools and best practices used by risk assessors to address the implications of nanotechnology. The workshop was successful in providing a venue for a wide range of stakeholders including Federal and State regulators, small and large businesses, insurance companies, academic researchers, occupational safety specialists, and public and environmental advocacy groups to share their perspectives on the risk management process and to discuss strategies and approaches for improving risk science methods. Another important outcome was the discussion of ways that NNI agencies can assist stakeholders in the responsible development of nanotechnology.

Stakeholders participating in the workshop presented their perspectives and methods used to assess and manage the potential risks of nanotechnology. Difficulties in applying commonly used risk assessment approaches where risk is quantified as the probability of specific impact (e.g., cancer) were noted due to the lack of validated risk benchmarks that can be used as references. Screening-level risk assessment methods (e.g., control banding) incorporate risk severity scores on individual risk metrics to quantify overall risk, while comparative risk assessment processes and multicriteria decision analysis (MCDA) tools can be useful in prioritization of alternative materials or technologies. For example, control banding or MCDA tools can be used to screen and communicate hazard information on nanomaterials in the face of missing data. The use of relevant risk assessment tools, e.g., industry standards, guidance documents, and reference nanomaterials, was also discussed. Life cycle assessment (LCA) for risk-based nanotechnology development decision making was mentioned as a practice common across stakeholder groups. A complete list of the tools, standards, and informational repositories that were discussed can be found in Appendix D (p. 72).

Research presented at the workshop shows that technical risk data alone will not enable decisions; risk evaluations by different stakeholders with varying biases, values, and stances can affect the perceptions and behaviors (e.g., investment or personal safety decisions) of consumers, regulators, developers, manufacturers, and insurers.

As highlighted by the keynote speakers, stakeholder perceptions and risk communication are complex issues that require expert analysis to understand potentially subtle or obscure ethical complexities. Empirical evidence indicates that using an intuitive understanding of "risk" to respond to societal needs results in erroneous conclusions for nanotechnology implications, thus outlining the need for more robust approaches for communicating risk information to the lay public. When these considerations are integrated early on in the risk management process using effective risk communication, they can help align actual risk and perceived risk. Overall, better outcomes, such as improved understanding of potential risks by stakeholders, will result if these issues are explicitly addressed.

The dialogue at the workshop between participants was robust, and although various perspectives were presented, some stakeholder participants emphasized the importance of developing more information on the potential hazards and exposure potentials of nanotechnology and how this information can improve existing risk analysis approaches. In cases where data are available, decision makers may not be clear what weight or value is appropriate to place on certain criteria or metrics in the decision

framework when setting safety standards and regulatory policy. For the business community, data gaps and public perception of risk are both highly important in terms of sustainable development, regulatory compliance, and market acceptance.

Participants from the various stakeholder communities identified needs in four areas (the list below is not prioritized):

- Communication Resources
  - Communication and decision tools for improved stakeholder communications and collective risk-based decision making.
  - Improved transparency in reporting the presence of engineered nanomaterials (ENMs) in applications across the supply chain.
  - Continued collaboration and communication among diverse stakeholder groups.
- Decision Tools
  - Improved detection and characterization tools and methods for assessing exposure and the potential risks of ENMs.
  - Tools to address nanotechnology-related environmental, health, and safety ("nanoEHS") issues at an earlier stage of product development.
  - Better integration of life cycle assessment tools and decision analysis tools with risk assessment to support regulatory decision making.
- Data Resources
  - Repositories or databases to facilitate access to or organization of existing information on nanoEHS.
  - Methods for accessing and investigating information that could be restricted as a result of issues such as confidential business information (CBI) or intellectual property (IP) protection.
  - Continued toxicology studies on the effects of ENMs.
- Standards and Guidance Resources
  - Standards and guidances to facilitate navigation of nanotechnology-enabled applications through the regulatory process.
  - Improved data quality and methods for reporting data used in nanomaterial risk assessment.

This report paraphrases statements made by the presenters and participants. Statements should be taken as expressions of the views of the speakers and not the positions of the NSET Subcommittee, NNCO, or the NNI agencies. Chapter 9 of this report provides additional details on common themes discussed during the workshop. In particular, Table 9.1 (p. 52) includes a list of topics discussed by breakout session and stakeholder/decision-maker groups.

1. Introduction

Nanotechnology holds the potential to impact many fields of science and technology, with exciting applications in medicine, sensing, and battery technology, among many others. However, as products enter the global market, there are still questions about the potential risks and benefits of nanotechnology to consumers, workers, and, more generally, human health and the environment.

The National Nanotechnology Initiative (NNI) recognizes the critical importance of environmental, health, and safety (EHS) research in support of the responsible development of nanotechnology. The 2011 NNI EHS Research Strategy [*1*] supports the use of science-based risk analysis and risk management to protect public health and the environment while fostering technological advancements that benefit society. Engagement of all stakeholder groups in developing and communicating up-to-date EHS research, best practices, and applicable regulations in the area of nanotechnology risk science is essential to continuing the responsible development of nanotechnology. Such stakeholder communities include innovators, scientists, nongovernmental organizations (NGOs), industry, regulators, and the general public. To foster this engagement, the NNI organized a Workshop on Stakeholder Perspectives on Perception, Assessment, and Management of the Potential Risks of Nanotechnology (the "R3 Workshop") to gather information on the current state of practice in nanotechnology risk science and the values and perceptions of risk among the various NNI stakeholder groups. Additionally, NNI agencies sought stakeholder input on steps to improve the linkage of risk assessment to risk management and risk communication.

WHAT IS NANOTECHNOLOGY?

Nanotechnology is the understanding and control of matter at dimensions between approximately 1 and 100 nanometers, where unique phenomena enable novel applications. Encompassing nanoscale science, engineering, and technology, nanotechnology involves imaging, measuring, modeling, and manipulating matter at this length scale.

A nanometer is one-billionth of a meter. A sheet of paper is about 100,000 nanometers thick; a single gold atom is about a third of a nanometer in diameter. Dimensions between approximately 1 and 100 nanometers are known as the nanoscale. Unusual physical, chemical, and biological properties can emerge in materials at the nanoscale. These properties may differ in important ways from the properties of bulk materials and single atoms or molecules.

About the Workshop

The NNI R3 Workshop was held on September 10 and 11, 2013, in Washington, DC, and was sponsored by the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the National Science and Technology Council (NSTC) Committee on Technology (CoT). The meeting was organized by a multisector planning team composed of representatives from academia, industry, NGOs, and members of the interagency Nanotechnology Environmental and Health Implications (NEHI) Working Group of the NSET Subcommittee. The Consumer Product Safety Commission (CPSC) and the Department of Defense (DOD) co-chaired the planning team, bringing together more than 130 participants from national and

State governments, organized labor, the insurance industry, small businesses, and academia. An additional 106 viewers participated via a live webcast [*2*].

This workshop builds upon a previous series of meetings on nanotechnology environmental, health, and safety (nanoEHS) research and risk assessment held by the NNI, which culminated in a March 2010 "capstone" workshop [*3*]. The goal of this series of meetings was to gather input from the research and other stakeholder communities on nanoEHS research needs—input that was taken into account in the development of the 2011 NNI EHS Research Strategy. The R3 Workshop aimed to assess the status of nanoEHS risk practice three years after the development of the 2011 NNI EHS Research Strategy. The workshop was deliberately participatory, with collaborative discussions, presentations, and breakout sessions involving multiple stakeholder groups.

This workshop was designed to gather data in a "top-down" fashion that focuses on decision makers, rather than a "bottom-up" approach that begins with data collection ([*4*], see Figure 1.1;). This method puts the focus on identifying types of decisions and decision-maker needs in order to guide nanotechnology risk assessment and risk management going forward.

With these considerations in mind, the agenda included the following sessions:

- Introductory Session: NNI Needs.
- Plenary: Stakeholder Perspectives.
- Keynotes: Stakeholder Risk Perception.
- Breakouts: Types of Decisions and Types of Decision Makers.
- Roundtable Discussions and Summaries.

Workshop planners and the NNI agencies aimed for the R3 Workshop to achieve the following:

- Facilitation of stakeholder inputs on the state of progress of tools and methods used in risk analysis.
- Identification of stakeholder values that inform risk-based decision making, and potential integration of these values and perceptions into a practical framework for risk communication.
- Determination of steps to improve the linkages of risk assessment to risk management and risk communication.
- Highlighting of ongoing and future challenges impacting the assessment, management, and communication of the potential risks of nanotechnology.

The above outcomes are needed to help advance the NNI's nanoEHS risk assessment and risk management strategy.

About the Report

This report is a summary of the key topics discussed at the NNI R3 Workshop and paraphrases statements made by the presenters and participants. Statements should be taken as expressions of the views of the speakers and not the positions of the NSET Subcommittee, the National Nanotechnology Coordination Office (NNCO), or the NNI agencies. Chapter 1 summarizes the workshop objectives, methodology, and anticipated outcomes. Chapters 2 and 3 summarize the keynote presentations: Chapter 2 discusses the process of risk analysis and the characteristics of effective risk analysis and risk communication methods; Chapter 3 reviews NNI-funded empirical data on nanotechnology risk perception among NNI stakeholder groups and several related implications. Chapter 4 summarizes the

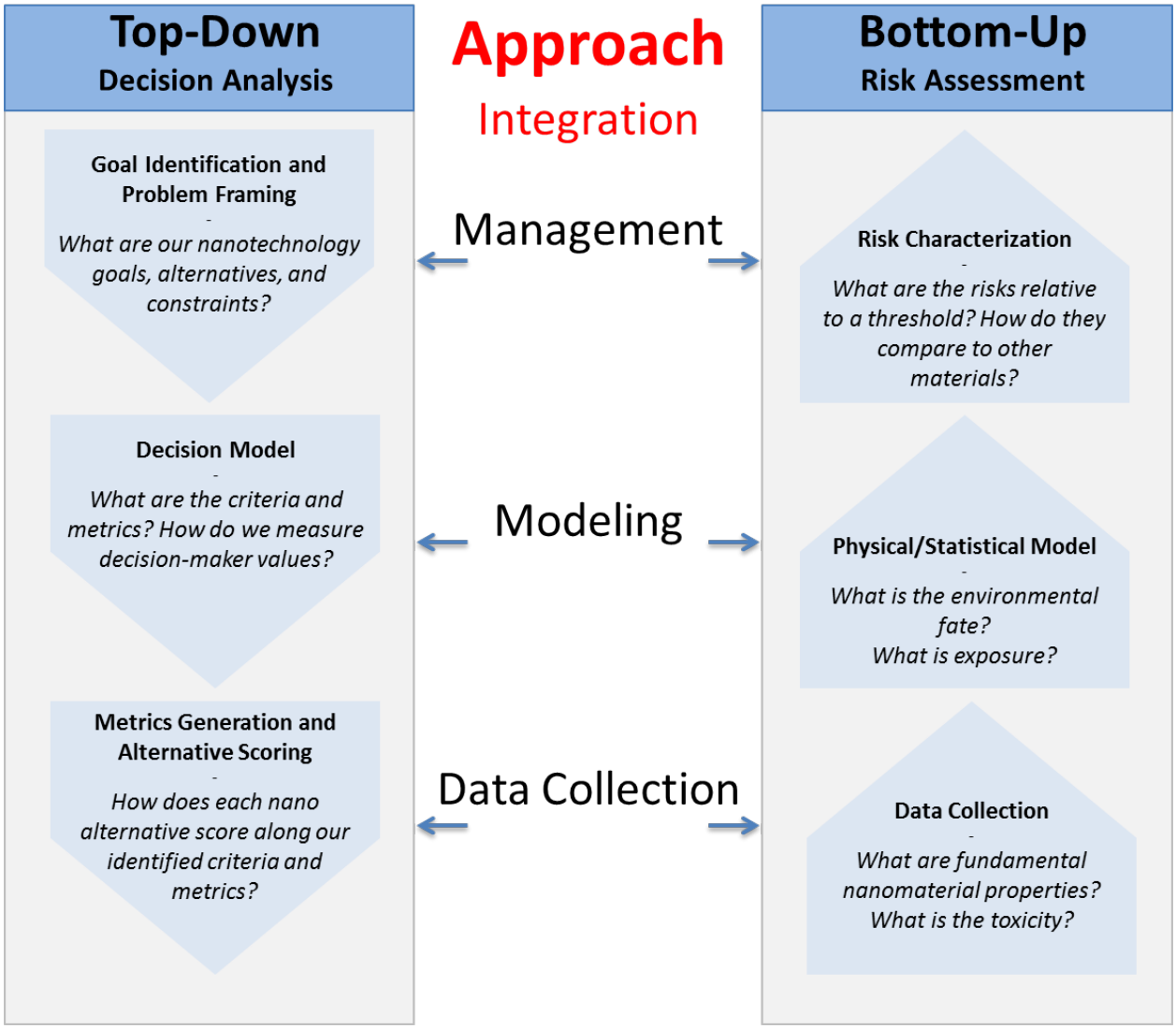

Figure 1.1. Comparison of approaches to risk management. *Top-down*: Identifying types of decisions and decision-maker needs to guide risk assessment and risk management. *Bottom-up*: Moving from hazard identification, exposure assessment, and risk characterization toward informed decisions. (Republished with permission of Springer, from Risk-based standards: integrating top–down and bottom–up approaches, Linkov, et al., *Environment Systems and Decisions* 2014; permission conveyed through Copyright Clearance Center, Inc. [*4*].)

perspectives of multiple stakeholder communities on the perception, assessment, and management of the potential risks of nanotechnology. Chapter 5 outlines the methodology of the stakeholder breakout sessions involving discussion of a hypothetical "Nanoparticle X" (see sidebar on p. 25) and the charge to the participants in those breakouts. The discussions from the breakouts are summarized by risk decision type in Chapter 6 and by stakeholder community in Chapter 7. Chapter 8 discusses the outcomes of the roundtable discussions. In Chapter 9, recurring themes across all sessions are summarized. Appendices include (A) the workshop agenda, (B) a list of workshop participants, (C) a list of acronyms and abbreviations used in the report, and (D) a list of available tools and information repositories mentioned at the workshop. Additional materials related to the workshop are available at www.nano.gov/R3workshop [*5*].

2. Keynote—Risk Analysis

Summary of Remarks by Baruch Fischhoff, PhD
Howard Heinz University Professor
Social and Decision Sciences and Engineering and Public Policy
Carnegie Mellon University

The field of risk management has been developing for about half a century. Most large English-speaking countries have produced some type of document with similar steps for effective risk management, in which (1) the size of the risk is characterized, (2) the value of the risk is assessed, and (3) the risk is somehow controlled. One preferred model is from the Standards Council of Canada ([*6, 7*], see Figure 2.1), which strives for overall management of risk by focusing on communication at each step. Specifically, the model (1) calls for the evaluation of benchmarks after each stage of the process (a "reality check") and (2) includes an explicit expectation of risk communication with stakeholders so that the public is not "blindsided" by a decision. This approach ensures that both actual risks and the concerns of the public are addressed. It can also allow technologists to solve potential problems early in the product design process, before financial, staff, and structural investments are made.

The Fischhoff research group's work on risk associated with the microscopic parasite *Cryptosporidium* in water supplies [*8*] illustrates how an explicit risk management model can assist the risk assessment process. The analysis can begin with either a bottom-up or a top-down approach; bottom-up by identifying the event and its potential outcomes (an analysis based on an event tree) or top-down by starting with an outcome and identifying the scenarios that might cause the outcome (an analysis based on a fault tree). Both methods can be used in concert to define the major risk-based determinant(s). Ultimately, this two-way process ensures that analysts integrate a variety of factors that are essential to risk analysis (e.g., characteristics of a local public health system, relevant regulations, and self-protective mechanisms—effective or not—that consumers could implement). An adequate risk model should be explicit and should accomplish the following:

- Create clear, shared definitions of variables and relationships.
- Identify critical expertise.
- Organize existing evidence.
- Organize emerging evidence.
- Estimate risk and uncertainty.

Assuming that quantitative data exist for every factor relevant to the risk analysis process, the model can be used to obtain absolute risk levels.

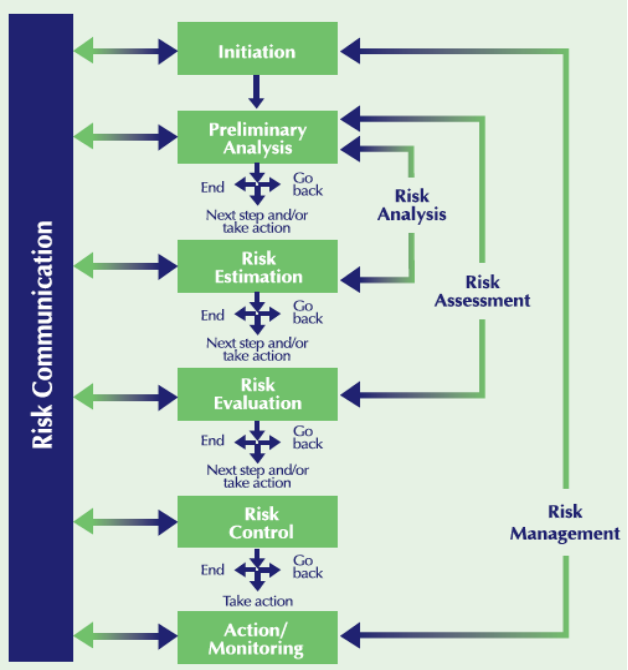

Figure 2.1. Fischhoff's preferred model of the risk management process, with a focus on communication. The flow chart shows six steps: initiation, preliminary analysis, risk estimation, risk evaluation, risk control, and action/monitoring. During the entire process, all of these steps interact with risk communication. (Reproduced from Figure 18 in [*6*], based on [*7*], courtesy of the Canadian Standards Association group.)

However, even in the absence of quantitative data, this model can still allow analysts to assess relative risk by (1) providing a general assessment of effectiveness for selected precautions or safeguards, and (2) helping to identify as well as gather relevant decision makers who can influence the risk level in the situation of interest. An adequate communications strategy must accompany an adequate risk model. This strategy includes providing the information that people need in accessible places and in a comprehensible form and using their feedback to inform risk managers early enough in the process to affect the design of the risk management framework.

Common Pitfalls

Assuming that risk can be defined objectively: The term "risk" can mean different things to different stakeholders, such that no single definition is objectively correct. The National Research Council (NRC) Committee on Risk Characterization recognized the critical importance of defining risk in its influential report, *Understanding Risk* [*9*]. This report overturned the conventional risk management model by suggesting that defining risk (i.e., engaging in explicit risk characterization) in the context at hand is the first step that risk managers must undertake. The NRC report also indicated that because risk is informed by public values, communication with the public and stakeholder engagement must occur in order to define risk correctly.

For instance, whereas certain risk analysts may implicitly assume that risk is defined as the probability of premature death (i.e., the probability that someone in a given population will die as a result of the new technology), others may assume that risk is defined as the expected life years lost (i.e., the number of years of life lost as a result of the new technology, which will be higher when younger people die). In the late 1970s and early 1980s, researchers addressing risk in the context of the nuclear power industry modeled risk differently if deaths occurred catastrophically (i.e., all at once), as opposed to chronically (i.e., over an extended period of time). Thus, a catastrophic but very low-probability event may be weighed differently than an event causing the same number of deaths distributed across several years, depending on societal needs or values. Risk analysts also should consider how outcomes are distributed over time: should risk that will only be realized at a future date be given the same weight as immediate risk [*10*]? There are many possible risk outcomes, including injuries, illnesses, preterm births, child abuse and neglect, and unrealized potential; deciding which definition to accept is a non-trivial, ethics-based choice.

When defining risk, consideration should be given as to whether the risk is either [*11*]:

- Distributed equitably.
- Assumed voluntarily.
- Catastrophic.
- Well understood.
- Controllable.
- Dreaded.
- Borne by future generations.

Any decision regarding the definition of risk will be controversial and will likely not be ethically or socially acceptable unless stakeholders are involved in defining that choice. Even in the presence of an open dialogue, the terms of any analysis will embody values that favor certain interests. As a result, common metrics across contexts will obscure ethical issues unless adopted by a credible public process because every context has its own complexity. For example the many different ways that one might

want to "discount" future outcomes in a risk analysis [*10*] demand communication and stakeholder involvement so that this consideration can be explicitly addressed when defining risk.

Limiting analyses to readily available experts and evidence: Most organizations initially approach risk with their preexisting set of experts. Because risk analysis depends on a vast array of factors, it is unlikely that any one organization will have a full set of experts capable of providing all of the relevant proficiency. The Fischhoff research group's work on the public health risk posed by *Cryptosporidium* intrusion into domestic water supplies illustrates this point [*8*]. This risk analysis model depended on factors including utility treatment options, health department awareness, and media coverage. Although the research team had reviewed the literature and had created putative estimates of risk, experts familiar with each system were also consulted. Without these other experts, this model would have been incomplete and potentially misleading; the researchers would not have discovered a fundamental flaw in their system for developing public warnings regarding *Cryptosporidium* contamination.

In terms of only using readily available data, summary measures of uncertainty are difficult to find, even though they are badly needed by decision makers. For various reasons, an organization's leaders might not feel that representing uncertainty is justified. However, the behavioral literature shows that much of the difficulty in understanding uncertainty comes not from numbers or concepts, but from the murkiness of the events being described [*12*]. An organization that does not support the representation of uncertain knowledge may develop a communication problem. Therefore, researchers should make an effort to effectively communicate uncertainty to decision makers and the public [*13*].

Choosing to "fly blind" when communicating with stakeholders: To communicate responsibly with stakeholders, risk managers must do stakeholder research. There are two main reasons for this: (1) personal intuitions regarding communication, even with people we know well, are often faulty and (2) human behavior is always complex. Much of psychology is dedicated to documenting ways in which we misunderstand one another. Misunderstandings can be exacerbated when the audience does not trust the communicator, does not know the communicator, has a different background than the communicator, or has other goals in mind. One major reason for miscommunication is the "common knowledge effect." This occurs when the communicator overestimates the extent to which the audience shares his or her knowledge and may result in the communicator failing to provide critical information. It is difficult to predict how communicating information will affect human behavior. Based on the literature, several principles guide people's judgments and choices:

- Principles of judgment
  - People are good at tracking what they see but not at detecting sample bias.
  - People have difficulty projecting nonlinear trends.
  - People have a limited ability to evaluate the extent of their own knowledge.
  - People have difficulty imagining themselves in other visceral states.
  - People can be affected by transient emotions.
- Principles of choice
  - People can be prisoners to sunk costs, hating to recognize losses.
  - People dislike uncertainty.
  - People consider the return on their investment in making decisions.
  - People are insensitive to opportunity costs.
  - People may not know what they want, especially when asked novel questions.

A priori, even if you know the literature, you cannot predict which principle will be important and how it will interact with a particular audience and a particular message. There is no responsible way of communicating without collecting evidence. Just as a risk manager has a fiduciary responsibility to prevent rejection of his or her client's product by an uncomfortable public, anybody who puts others at risk or is trying to provide benefits that might be lost if the process fails has an ethical responsibility. Risk managers who choose not to test their message are choosing to "fly blind," putting their own enterprise and their stakeholders in peril.

Proposals for Avoiding the Pitfalls

Overall, a risk management framework requires domain and subject matter experts, risk and decision analysts who can identify the relevant facts, behavioral scientists who can create an effective communications strategy, and systems specialists and practitioners who can ensure that the entire enterprise is functional.

Create an independent resource center: An independent, permanently funded resource center with scientific support would assist the risk management process. An effective risk management endeavor requires a fairly complicated skill set that is best satisfied by experts in each area. These groups are not often in communication with each other and do not know how to initiate a joint risk management endeavor. A competent resource center should have sufficient resources and participants to handle outreach to stakeholder communities and to serve as a point of contact for "inreach" among experts capable of providing publication-quality scientific support. The envisioned resource center should have the following functions:

- Provide quality assurance from researchers willing to commit a portion of their time for the public benefit (hopefully with institutional support).
- Facilitate economies of scope.
- Pool lessons learned.
- Anticipate problems.
- Involve academic researchers who are not willing or able to commit time or resources to applied research.

Standardize procedures for making and communicating decisions: When multiple groups involved in a single endeavor communicate in different ways, the audience will have to orient itself to each style. This makes the decision-making procedure challenging. If a standard procedure for making and communicating decisions were implemented, the efficiency of the process could be significantly improved. One example of an effort to standardize communication is the process promulgated by the Food and Drug Administration (FDA) for both conducting and communicating its licensing decisions under the Prescription Drug User Fee Act [*14*]. This process is an interesting compromise between making it comprehensible to people and making something experts are comfortable saying. In the FDA process, all evidence must be accompanied by an assessment of uncertainty. The FDA method also clearly distinguishes between the evidence and the reasons and conclusions that lead to each decision. Another group systematically summarizes drug testing evidence specifically for patients [*15*]. Complex information can be understood by most of the public if the communicator uses effective communication methods informed by research.

Develop a shared understanding by developing a common knowledge of essential scientific approaches: Risk managers should seek fluency, rather than technical mastery, in a range of risk

management and analytical methods. Few analytical approaches have made their way through peer review; therefore, it is advantageous and not prohibitively difficult for risk managers to know a little bit about different analytical methods so that they can recognize classes of problems that they might not otherwise detect [*16*, *17*]. Every competent risk manager should know something about the following essential analytical methods:

- Risk analysis.
- Decision analysis.
- Signal detection theory.
- Game theory.
- Economics.
- Behavioral psychology.
- Communications.

In conclusion, the development of a common knowledge of essential scientific approaches can allow for efficient risk management by enabling the sharing of information among stakeholders. Such an understanding will enable effective communication and create more informed stakeholder communities. Finally, several resources that are points of access for understanding risk management methods are provided in Table 2.1.

Table 2.1. Resources on risk management

Title of Resource	Author(s)
The Science of Science Communication *PNAS* [*18*]	Fischhoff, B., & Scheufele, D. (Eds.), 2013
***Communicating Risk and Benefits: An Evidence-Based User's Guide* (FDA) [*19*]**	Fischhoff, B., Brewer, N., & Downs, J. (Eds.), 2011
***Risk: A Very Short Introduction* [*7*]**	Fischhoff, B., & Kadvany, J., 2011
***Thinking, Fast and Slow* [*20*]**	Kahneman, D., 2009
***Uncertainty* [*21*]**	Morgan, M. G., Henrion, M., & Small, M., 1990

3. Keynote—Nanotechnology Multi-Stakeholder Risk Perception: Implications for Risk Analysis, Management, and Communication

Summary of Remarks by Barbara Herr Harthorn, PhD
Professor of Anthropology
Director, Center for Nanotechnology in Society
University of California, Santa Barbara

Responsible and ethical risk analysis and communication is a key part of responsible development of nanotechnology. These require having good, empirical evidence about both the technical risks and about society's perceptions of risk. Both actual and perceived risk are important not only for normative, ethical reasons but also for instrumental reasons, to achieve better outcomes. This overview of the diverse stakeholder perceptions of nanotechnology risks and their potential implications for risk management and decision making is based mainly on the research of the Center for Nanotechnology in Society at the University of California, Santa Barbara (CNS-UCSB), funded by the National Science Foundation.

The need for a common language is evident throughout the discussions of this workshop. The definition of "responsible development" endorsed by the National Research Council (NRC) of the National Academy of Sciences provides an ethical framework for the NNI risk management endeavor. According to a 2006 NRC report, responsible development of nanotechnology "implies a commitment to develop and use technology to help meet the most pressing human and societal needs, while making every reasonable effort to anticipate and mitigate adverse implications or unintended consequences" [*22*]. Based on this definition, responsible development is entwined within a risk–benefit framework where the benefits aim to answer the needs of society. The empirical evidence indicates that one cannot rely on intuitive understanding of "risk" or "benefit" to respond to societal needs. Various stakeholders with diverse backgrounds will likely have differing perceptions with respect to what constitutes both benefits and risks in nanotechnology development. CNS–UCSB has investigated the risk/benefit perceptions of six stakeholder groups:

- **Scientists and engineers** synthesizing novel materials and incorporating them into increasingly complex molecular devices and systems.
- **NanoEHS researchers** (toxicologists) working to characterize the hazards of numerous manufactured nanomaterials and nanotechnology-enabled products in a large range of environmental contexts.
- **Regulators** attempting to determine a safe course forward that will ensure public safety without impeding economic development.
- **Industry** leaders and workers concerned with safety and quality control while maintaining an economically viable future.
- **NGOs**, or the "activated public," focused primarily on environmental and consumer product safety risks or about democratic participation itself.
- **Lay publics**, who generally are not included in these discussions but often are implicated as participants, as imagined downstream consumers.

In order to obtain an accurate, representative sample of public perceptions of emerging technologies, research must be comprehensive and deliberative. Relevant publics include representative sample groups, "invited publics" (quasi-representative), and "self-selected" publics. The self-selected public comprises individuals who are self-motivated to attend advertised events, including NGOs, whereas the invited public may not even know that the research topic qualifies as, for example, an emerging technology. It is important to note that at least one study in the UK has indicated that self-selected public groups tend to have a perception of risk that is higher than that of the general public [*23*].

Studies on Stakeholder Risk Perception

Summarized here are several CNS-UCSB studies on public perceptions of risk and the complex cognitive and affective drivers of risk perception, conducted through both survey-based, experimental quantitative research and qualitative/deliberative evaluations (i.e., mixed methods research).

Risk perception among members of the public: A meta-analysis of 22 surveys on public perception of nanotechnology was conducted between 2002 and 2009 [*24*]. These surveys were conducted in North America, Europe, and Japan. The results showed that public perception of nanotechnology was benefit-centric: Among those who did not indicate uncertainty, members of the public who believed that the benefits outweighed the risks outnumbered those who believed that the risks outweighed the benefits by a ratio of approximately three to one ([*24*], see Figure 3.1). However, because on average 44% of people indicated uncertainty, this analysis also highlights the potential for a future change in public perception and probably indicates that large portions of the public are unfamiliar with nanotechnology (over 50% in some surveys). The large "not sure" results of this study are unusual in the risk analysis arena when conducting this type of study.

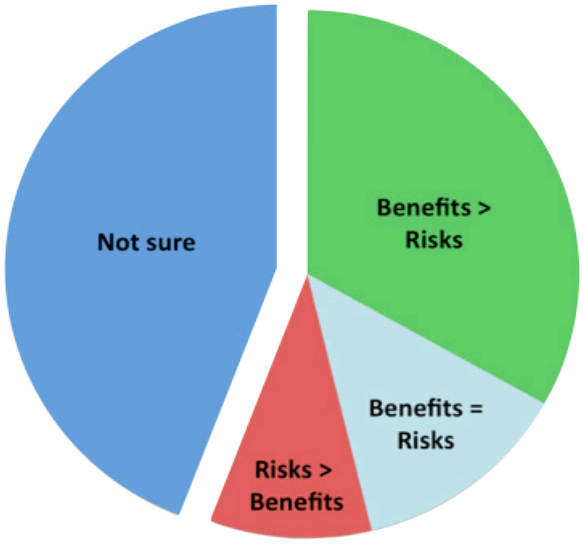

Figure 3.1. Pie chart showing public perceptions of nanotechnology risks and benefits. The results are based on a quantitative meta-analysis of 22 studies from 2002–2009 in North America, Europe, and Japan. The responses were benefit-centric, with nearly half of respondents stating that the benefits are equal to or greater than the risks. However, the most frequent response was that of uncertainty, showing a high potential for opinions to shift. (Figure courtesy of B. Herr Harthorn.)

A comparative review of 18 different deliberative research projects also found benefit centricity to be widespread with respect to nanotechnology risk perception [*25*]. However, the same study also discovered a phenomenon of "latent ambivalence," which manifests around three views: (1) skepticism toward the government and industry, (2) a concern about who represents the public's interests, and (3) questions regarding whether a product is needed at all. These concerns represent social, not technical, risk issues, and they are the predominant concerns voiced in deliberative forums, even when technical risk information is presented during the deliberations. Thus, increased knowledge and awareness do not affect this latent ambivalence.

Another research example indicated that the trust asymmetry principle (i.e., that trust is much easier to lose than it is to gain) will prevail in the nanotechnology context. In one of their studies, CNS-UCSB researchers conducted a phone survey to assess how plausible positive and negative

scenarios relating to nanoEHS effects, nanotechnology-related industry actions, and nanotechnology regulation would affect public perceptions of nanotechnology [*26*]. The negative scenarios decreased public trust more than the positive scenarios increased public trust, and trust was lost more easily when bad news followed good news. For example, if the benefits of new technology were advertised and emphasized to the public and news about risk or adverse effects followed, public trust would suffer a greater amount of damage than if balanced news were given throughout the process.

The results of an in-progress web survey by CNS-UCSB researchers reveal interesting aspects of the public's opinion about what constitutes an acceptable amount of environmental risk [*27*]. The results show that the public has a fairly nuanced idea of what constitutes "responsible development" of new technology. Specifically, the public is interested in the degree to which informed consent is given to develop new technology, the degree to which issues of equity and power are resolved ethically, the value given to the public's role, and the amount of trust that is held by the acting institutions.

Race and gender can also be important in public deliberation about risk [*28*], resulting in subtle and overt group dynamics. For example, men speak more than women and use more intrusive interruptions during deliberations about nanotechnology; whites use more intrusive interruptions than people of color; women use more backchannels, cooperative overlaps, and self-disclosure when discussing health and human enhancement applications as opposed to energy and environmental applications; and men's patterns of talk do not vary when the application discussed varies. These dynamics are found in many other decision-making situations regarding social issues; their significance is that both subtle and overt group dynamics play major roles in deliberative settings, are very difficult to disentangle, and are not well studied. The important aspect is that these studies show the dynamic that one can expect when dealing with decision makers who have varying social positions. Ultimately, the public dialogue on nanotechnology, particularly early in development, is likely to veer from technical risk to societal implications.

Risk perception among NGOs: The CNS-UCSB research group is approaching the topic of nanotechnology risk perception among NGOs by analyzing English-language publications from 183 NGOs, 88 of which are specifically "nano engaged" [*29*]. Of this sample, the researchers have preliminarily chosen 20 predominant groups and have summarized how those NGOs focus on consumer and environmental safety. Common goals among these groups include the following:

- Increasing the amount of nanoEHS research.
- Promoting labeling of commercial products containing nanomaterials.
- Increasing government oversight of nanotechnology.
- Engaging the public in dialogues on nanotechnology.

The CNS-UCSB researchers found that NGO groups have paid little attention thus far to worker safety issues. Also, they found that in general, NGOs do not restrict their activities to specific nanomaterials, with the exception of nanosilver and titanium dioxide. Finally, these groups often advocate government action as the main focus of their social action.

Risk perception within industry: Not much work has been done with industry. CNS-UCSB has completed two international surveys, in 2006 [*30*] and in 2010 [*31*]. In the more recent study, the researchers interviewed industry leaders from companies that handled or produced engineered nanomaterials (ENMs) about issues relating to risk perception for six classes of nanomaterials: carbon nanotubes (CNTs), heavy metals, dry powders, quantum dots, metal oxides, and other carbonaceous nanomaterials.

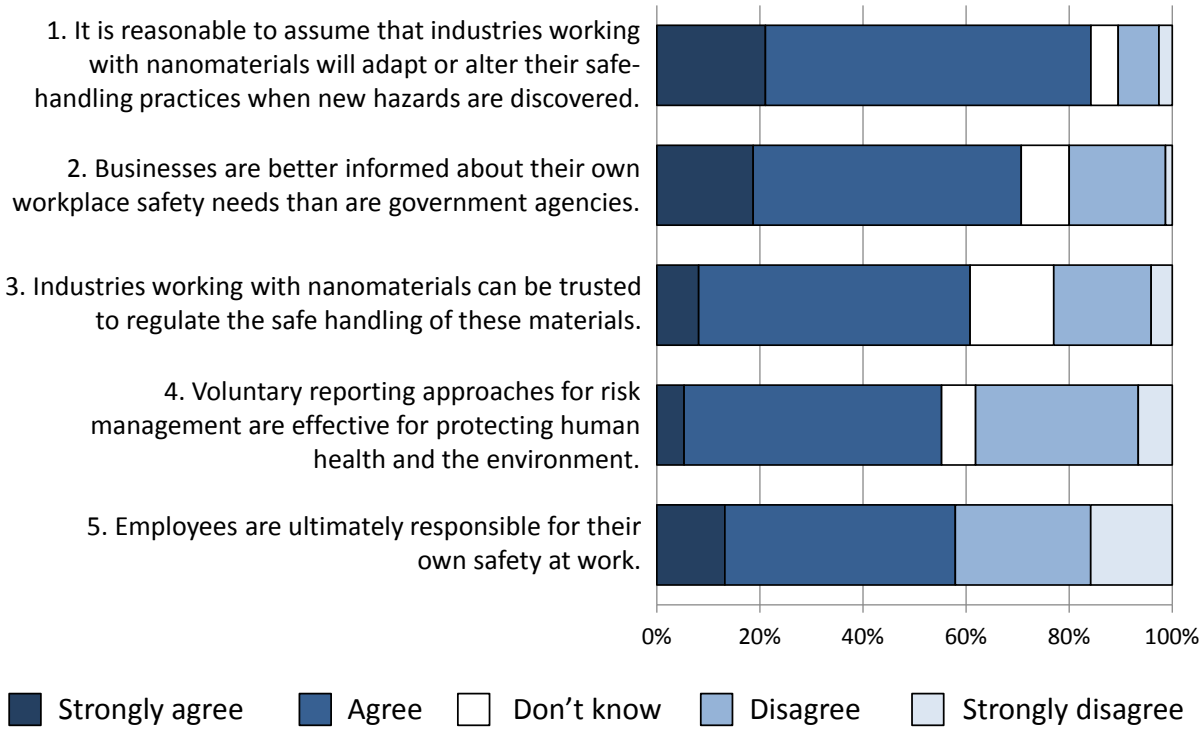

Figure 3.2. Industry perceptions of risk and regulation show a preference for autonomy over regulatory oversight. The study asked nanotechnology companies to rank their agreement with each of statements 1–5 on a scale of *strongly disagree*, *disagree*, *don't know*, *agree*, and *strongly agree*. The statements implied a desire for independence from regulation, and the majority of respondents (over 50%) agreed or strongly agreed with each statement. (Figure courtesy of B. Herr Harthorn.)

Results showed that 75% of respondents were either uncertain about the risks or that they believed that the risks of nanomaterials were "moderate to high." This trend was fairly uniform across the six surveyed materials, indicating that risk perception among these industry leaders was not dependent on the materials that their companies were handling.

The researchers then asked a series of questions regarding regulations ([*31*], Figure 3.2). The answers provide evidence that the industry prefers autonomy from governmental regulation. Typically, individuals with high perceived risk favor self-protection through regulation. At the same time, there was strong concern regarding the public response ([*29*], Figure 3.3). In particular, the majority of respondents were concerned about unwarranted public backlash and believed that the direct involvement of citizens in technology policy is not beneficial.

Risk perception among experts: Three stakeholder groups may be termed "experts," including (1) nanotechnology scientists and engineers, (2) regulators involved in nanotechnology-related regulation and nanotechnology risk assessors in the government, and (3) nanoEHS researchers. A study by CNS-UCSB researchers surveyed over 400 experts about their risk perceptions relating to nanotechnology [*32*]. The results of this study indicated that expert views on nanotechnology-related risk are significantly different from the views held by the general public, particularly in terms of uncertainty regarding the risks and benefits. In total, 23% of nanotechnology-related regulators, 16% of nanoEHS researchers, and 11% of nanotechnology scientists and engineers indicated that they "didn't know" or "weren't sure" whether the risks of nanotechnology would outweigh the benefits ([*33*], Figure

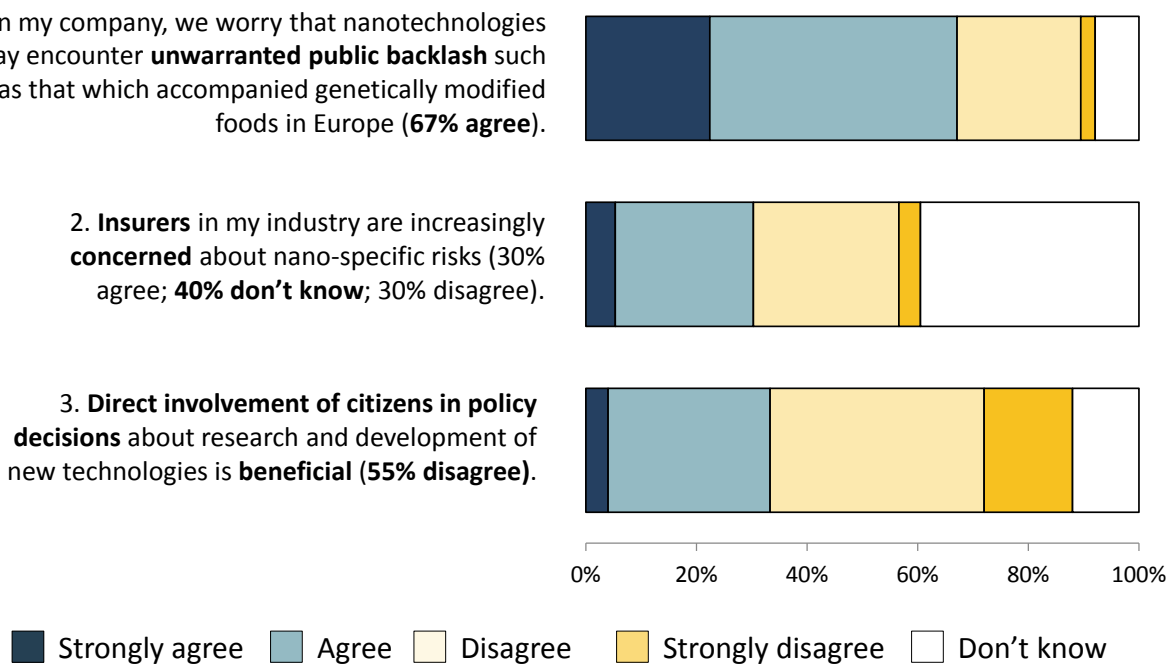

Figure 3.3. Industry concern about the public response. The study asked nanotechnology companies to rank their agreement with each of five statements on a scale of *strongly disagree*, *disagree*, *don't know*, *agree*, and *strongly agree*. These results indicate that most companies are worried about public backlash and do not trust the public to be involved in policy decisions. (Figure courtesy of B. Herr Harthorn.)

3.4). In contrast, the surveyed members of the public who provided the same ambivalent responses constituted nearly the majority of respondents in a 2009 meta-analysis of 22 surveys (Figure 3.1).

Overall, the majority of respondents from each expert community believed that the benefits of nanotechnology will outweigh the risks. Nanotechnology scientists and engineers—the group actually "in the labs"—generally showed less concern about the potential risks posed by nanotechnology than the other two groups did, and regulators and risk assessors in the government showed the most concern. The results of this study show that among experts, regulators have the least amount of confidence in the ability of the regulatory system to handle the challenges posed by nanotechnology.

Additionally, the study revealed gender differences with respect to experts' nanotechnology risk perceptions. The survey indicated that female experts generally perceived risk to a greater extent than male experts did, a finding that replicates the results of the vast majority of risk perception surveys considering gender. The point of this result is not just about gender, but rather that a person's social position matters when making decisions about risk, even among scientists and regulators. This finding indicates that social position is a relevant consideration when investigating how individuals perceive and communicate risk.

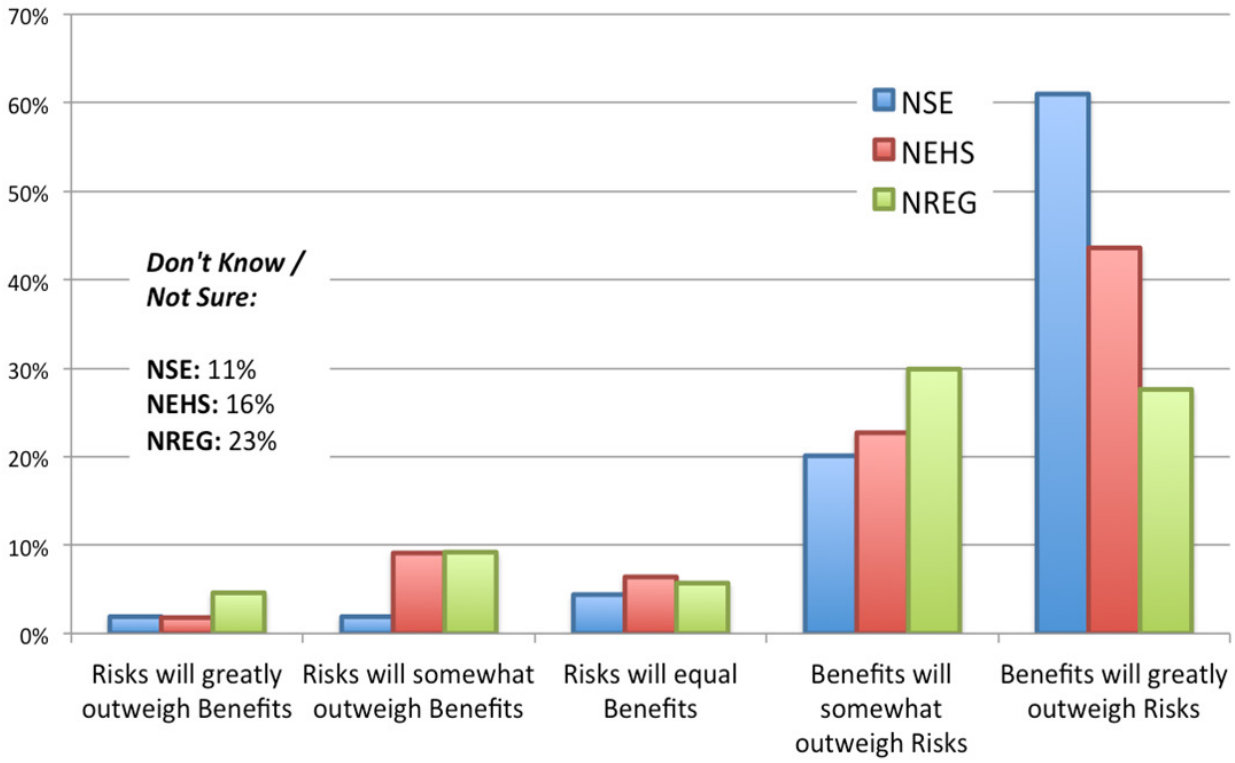

Figure 3.4. Expert perceptions of ENM risks and benefits. Scientists and regulators were asked to rank the relative risks and benefits of ENMs. Although the majority of experts agreed that the benefits will greatly outweigh the risks, nanotechnology scientists and engineers felt more strongly (60%) than regulators (27%) did in this regard. NSE: nanotechnology scientists and engineers, NEHS: nanotechnology EHS researchers, NREG: nanotechnology regulators. (Figure courtesy of B. Herr Harthorn.)

The main point is that all stakeholders have motivated cognition that affects the way they engage in decision making. Therefore, biases need to be accounted for in a structured way, using explicit analytics for the decision-making process. Under development at CNS-UCSB is a nanotechnology risk screening tool [*33*] for structured decision making. Technical risk data alone will not affect decisions; judgments by different stakeholders with varying biases, values, and stances, and differing levels of power and interest, will also be involved. Overall, better outcomes will result if these issues are explicitly addressed.

4. Plenary Presentations—Stakeholder Perspectives

A Perspective from Industry (Microelectronics Business Perspective)

Regulatory Challenges and Impacts on Carbon Nanomaterial Development

Summary of Remarks by Stephen Gibbons, PhD
Director of Technology, Carbon Electronics Center
Brewer Science, Inc.

Brewer Science conducts research in, develops, and manufactures advanced materials and equipment for making devices used in microelectronics. The company's core competencies are in materials innovation, design, manufacturing, and process integration, and its patent and commercialization portfolio includes supplying the first microelectronics-grade carbon nanotube (CNT) solutions on a commercial scale.

Limited data exist for determining the EHS, regulatory, and business implications of nanotechnology products and processes. Brewer Science has investigated EHS impacts of nanomaterial release into air, water, and soil; impacts on both humans and wildlife; and environmentally friendly methods for the effective and efficient disposal of nanotechnology-related solid and liquid wastes. Newer approaches have involved gap analysis to determine what types of data are needed for the efficient risk management of CNTs. Potential gaps include the following:

- Unknown baseline environmental exposures for various kinds of nanoparticles.
- Lack of life cycle studies based on realistic scenarios for the microelectronics industry.
- Lack of well-understood exposure limits.
- Lack of differentiation between the hazards associated with different CNT chemistries [*34*].

The NNI agencies could help in several areas to support industry in responsible, effective, and profitable development of nanotechnology. First, they could help in terms of education. Second, they could help regulators to realize that different nanomaterials and different functionalizations of nanomaterials pose different potential risks. Third, given that many regulatory frameworks are based on theoretical models, due to a lack of conclusive EHS data, it would be extremely beneficial to have a widely accessible, searchable information repository on the EHS implications of various nanomaterials. Finally, the NNI agencies could help devise a consistent set of criteria with which nanomaterials can be assessed for EHS implications—criteria that should take into account life cycle analyses, nanomaterial volumes in consumer devices, and other relevant variables.

A Perspective from the Consumer Community

Summary of Remarks by Michael Hansen, PhD
Senior Staff Scientist
Consumers Union

Products that contain nanomaterials are not sufficiently labeled, as demonstrated by results from the 2008 Consumers Union test of commercial sunscreens ([*35*], see Figure 4.1 and Table 4.1). In a December 2008 study, Consumer Reports tested five sunscreens containing titanium dioxide and zinc oxide. None of the products tested had a "nano" claim on its label, and when asked by Consumer Reports, customer

service representatives from five companies stated that each did not contain nanoparticles. Tests showed that nanoparticles were present, at least to a limited extent, in four out of the five products. Additionally, Consumer Reports tested one sunscreen that did make a nano claim on its label and found that it did contain nanoparticles. However, a customer service representative stated that the nanoparticles of titanium dioxide are coated with wax and thus cannot enter the skin.

Figure 4.1. Image of six sunscreens tested by Consumer Reports for the presence nanoparticles. ©2008 by Consumers Union of U.S., Inc. Yonkers, NY 10703-1057, a nonprofit organization. The December 2008 study looked for the presence of nanoscale titanium dioxide and zinc oxide [*35*]. Reprinted with permission from the December 2008 issue of Consumer Reports for educational purposes only. No commercial use or reproduction permitted.

Although more risk assessment research is now being funded by NNI agencies, more work is needed concerning the detection of nanoparticles as they are functionalized in consumer products on the market. This will facilitate assessment of potential impacts on consumers in realistic exposure scenarios (once nanoparticles have been incorporated into the food or product matrix). Although toxicity and exposure testing using commercially available standardized nanoparticles is becoming more common, the available samples need to be better aligned with nanomaterials actually on the market, especially in products used on or in the human body. Further, all functionalized forms need to be looked at separately. The NNI website and NNI brochures need to be more user-friendly in terms of making it easier to find the research on hazard and risk assessment. Likewise, the good work by CPSC in the area of nanotechnology risk assessment [*36*] should be easier to find online.

Table 4.1. Consumer Reports test results for the presence of nanoparticles in sunscreens (Reproduced from [*35*])

Product	Nano claim	Our findings
Aubrey Organics Natural Sun SPF 25 Green Tea Protective Sunscreen	**No.** A company representative said the titanium dioxide is not in nano form.	**Yes**
Badger SPF 30 Sunscreen	**No.** A customer service representative said the product has micronized zinc that sits on the skin and is not absorbed.	**Yes**
California Baby SPF 30+ Sunscreen	**Yes.** In its raw form the titanium dioxide is nano, but it is coated with waxes so that it does not enter the skin, a company representative said.	**Yes**
Kiss My Face SPF 30+ Sun Screen	**No.** The product does not contain nanoparticles of titanium dioxide, a customer service representative said.	**Yes**
Mexitan SPF 30 Sunscreen	**No.** The titanium dioxide and zinc oxide used are not nano-particles, according to a customer service representative.	**Yes**
Zinka Colored Nosecoat*	**No.** The product contains no nano, a customer service representative said.	**No**

None of the products tested had nano claims on its label.
*Zinka makes no SPF claim on the package.

The International Life Sciences Institute (ILSI) has initiated two "NanoRelease" projects, one themed "Consumer Products" [*37*] and one themed "Food Additives" [*38*], both of which aim to develop methods to detect nanomaterials in consumer products and in the human body following product use. The ILSI

model is a good one in that these projects have broad participation from all sectors in their steering committees and are looking at items in actual commercial use. The ILSI studies are crucial from a consumer perspective because there are so few studies on detecting nanoparticle uptake in the human digestive system. If you can't detect the nanoparticle, you can't measure exposure or determine risk.

The current regulatory framework is not sufficient for assessing the risks of nanotechnology-enabled consumer products, especially for nanoparticles that are actually in use in cosmetics, foods, food additives, etc. In April 2012, FDA released two draft guidance documents [*39*, *40*]. Both included consideration of deliberately manipulated materials up to 1000 nm in size. The first document, which addresses food additives, states that ENMs "likely would not be covered" by existing "generally recognized as safe" (GRAS) standards, making these materials subject to formal premarket review [*39*]. The second document, covering cosmetics, suggests that industry should revise its safety testing using a "tiered testing" approach due to the unique properties of ENMs [*40*]. FDA has no authority to require premarket testing for cosmetics under the Federal Food, Drug, and Cosmetic Act (FFDCA), and FDA assumes the existing battery of tests are "probably adequate" for testing of ENMs. A bill called the Safe Cosmetics and Personal Care Products Act of 2013 [*41*, *42*] has been introduced in the U.S. Congress that would give the FDA the regulatory authority to require testing and labeling of ENMs in cosmetics.

The Environmental Protection Agency (EPA) Nanoscale Materials Stewardship Program (NMSP) [*43*] has released an interim report on the NMSP indicating that 90% of likely commercially available nanoscale materials are not reported by companies at all [*44*]. This low rate of engagement suggests that companies are not inclined to voluntarily test their nanomaterials, and efforts in the UK and Denmark to utilize voluntary reporting schemes have also proven unsuccessful. Mandatory approaches are needed. France requires industry reporting of the identity, quantity, and uses of ENMs. Canada has a mandatory safety reporting system for import and production of ENM amounts greater than one kilogram.

EPA has authority over ENMs under the Toxic Substances Control Act (TSCA). However, standard toxicology testing for ENMs is not based on volume or quantity but on surface area, making the low-volume and low-release/low-exposure exceptions[1] inappropriate for nanoscale materials. Consequently, these exemptions need to be reconsidered for ENMs. EPA has thus attempted to recognize that nanoscale materials may pose different risks than bulk-scale materials in its regulations. In 2011, EPA promulgated significant new use rules (SNURs) [*45*] under TSCA [*46*] for multiwalled CNTs. Subsequently, EPA has proposed SNURs for 37 other chemicals, including 14 nanomaterials [*47*]. While these SNURs are being reviewed by the Office of Management and Budget (OMB)[2] [*48*], EPA has begun product-by-product data call-in notices for nanosilver products under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) section 3(c)(2)(B)[*49*].

Since ENMs are different than bulk materials, the U.S. Government should mandate testing and reporting to determine how much is in use and develop protocols, even if just to find that ENMs are not problematic.

[1] Chemical substances manufactured in quantities of 10,000 kg or less per year and chemical substances with low environmental release and human exposure, 40 C.F.R. §723.50 (2012).

[2] On February 25th, 2013, EPA announced Proposed Significant New Use Rulings (SNURs) for 37 chemical substances, including 14 substances whose reported chemical names include the term "carbon nanotube" or "carbon nanofibers." These rules became final on September 2, 2014, for 36 of those substances, including all of the nanomaterials. An additional set of SNURs for 52 chemical substances, including one nanomaterial (functionalized carbon nanotubes generic PMN No. P-13-793), was promulgated on October 27th, 2014. This SNUR was partially withdrawn for 30 of these chemicals (including PMN No. P-13-793) on December 23rd, 2014, because EPA received a notice of intent to submit adverse comments.

A Perspective from the Labor Community

Assessment and Management of the Potential Risks of Nanotechnology

Summary of Remarks by Darius Sivin, PhD
Health and Safety Department
International Union, United Auto Workers

Our ability to measure, manipulate, and process at the nanoscale is new. The United Auto Workers (UAW) is concerned that the lack of data regarding ENMs could present problems for auto workers. This includes potential hazards of exposure and the ability of workers to know which materials are present in specific products they handle. The Occupational Safety and Health Administration (OSHA) Hazard Communication Standard (i.e., the "right-to-know standard") requires manufacturers who sell materials utilized in the workplace to provide "safety data sheets" (SDSs) to employers [*50*]. These SDSs provide information about the material composition and potential hazard(s) of each component. Employers are then required to train and inform their workers regarding what potential hazards exist in the work environment in order to minimize any risk of exposure associated with such hazards. One problem is that in the OSHA regulation an "article" is exempt from reporting requirements.[3]

"Articles" are typically manufactured products, such as an engine or a dashboard, that arrive at a factory as a unit, the assumption being that they will not be further processed.[4] However, articles often require physical modifications (i.e., grinding, cutting, or buffing the material) to ensure that they fit properly, thereby creating new opportunities for hazard exposure in the absence of potential hazard information (for example, what the articles are coated with).

Another problem is that SDSs are often incomplete ([*51*], Figure 4.2). The Hazard Communication Standard does not clearly indicate whether a manufacturer or distributor is responsible for indicating that a material is a nanomaterial. The chief science advisor for the Project on Emerging Nanotechnologies, Dr. Andrew Maynard, stated that "carbon nanotubes are as similar to pencil lead as the soot on my grill at home is to diamonds" [*52*]. One review of SDSs by the Lippy Group revealed that 33% of these sheets failed to identify a nanoscale component as present and that 52% did not include any cautionary language [*53*]. Furthermore, the National Institute for Occupational Safety and Health (NIOSH) performed a review of 26 SDSs that revealed that 58% of the documents contained occupational exposure limits (OELs) for the bulk material without providing

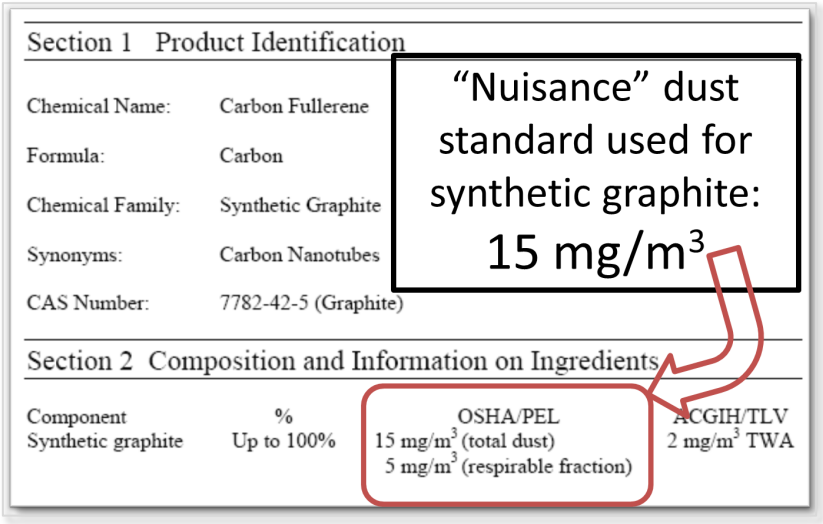

Figure 4.2. An example of a safety data sheet (SDS) using an inappropriate synonym for a nanomaterial. This safety data sheet for carbon nanotubes uses the 15 mg/m^3 nuisance dust standard for synthetic graphite [*51*]. (Figure courtesy of D. Sivin.)

[3] Hazard Communication, 29 C.F.R. §1910.1200(b)(6)(v)
[4] Hazard Communication, 29 C.F.R. §1910.1200(c)

guidance that the OELs may not be appropriate for the nanoscale material. Overall, 69% of the 26 sheets were classified as "in need of serious improvement," and none were classified as "good" [*54*]. Ultimately, documentation practice does not adequately communicate the potential for nanomaterial exposure among workers in the automotive industry; thus, it does not allow workers or the union to know the possibilities for nanomaterial exposure. As such, the union cannot encourage employers to take appropriate precautions, despite the highly developed occupational safety and health programs that are jointly administered by the union and the big three auto manufacturers. This problem is compounded when more and more work is outsourced to owner-run suppliers with less knowledge, ability, and on-site staff to address possible ENM hazards.

How do we address the lack of data about ENM hazards? A lesson learned from the petrochemical industry experience is that regulatory regimes must be devised early on to adequately distinguish between beneficial and harmful technologies and be able to restrict harmful ones before exposure is widespread. We need to be willing to act on incomplete knowledge to protect people. Control banding, which incorporates Lawrence Livermore probability and risk severity scores, is one promising method for risk assessment in the face of incomplete information and uncertainty [*55*].

In summary, we need more information about which products contain what nanomaterials. In addition, improved risk communication is necessary to mitigate the "where" and "when" of worker exposure to nanomaterials. This goal can be accomplished in part through full disclosure of nanomaterial safety information in SDSs. Suppliers and employers can assist in this effort by tracking who is exposed to nanomaterials and when exposure can potentially occur. And we need to learn from past mistakes and be more proactive about instituting some level of protection while data are still being acquired.

A Perspective from the Standards Community

The Role of Standards in Addressing Issues Relating to Risk and Nanotechnology

Summary of Remarks by Ajit Jillavenkatesa, PhD
Senior Standards Policy Adviser, Standards Coordination Office
National Institute of Standards and Technology

Standards provide confidence in the efficacy of tools used to assess and mitigate the potential risks of nanotechnology. However, they are only as good as the community's engagement in their development, in their use, and in publishing both successes and failures. "Documentary standards" are composed of agreed-upon and documented principles, approaches, and tests established by consensus and approved by a standards development body [*56*]. Such standards are generally formed by experts on the basis of sound scientific data. Regulators sometimes choose to refer to these standards for guidance.

Standardized approaches are very important in assessing risk. They enable clarity in communication, which enables the protection of human and environmental interests when used by regulators. Standards are also important for technology innovation, allowing developers to work on common platforms or foundations that are established by these standards. Finally, when standards are harmonized on a global scale they facilitate communication and trade among stakeholders and provide broad benefit.

Standardization activities relevant to the nanotechnology risk management process are being developed in a wide range of standards organizations. ASTM International [*57*] and the International Organization for Standardization (ISO) [*58*] are two such organizations with significant efforts relating to nanotechnology standards development. Efforts in three major areas worth noting relate to terminology, measurement, and EHS characterization (see Table 4.2). Both of these organizations

develop standards using open, transparent, consensus-driven processes involving multiple stakeholders to develop terminology, characterization, and measurement guidelines to assist EHS research and risk management for nanotechnology [*59*]. A standards document on general risk management principles has also been published [*60*]. Several documentary standards resources are the Nanotechnology Standards Database, sponsored by the American National Standards Institute (ANSI) Nanotechnology Standards Panel [*61*]; the ISO online browsing platform [*62*], which provides access to standards documents; the Nanomaterial Registry [*63*]; Germany's Federal Institute for Materials Research and Testing (BAM) Nanoscale Reference Materials [*64*] website, and a Nanostandards Wiki [*65*].

Table 4.2. Illustrative examples of documentary standards available for nanomaterials (current at the time of the workshop, and subject to revision and updates)

Type of Standard	Unique Identifier	Title
Terminology	ASTM E2909-13	Standard Guide for Investigation/Study/Assay Tab-Delimited Format for Nanotechnologies (ISA-TAB-Nano): Standard File Format for the Submission and Exchange of Data on Nanomaterials and Characterizations [*66*]
	ISO/TS 80004-1:2010	Nanotechnologies -- Vocabulary -- Part 1: Core terms [*67*]
	ISO/TR 14786	Nanotechnologies -- Considerations for The Development of Chemical Nomenclature for Selected Nano-objects [*68*]
	ISO/TS 80004-3:2010	Nanotechnologies -- Vocabulary -- Part 3: Carbon Nano-objects [*69*]
Measurement	ASTM E2578 - 07(2012)	Standard Practice for Calculation of Mean Sizes/Diameters and Standard Deviations of Particle Size Distributions [*70*]
	ASTM E2864-13	Standard Test Method for Measurement of Airborne Metal and Metal Oxide Nanoparticle Surface Area Concentration in Inhalation Exposure Chambers using Krypton Gas Adsorption [*71*]
	ISO/TR 13014:2012	Nanotechnologies -- Guidance on Physico-Chemical Characterization of Engineered Nanoscale Materials for Toxicologic Assessment [*72*]
	ISO/TS 14101:2012	Surface Characterization of Gold Nanoparticles for Nanomaterial Specific Toxicity Screening: FT-IR Method [*73*]
EHS Effects	ASTM E2535-07(2013)	Standard Guide for Handling Unbound Engineered Nanoscale Particles in Occupational Settings [*74*]
	ASTM WK 34427	New Guide for Nanotechnology Workforce Education in Health and Safety (*under development*) [*75*]
	ISO/TR 13121:2011	Nanotechnologies -- Nanomaterial Risk Evaluation [*76*]
	ISO 10808:2010	Nanotechnologies -- Characterization of Nanoparticles in Inhalation Exposure Chambers for Inhalation Toxicity Testing [*77*]
	ISO/TS 12901-1:2012	Nanotechnologies -- Occupational Risk Management Applied to Engineered Nanomaterials -- Part 1: Principles and Approaches [*78*]

For effective standardization, several questions must be considered and addressed:

- What needs to be standardized?
- By when is it needed?
- Are there priorities for certain standards?
- Are there good data on which to base the standards?
- Is there a consensus on techniques?

- How will the standards be used?
- Will the community participate in the validation and adoption of the standards?

Certain guidance can be gained by referencing past successes and failures from other sectors, including the experiences of the information security and financial industries, among many others. Inputs from all stakeholder groups should inform and support the process of creating standards; their continual engagement is essential for effective standardization.

A Perspective from the Regulatory Community

Assessment and Management of Nano Risk: A Regulatory Perspective

Summary of Remarks by Tim Malloy, JD
Professor of Law; Faculty Director, Sustainable Technology and Policy Program
University of California, Los Angeles

Regulations should follow the principles of transparency, flexibility, pragmatism, consistency, and rigor, with the ultimate goal of being protective. Other than direct regulation by the Federal Government or States, there are other, less-examined, ways of regulating risk. The first is a more decentralized mechanism, tort liability. The NNI might want to further examine this mechanism. Torts are civil wrongs that place the regulation of risk in the hands of the judicial system. Information disclosure is another way of regulating risk, such as in the form of SDSs. There are also more direct regulatory mechanisms; for example, at the Federal level, EPA manages CNTs in a new chemical program under TSCA [*79*], and the review of food additives by FDA may result in the regulation of nanomaterials [*80*].

California has been very active with respect to nanotechnology-related information disclosure. One California statute allows the State's Department of Toxic Substances Control (DTSC) to obtain information about nanomaterials from manufacturers.[5] However, limited information has been obtained regarding the production volume of these nanomaterials, their application, and risk assessment and risk management practices. Although the statute does provide DTSC with the power to require manufacturers to develop analytical detection methods, such power has not been exercised to its full extent.

In terms of direct regulation, most regulations are composed of four steps:

1. Identify the product or process of concern.
2. Prioritize the potential hazards.
3. Assess the risk.
4. Manage the risk.

In California, the "Safer Consumer Products Regulation" [*81*] process is similar yet different in the two steps related to assessing and managing risk (steps 3 and 4). In Step 1, a "chemical of concern" is identified if a material exhibits what is known as a "hazard trait," one of which is particle size or fiber dimension at the nanoscale. After the chemical or process of concern has been identified and has undergone prioritization (Step 2) instead of the classical risk assessment in Step 3, a "comparative risk assessment" is performed (also called an "alternatives analysis"). This assessment compares the product with alternative functionalizations, non-nanoscale versions, or other substitutes to determine if there is a safer alternative to the "chemical of concern."[6] The product under consideration and the alternatives

[5] Cal. Health & Safety Code §§57018-57020 (2007)
[6] Safer Consumer Products Regulation, Cal. Code Regs. tit. 22, § 69505-69509 (2013)

are evaluated using a ranking system in light of major criteria reflected in the statute, such as the human health impact, ecological impact, environmental impact, technical performance, and economic impact of the product.[7] This process requires regulators to identify materials of concern and to prioritize the risks presented by these various materials. Some resources that address these issues are provided in Table 4.3. This approach might be better than quantitative risk assessment because a classical risk assessment is often viewed as being too data dependent or driven by hidden assumptions. Step 4 is also approached differently than in a quantitative process because the preference is for inherent protection rather than managing risk by controlling exposure.

Regulatory agencies may encounter structural and administrative constraints when implementing regulations. They often face limitations with respect to funding, staff expertise, and collection of the right information. These limitations must be taken into account when designing and selecting a regulatory structure for nanotechnology risk management.

Table 4.3. Resources for alternatives risk analysis

Purpose	Title
Identifying materials of concern, their uses, and their fate	Global life cycle releases of engineered nanomaterials (2013) [*82*]
	Modeling approaches for characterizing and evaluating environmental exposure to engineered nanomaterials in support of risk-based decision making (2013) [*83*]
Prioritizing materials of concern	Risk-based classification system of nanomaterials (2009) [*84*]
	The use of Bayesian networks for nanoparticle risk forecasting: Model formulation and baseline evaluation (2012) [*85*]
Evaluation of an approach for conducting the alternatives analysis	Use of multi-criteria decision analysis in regulatory alternatives analysis: A case study of lead free solder (2013) [*86*]

A Perspective from the NGO Community

A GreenScreen™ Hazard Assessment Approach for Nanomaterials—Nanosilver Case Study

Summary of Remarks by Jennifer Sass, PhD
Senior Scientist, Health and Environment Program
Natural Resources Defense Council

A novel tool called GreenScreen™ [*87*] can be used to screen and communicate hazard information on specific classes of nanomaterials in the face of missing data. It can be used to make informed decisions with respect to material selection, to encourage transparency with respect to the EHS implications of new materials, and to ultimately help decision makers move toward the adoption of safer technologies. This tool is free and publicly accessible, transparent, and peer reviewed, ultimately providing a standardized framework that can be used to conduct a comparative chemical hazard assessment.

GreenScreen helps to facilitate alternatives analysis by providing a screening measure in the face of data gaps, but the tool does not generate new data. Instead, it uses data that are already available and substitutes for missing data when certified profilers believe that this substitution can be performed scientifically. The certification of profilers ensures the operational credibility of the tool.

[7] Safer Consumer Products Regulation, Cal. Code Regs. tit. 22, § 69505.5-69505.9 (2013)

The GreenScreen assessment is based on 18 environmental and human health endpoints, which are divided into four categories: two categories for human health hazards, one for environmental toxicity and fate, and one for physical hazards. These endpoints include carcinogenicity; genotoxicity; endocrine disruption; reproductive toxicity; and persistent, bioaccumulative, and toxic (PBT) effects [*88*]. If a material ranks highly in any of these categories, it is labeled "highly toxic," following the same model as the European Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) program [*89*]. The process also includes a life cycle analysis by examining the constituents and breakdown products that emerge during processing, manufacturing, or disposal. Based on the overall assessment, GreenScreen provides an overall benchmark score that supports a course of action [*90*].

The tool can be used to help individuals who are not toxicology experts to make product design and regulatory decisions. For example, GreenScreen is used by a number of organizations, including the EPA Design for the Environment program; the U.S. Green Building Council; and companies in the private sector, including Hewlett-Packard, Staples, and IBM. Several State regulatory agencies also use GreenScreen; for example, the tool will be used in the implementation of the California "Safer Consumer Products Regulation" [*81*].

GreenScreen was used to assess nanoscale silver materials. Nanosilver was selected due to its known stability in various environments and media, as well as its potential for release in consumer products. The GreenScreen analysis included a comparison of (1) conventional silver (low-solubility dispersed non-nanoscale silver and silver salts), (2) nanoscale metallic silver, and (3) a nanoscale silica-silver composite. The decision to test conventional silver was informed by stakeholder inputs; the release of silver ions from the selected nanomaterials could be considered a source of toxicity, and because conventional silver also releases silver ions, it served as a control.

The GreenScreen results for nanosilver indicate that with respect to judging acute inhalation hazards, the structural form is a critical factor to consider. These material assessments are discussed on the Jennifer Sass blog [*91*] and in other documents [*92*]. Researchers can use GreenScreen to facilitate safer design approaches, enable hazard screening before humans or the environment are exposed to nanomaterials, and identify crucial data gaps.

5. Breakouts—Approach and Charge to Participants

Approach to the Breakout Sessions

The purpose of the parallel breakout sessions held on Day 1 and Day 2 was to gather inputs on tools, methods, and practices that support risk-based decision making for various types of decisions and by various communities of decision makers. Considering a product life cycle approach ([*93*, *94*], Figure 5.1), the breakout groups were organized in two ways:

- **Day 1: Breakouts by Decision Type** to gather inputs from the perspectives of three different frameworks in which decisions are made: occupational risk analysis, the commercial product life cycle, and the environmental life cycle.
- **Day 2: Breakouts by Decision-Maker Community** to gather inputs from each of seven types of stakeholder communities, loosely defined as follows:
  - *Research community*: academia, national laboratories, research institutes, and intramural government research facilities.
  - *Regulatory community*: Federal regulatory agencies, State and local governments, multinational organizations (e.g., the European Union and the Organisation for Economic Cooperation and Development), and lawyers.
  - *Nanomanufacturers*: primary manufacturers of engineered nanomaterials (ENMs), manufacturers of nanotechnology-enabled products, the military, and trade associations.
  - *Small business*: start-ups and businesses with less than 50 employees.
  - *Financial risk community*: insurance agencies, venture capitalists, and lawyers.
  - *NGO community*: consumer and environmental protection groups and other public interest groups.
  - *Other public communities*: consumers, nanotechnology production workers, labor unions, and the collective public.

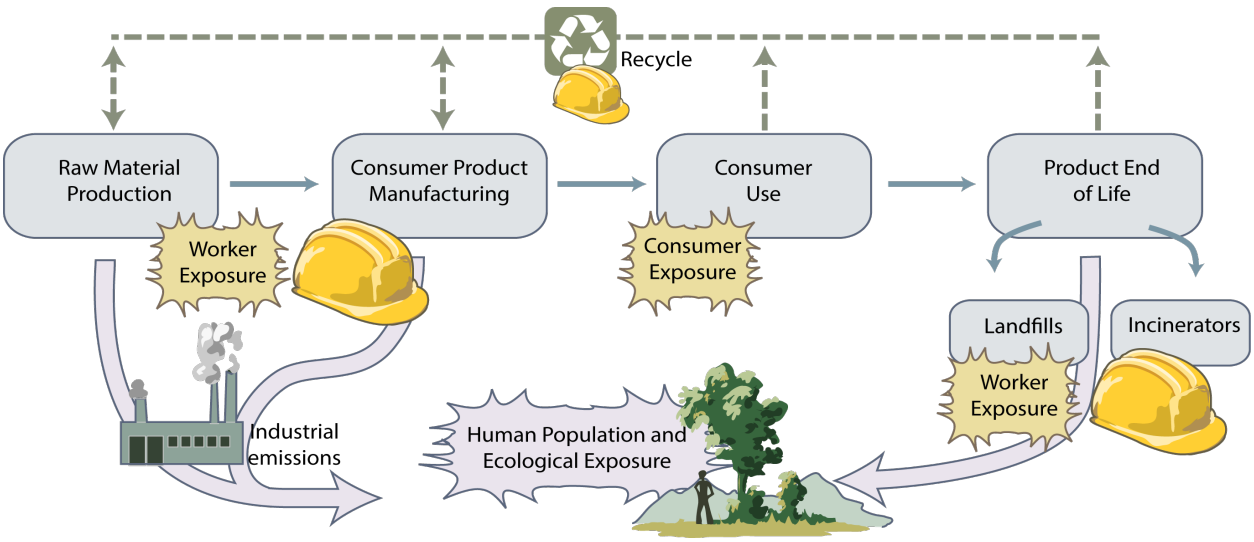

Figure 5.1. Product life cycle showing different points for EHS evaluation. (Source: 2014 NNI Strategic Plan [*94*], adapted from [*93*].)

Breakout Session Structure

The breakout sessions on both days were composed of two parts: (1) an introduction involving a real-world case study to provide background and a working framework for participants, followed by (2) an exercise involving a theoretical vignette.

Real-World Case Study

The session co-chairs were asked to provide a practical/real case example relevant to nanotechnology risk management and what approach/solution they had adopted in their consideration of risk. Specifically, they were asked to discuss the tools or methods that they had adopted when handling the case and the solutions that they had developed as a result. Participants were encouraged to share as much real-world experience as possible to move beyond generic discussions of risk analysis and towards navigating actual situations and knowledge gaps. After the case study was discussed by the group, the co-chairs led participants through an interactive study of the theoretical vignette.

Theoretical Vignette Exercise

The vignette exercise aimed to focus the discussion and elicit concrete, fact-driven information relating to real-world experiences. Used in all of the breakout sessions on both days, the exercise was developed with the following criteria in mind:

- The vignette should be general enough so that it does not implicate a specific individual, organization, product, or material.
- The vignette should present the potential for the release of a material and, therefore, an opportunity to consider fate, exposure, and toxicity.
- The vignette should have applications that all participants can relate to easily.
- The vignette should involve an application, not just a specific nanoparticle.
- There should be compelling societal benefits as well as potentially serious risks associated with the application/nanoparticle.

Based on these criteria, the following vignette was presented to breakout session participants to be considered in the context of their stakeholder community:

> Nanoparticle X is a new nanoparticle that is being produced by several companies and added to drywall and paints to provide excellent energy-saving insulating properties. It is also being considered in food packaging to keep foods cold on the shelf and in blood bags to preserve donated blood. It is sold as a powder that is stirred into paint or added to thermoset polymers for packaging. One rat inhalation study of a similar but slightly different particle found a considerable increase in lung tumors in exposed animals. Some companies have added a proprietary functional group to the particle or encapsulated the particles in an effort to minimize the compound's reactivity. The discrete nanoparticle is highly reactive, but becomes very stable in cured polymer matrices. Durability of its insulating properties reflects the properties of the matrix, so that it is potentially released when the end product degrades.

The stakeholder and decision-type communities were then asked to use their experiences in their various roles in nanotechnology development to answer the same four questions with regards to the vignette. The four thematic questions were as follows:

A. What types of risk assessment processes, if any, are being used in decisions about the commercialization/development/use of Nanoparticle X?

B. What are the tools/approaches/models and information needed for risk assessments and risk-based decision making?

C. How are risk information and uncertainty factored into the decision?

D. How can the NNI best support risk-based decisions?

Breakout Reports

After each day of breakouts, the breakout co-chairs provided a report to the main group on the results of their discussions. The goal was to gather each group's perspective on approaching risk, including risk-based questions, decisions to be made, relevant tools and methods, and decision drivers, and then to compare those inputs across the various breakout groups to identify commonalities in processing risk-based information.

6. Breakouts Focused by Decision Type

The first set of breakout sessions focused on the types of decisions made when approaching the potential risks of nanotechnology. Stakeholders were split into three concurrent sessions addressing the following decision frameworks: (1) occupational risk analysis, (2) the commercial product life cycle, and (3) the environmental life cycle. Each group began with a presentation from the co-chair(s) on a real-world case study related to the breakout framework. Following this, all groups were asked to work through the same hypothetical "vignette" in the context of the session framework and were charged with answering four discussion questions, as noted in Chapter 5. The discussions are summarized below.

Group 1: Occupational Risk Analysis and Decision Making

Co-Chairs:
Paul Schulte, PhD, National Institute for Occupational Safety and Health
Bruce Lippy, PhD, CPWR—The Center for Construction Research and Training

Occupational Risk Framework

The co-chairs noted that the data gaps associated with emerging technologies have presented a significant challenge with respect to risk-based decision making and that what little is known must be used to make decisions to protect workers at all stages of the product life cycle. In the case of "Nanoparticle X," a number of assumptions must be made throughout the risk management process due to a lack of information. The co-chairs made several general points during the case study discussion:

- The hierarchy of controls, which has been a guiding principle for industrial hygiene, has been recommended as a model for nanoparticle control in most international guidance.
- Hazard and control banding tools can assist nanotechnology-related risk management in the occupational context. One example is the "Control Banding Nanotool" ([*55*], Figure 6.1).

Severity	**Probability**			
	Extremely Unlikely (0–25)	Less Likely (26–50)	Likely (51–75)	Probable (76–100)
Very High (76–100)	RL 3	RL 3	RL 4	RL 4
High (51–75)	RL 2	RL 2	RL 3	RL 4
Medium (26–50)	RL 1	RL 1	RL 2	RL 3
Low (0–25)	RL 1	RL 1	RL 1	RL 2

Key to Risk Levels

RL 1: General ventilation

RL 2: Fume hoods or local exhaust ventilation

RL 3: Containment

RL 4: Seek specialist advice

Figure 6.1. Example of the control banding nanotool. Risk is calculated as the severity of the hazard scaled by the probability of exposure. The red cells show the highest risk (RL 4), and the green cells show the lowest risk (RL 1). (Redrawn with permission of the authors from Paik *et al*. Application of a Pilot Control Banding Tool for Risk Level Assessment and Control of Nanoparticle Exposures. *Ann Occup Hyg* (2008), and reprinted by permission of Oxford University Press on behalf of the British Occupational Hygiene Society [*55*].)

- Many nanomaterials, due to their effectiveness and high performance in a product, are unlikely to be eliminated or substituted by manufacturers without clear evidence that the materials pose a hazard. As an alternative to substitution, the National Institute for Occupational Safety and Health has demonstrated that engineering controls can be an effective way of managing risk with nanomaterials ([*95*]; see also Figure 6.2). Control methods to ensure industrial hygiene are listed in decreasing order of preference based on effectiveness: elimination, substitution, engineering controls, warnings, administrative controls, and personal protection. For example, CPWR—The Center for Construction Research and Training—has demonstrated that ventilation can be an effective engineering control for worker safety when handling construction nanomaterials [*96*].

Figure 6.2. CPWR demonstrates the effectiveness of ventilation with construction nanomaterials. Here, a worker using a tile cutter on a clay roofing tile and producing a large amount of clay dust (on the left) can control exposure using a fitted vacuum hood (on the right). (Images courtesy of B. Lippy.)

Vignette Discussion

A. *What types of risk assessment processes, if any, are being used in decisions about the commercialization/development/use of Nanoparticle X?* Initially, breakout session participants discussed many technical decisions that must be made when undertaking risk assessment, including determining the appropriate sampling strategies and equipment, specifying the toxicological studies that are needed, and assessing how much value can be assigned to data on analogous materials. Furthermore, participants suggested beginning the risk assessment process by asking who is being exposed and whether a product contains nanoparticles.

B. *What are the tools/approaches/models and information needed for risk assessments and risk-based decision making?* A number of approaches and tools were discussed:
   - The REACH program approach to nanomaterials, initiated through European legislation [*89*].
   - The collaborative approach of the Nano GO Consortium [*97*].
   - Qualitative risk assessment, serving as a key approach for testing a great number of ENMs, given data limitations.
   - The "Good Nano Guide," serving as an "Internet-based collaboration platform for experts to exchange ideas on handling nanomaterials in an occupational setting" [*98*].
   - Agency publications from NIOSH [*99*].

C. *How is risk information and uncertainty factored into the decision?* Some industry representatives discussed whether the business risk of using nanoparticles could be justified. Uncertainty may lead decision makers to err on the side of caution.

D. *How can the NNI best support risk-based decisions?* Participant suggestions included the following:

- Coordinate ongoing meetings with non-Federal stakeholders to discuss their needs and risk management approaches.
- Provide information about the risks directly to non-Federal stakeholder groups.
- Coordinate among NNI member agencies to disseminate key data and to facilitate an understanding of the agencies' respective roles.
- Support research on baseline environmental levels for key ENMs.
- Work with State governments to help to develop approaches for risk management.
- Facilitate the development of inventories (e.g., an inventory of SDSs).
- Support efforts to determine how intellectual property regulations are impacting EHS information collection and dissemination.

Group 2: Commercial Product Life Cycle

Co-Chairs:
Rick Canady, PhD, International Life Sciences Institute (ILSI)
Todd Kuiken, PhD, Woodrow Wilson International Center for Scholars

Commercial Product Life Cycle Stage Framework

The co-chairs focused on the risk of nanomaterial exposure from food packaging, referencing a 2008 study from the Wilson Center [*100*]. They suggested that a life cycle approach is important in this context because ENM introduction can occur during different life cycle stages, including handling, processing, packaging, ingredient introduction before and after processing, and intake/consumption. Considering these aspects, they reviewed the three hypothetical case studies in the 2008 report to help to identify regulatory and scientific needs to frame the breakout session discussion. The case studies in the 2008 report were the following:

- **Case 1**: A nanoscale sanitizer that prevents the contamination of packaging film used to wrap fresh produce or meat.

  Although the outside surface of this film is a conventional material, the inside (the food contact surface) is an ultrathin layer of nanoparticles functionalized as microbial inhibitors.

- **Case 2**: A packaging film that detects and quantifies microbial pathogens in products as they move through the food-processing chain.

  This nanobiosensor is based on enzyme-linked immunosorbent assay (ELISA) technology and is incorporated into the inner (food contact) surface.

- **Case 3**: Barrier packaging for carbonated beverages.

  The barrier material, used to prevent the permeation of water vapor, oxygen, and CO_2, has an inner layer of polypropylene embedded with nanoclay particles and sandwiched between conventional polyethylene layers.

In the 2008 study, each case was run through a mock regulatory submission to the Food and Drug Administration and the Environmental Protection Agency to determine if (1) the regulations seemed to be addressing the right issues, and (2) where science and methods could fill information gaps. The Wilson Center report contributed to the FDA guidance, adding language to call for data on particle characteristics and to clarify the relevance of existing data for evaluating the "generally recognized as safe" (GRAS) status of nanoscale materials.

Vignette Discussion

A. *What types of risk assessment processes, if any, are being used in decisions about the commercialization/development/use of Nanoparticle X*? Session participants discussed possible information gaps in assessing the risks posed throughout the course of the commercial product life cycle. They identified "who is being exposed to the ENM?" and "how is that exposure occurring?" as two central pieces of information that would be needed (Figure 6.3). When discussing factors affecting the success of risk-based decision making, some participants noted that the efficacy of risk communication and perception is critical because effective risk communication and perception help to align actual risk and perceived risk. They also identified the quality and reliability of available data as fundamental issues.

B. *What tools, approaches, models, and/or information are needed for risk assessments and risk-based decision making?* Both GreenScreen [*87*] and presubmission consultation with the FDA [*101*] were suggested as important tools, in addition to the nanotechnology-specific databases that are available, including the Nanomaterial Registry [*63*] and the publications database available at nanoHUB [*102*]. Some participants also cited PubMed [*103*] and other non-nanotechnology-specific databases as sources of information that may be relevant to risk assessment in this context.

C. *How are risk information and uncertainty factored into the decision?* Some participants named analytical techniques such as "fuzzy set theory" and structured decision making (SDM) as helpful in allowing decision makers to account for risk in the face of uncertainty, as well as guidance documents provided by organizations such as FDA [*104*]. Value-of-information analysis was cited as a tool to "quantify…the potential benefit of additional information in the face of uncertainty" [*105*]. Participants also discussed methods of communicating risk and uncertainty to decision makers:
   - Control banding, which is used "to guide the assessment and management" of risks [*106*], can assist in communicating risk and uncertainty to decision makers by providing a visual guide.
   - Risk information should be conveyed to decision makers in a way that allows them to engage in responsible governance. For example, researchers and developers should share relevant information to fill data gaps and should explain the robustness of the available data. This will help decision makers to understand the extent and causes of uncertainty for ENMs.

D. *How can the NNI best support risk-based decisions?*
   - A lack of agreed-to methods to measure nanomaterials in exposure conditions was identified as a key gap that affects safe product development. The co-chairs proposed specific support to methods development targeted at decision steps in a risk evaluation as a practical approach. For example, Figure 6.3 was presented as a decision sequence for which specific methods development could simplify product formulation and risk assessment approaches.
   - Some participants felt that NNI support could assist risk-based decision making by coordinating the identification of data and information gaps. They noted the following data gaps: exposure occurrence, exposure effects, ENM behavior before and after exposure, the presence of nanomaterials in existing products and environments, and the effects of regulatory responses.
   - It was suggested that the NNI also could facilitate the communication and dissemination of existing studies by supporting the development of inventories or repositories of information. In addition to a repository of EHS-related studies on nanomaterials (including both positive and negative results), an inventory of nanomaterial use could be created that keeps track of how certain nanomaterials are being used and implemented by consumers and industry, and how much of the nanomaterial is being used in each of these applications (e.g., the Wilson Center's "living" consumer products inventory [*107*]).

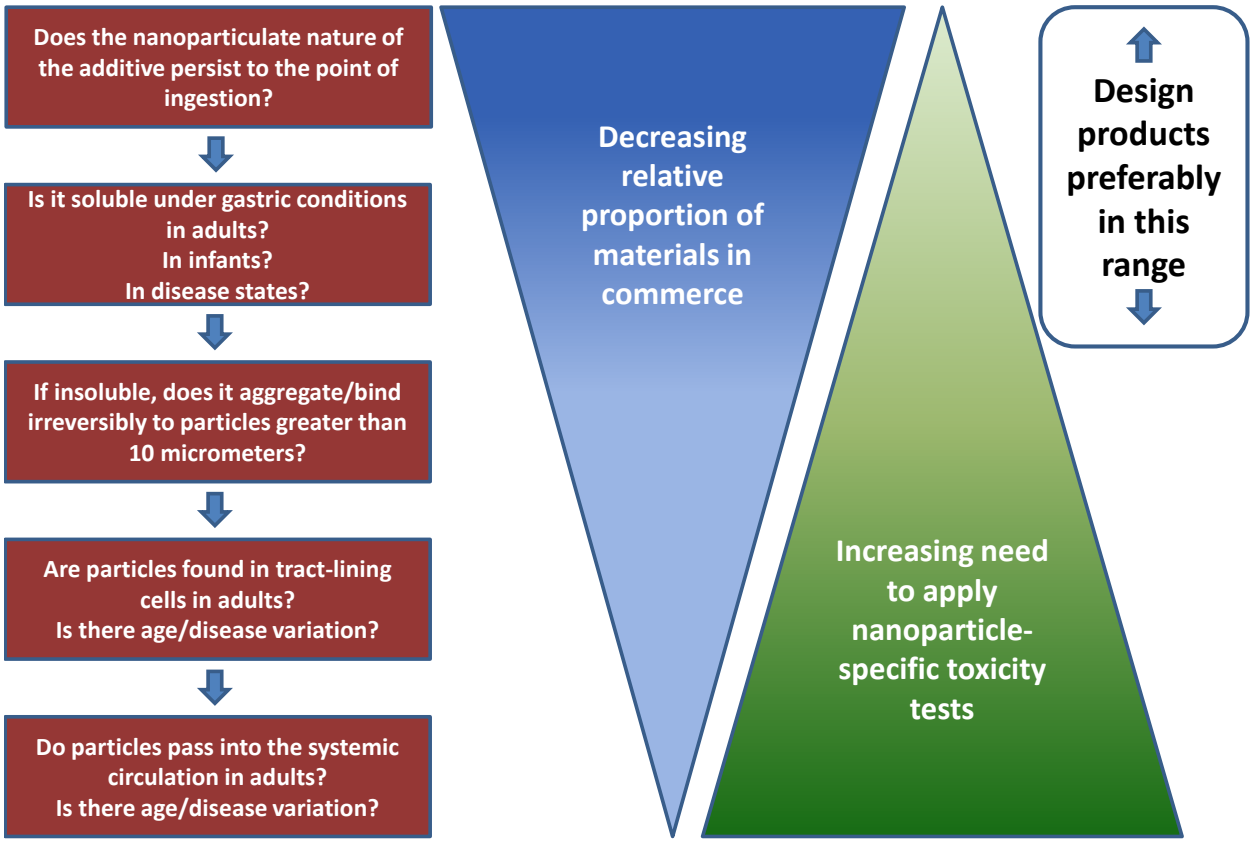

Figure 6.3. Hypothetical decision sequence for nanoparticle uptake assessment to prioritize data needs or to aid product development. There is an inverse relationship between the relative proportion of ENMs in commerce and the need to apply nanoparticle-specific toxicity tests. Ideally, products should be designed that have less need for specific toxicity tests. Product design and data needs depend on whether an ENM is persistent to the point of ingestion and on the behavior of the ENM after ingestion. (Figure courtesy of T. Kuiken.)

Group 3: Environmental Life Cycle Implications

Co-Chairs:
Tom Seager, PhD, Arizona State University
Matthew Hull, PhD, Virginia Tech

Environmental Life Cycle Implications Framework

The co-chairs framed the vignette in terms of a life cycle assessment framework that could be used to assess the potential EHS risks of emerging technologies. They began by explaining that traditional tools used to perform life cycle assessments are primarily retrospective, as they rely on data gathered from commercial applications. However, risk-based data are often unavailable for emerging technologies due to the short time they have existed and the limited scale at which they have been implemented.

To address this problem, Dr. Seager presented a life cycle assessment framework that assesses the EHS implications of a technology when data are sparse (see Figure 6.4). Despite uncertainty in many areas, this model can help to scale down data requirements for the risk management of emerging technologies.

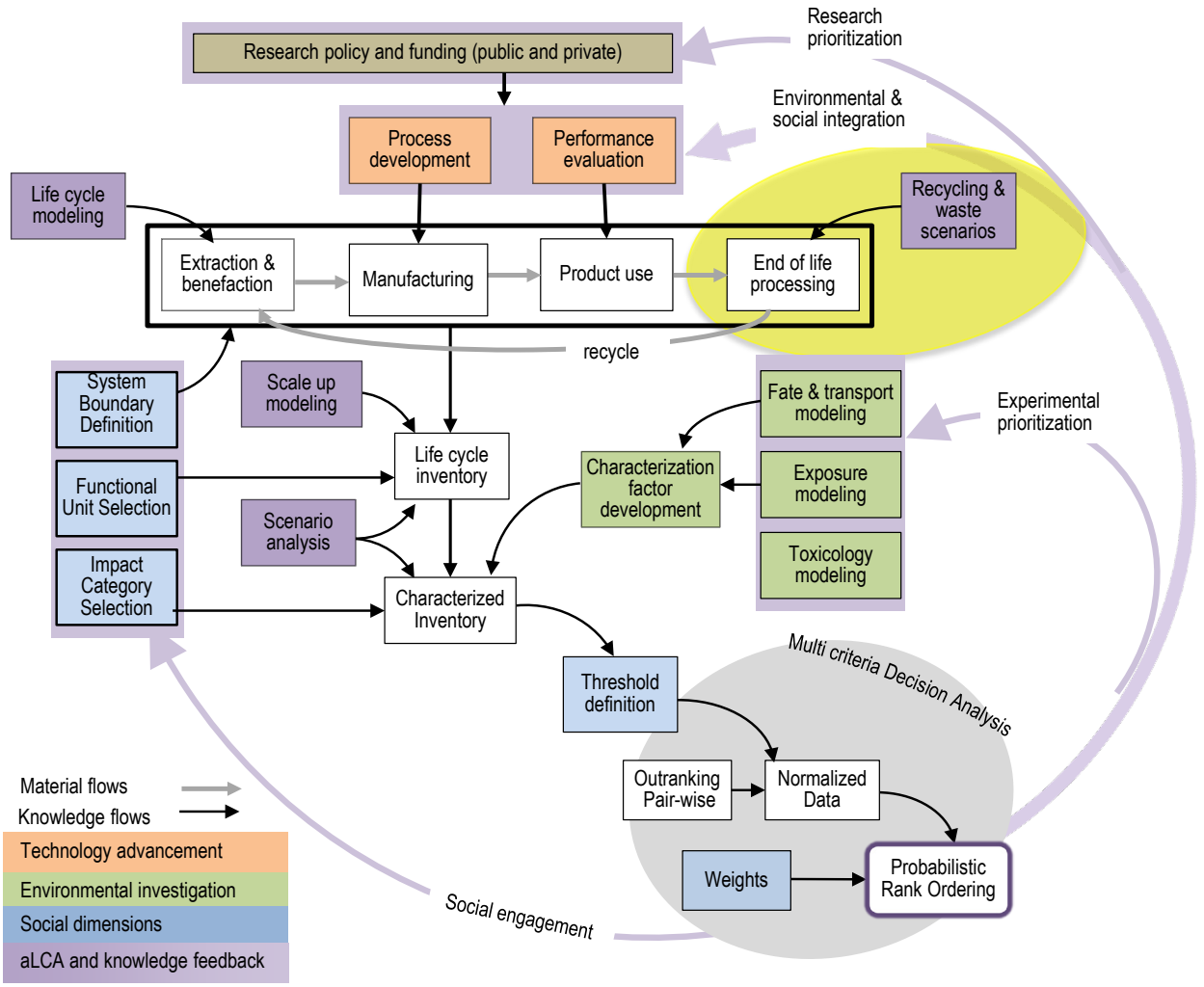

Figure 6.4. Life cycle assessment framework for emerging technology. This framework helps to facilitate life cycle assessment when data are sparse. The core of this framework is linear and traditional, comprising the extraction and benefaction, manufacturing, product use, and end-of-life processing stages of the life cycle. Not much research has been performed on manufacturing byproducts (yellow circle on the upper right). **aLCA**: abridged life cycle analysis. (Figure courtesy of T. Seager.)

Dr. Hull focused on the environmental life cycle issues posed by the production of metallofullerenes via arc discharge. A recent study showed that leachate prepared from the soot from metallofullerene production was toxic to EPA test organisms due mainly to the release of copper [*108*]. Engaging industry is important to identify priority areas of research for life cycle risk assessment. Several takeaways from this case study are as follows:

- Attention should be given to assessing the EHS risks presented by the manufacturing byproducts of engineered nanomaterials.
- Life cycle assessments of manufacturing processes should be conducted as manufacturers increase the scale of their endeavors to meet increased demand.
- More data on industrial activities must be gathered in order to advance environmental life cycle assessment research.
- Rules and regulations must be made clear so that manufacturers are aware of the applicable requirements in this arena.

Vignette Discussion

A. *What types of risk assessment processes, if any, are being used in decisions about the commercialization/development/use of Nanoparticle X?* Breakout participants commented that the types of decisions made about risk are often dictated by the information required by regulatory agencies. Furthermore, some industry representatives explained that decisions made in regard to market entry involve risk, given that evaluating the potential commercial applications of a nanomaterial involves an estimate of its market acceptance and potential based on product performance.

B. *What are the tools/approaches/models and information needed for risk assessments and risk-based decision making?* Several tools and approaches were discussed, including the following:

- The Swiss Precautionary Matrix for Synthetic Nanomaterials is a tool "made to support all interest groups having a responsibility for the safety of workers, consumers or the environment" [*109*].
- NanoRiskCat, a risk categorization framework developed in Denmark, is "able to identify, categorize and rank exposures and effects of nanomaterials used in consumer products based on data available in the peer-reviewed scientific literature and other regulatory relevant sources of information and data" [*110*].
- The publications database available at nanoHUB [*102*] is useful for access to nanomaterial-related information.
- Standard methods and protocols are provided by various Federal agencies for guidance. For example, DOD utilizes a "watch list" of EHS-risk materials [*111*, *112*].
- The method used by a 2012 EPA-funded study to prioritize risk based on stakeholder input is one example of prioritizing risk management needs. This study examined prioritizing research areas related to potential use of multiwalled CNTs in upholstery fabric [*113*].
- An "incremental approach" could be practical from both business and research perspectives. In such an approach, issues are prioritized by determining questions of immediate need. Chronological benchmarks are set for resolving these questions, and at each benchmark, progress and the costs and benefits of continuing the project can be evaluated.

C. *How are risk information and uncertainty factored into the decision?* Some participants noted that risk and uncertainty affect decision making when actors weigh the amount of work and funding needed to conform to information reporting requirements. Risk and uncertainty also could influence decisions when actors take into account how the developing regulatory framework could restrict future activities.

D. *How can the NNI best support risk-based decisions?* The discussion focused on increasing the accessibility and availability of relevant data. Organizing the available information and data (including "negative" or difficult-to-publish data showing no effect) into a central repository could greatly assist stakeholders. Some participants also identified confidential business information as a potential source of valuable information for risk management in this context and suggested that the NNI could investigate ways to identify common issues and trends reflected in this information, while still maintaining its confidential nature. Others expressed the view that basic research should continue to be funded so that fundamental data for risk assessment can be generated.

7. Breakouts Focused by Decision-Maker Community

Stakeholders have perceptions of benefit and risk that affect their views of problems, processes, and solutions. These breakout sessions used the same vignette about Nanoparticle X and the same charge questions to identify the needs, perceptions, and approaches of seven different stakeholder communities when making decisions about nanotechnology risk. Again, each session began with presentations from the co-chair(s) on a real-world case study, followed by a group discussion regarding the charge questions. The discussions are summarized below.

The Research Community

Co-Chairs:
Christie Sayes, PhD, RTI International
Jacqueline Isaacs, PhD, Northeastern University

Case Presentations

The co-chairs discussed using a life cycle approach (Figure 7.1) to understand the potential risks of two nanotechnology applications: the potential hazards of aerosol release from TiO_2-enabled coatings (e.g., paints) and the theoretical end-of-life fate of electronic devices (e.g., cell phones) containing carbon nanotubes.

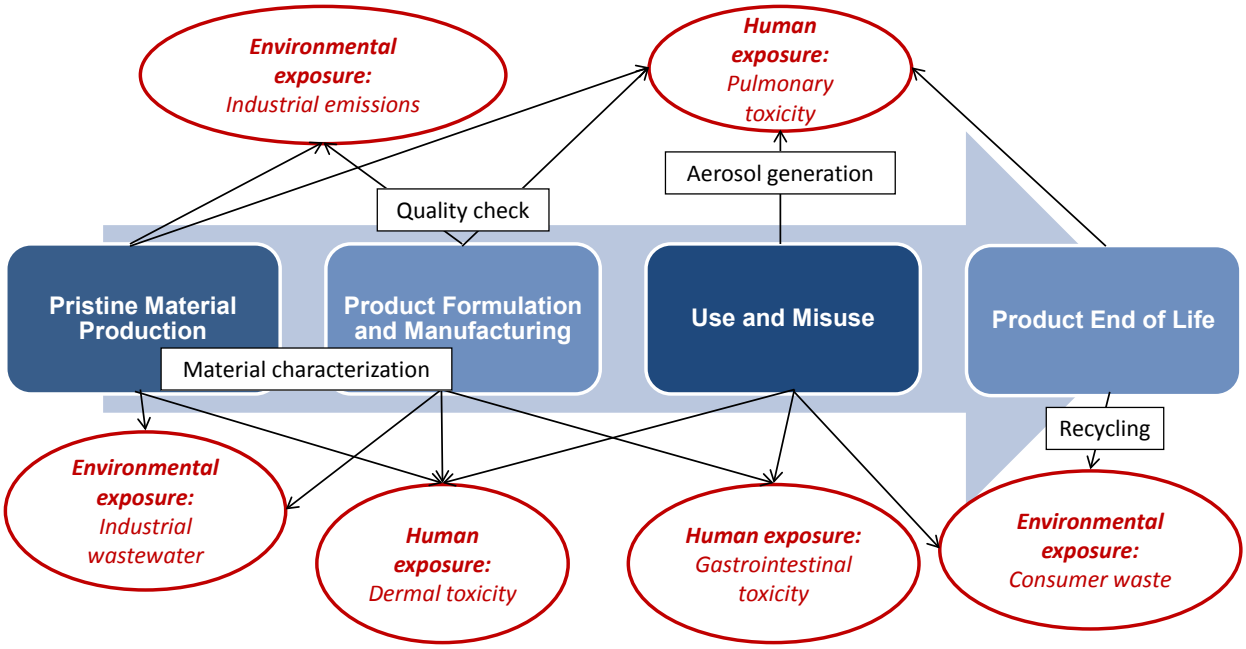

Figure 7.1. The product life cycle approach to understanding exposure risks. (Figure courtesy of C. Sayes and J. Isaacs.)

The comments from session participants during the case study presentations included (1) there is a need to create incentives for industry players to address the potential environmental risks posed by nanotechnology-enabled products, (2) the public's perception of a company's "goodwill" could also play a role in motivating industry behavior, and (3) insurance companies influence industry behavior due to liability and risk leading to higher insurance costs.

Vignette Discussion

Some breakout participants commented that risk-based decisions are essentially risk–benefit-based decisions. In particular, researchers may choose which nanomaterials to use in a given application based on the accessibility of the material, the challenge of incorporating it into a product, and the potential risks. Quantitative data on exposure at all stages of the life cycle and an ability to prioritize potential outcomes are critical for the decision-making process.

Some participants argued that the insurance industry has a significant influence over risk-based decisions and could be better informed by studies conducted by the research community. In this case, collaborations between the research community and the insurance community could better guide risk–benefit-based decision making, inclusive of the following:

- Safety data sheets (SDSs, formerly known as material safety data sheets, MSDSs).
- National Institute for Occupational Safety and Health Guidance documents [*114*].
- National Academy of Engineering (NAE) and National Academy of Sciences (NAS) reports.
- Organisation for Economic Co-operation and Development publications [*115*].
- National Institute of Standards and Technology (NIST) standard reference materials [*116*].
- The National Institutes of Health (NIH) Nanomaterial Registry [*63*].
- Other reports and peer-reviewed literature.

Session participants mentioned that limitations still exist for the tools listed above: inaccurate SDSs, cost-prohibitive reference materials, and insufficient characterization leading to irreproducible results. Comments from session participants on risk, uncertainty, and its communication on decision making included the following:

- There is a lack of information regarding when and how exposure occurs throughout the life cycle with regard to workers, consumers, and the environment. Risk–benefit-based information is missing.
- There is a need for data from case studies on realistic exposure scenarios, including hazard identification, in order to develop quantitative structure–activity relationships (QSARs).
- Researchers should engage all stakeholders early in the process, so that research activities can be tailored to making informed decisions.

Some participants recommended a number of steps that the NNI could take to assist the research community by making information available and accessible:

- Supporting a repository for peer-reviewed SDSs.
- Expanding the existing databases of information about ENMs (such as the Nanomaterial Registry [*63*]).
- Developing a directory of decision makers (including insurance companies, government agencies, and other stakeholders) to improve communication and enhance collaboration.[8]

[8] Contact information for Federal decision makers (www.nano.gov/partners), regional, State, and local resources (www.nano.gov/initiatives/commercial/state-local), industry collaborators (www.nano.gov/initiatives/commercial/industry-collaborations), and more can be found at www.nano.gov.

The Regulatory Community

Co-Chairs:
Janet Carter, MPH, Occupational Safety and Health Administration
Jim Alwood, MS, U.S. Environmental Protection Agency
Rick Reibstein, JD, Massachusetts Office of Technical Assistance and Technology

Case Presentations

Summary of Co-Chair Case Presentation—Ms. Carter

The Occupational Safety and Health Administration is developing a searchable database for identifying the potential hazards posed by nanomaterials. This database will provide information about ENMs in a format that is both searchable and sortable and that allows for a comparison of nanomaterials. In addition, the database will identify research gaps and inconsistencies in the literature. The project, which also involves assessing the quality of the data included in the database, has so far identified approximately 1800 studies that contain usable information for the database (Figure 7.2).

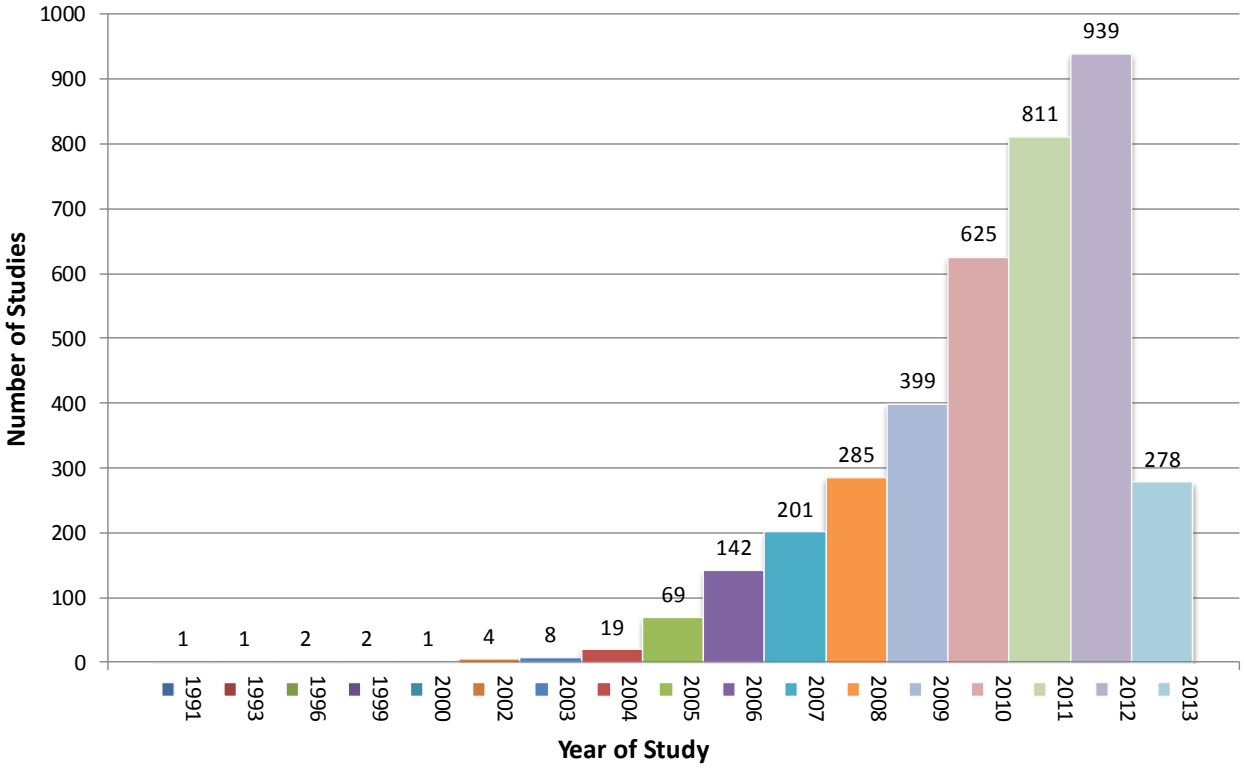

Figure 7.2. The number of studies addressing the toxicity of a nanomaterial to humans, organized by year of publication, as of September 2013. Approximately 1800 of these studies can be found in the searchable database being developed by OSHA. (Figure courtesy of J. Carter.)

Summary of Co-Chair Case Presentation—Mr. Alwood

EPA regulates carbon nanotubes under the Toxic Substances Control Act [*46*]. The agency has received new chemical notices under TSCA for over 150 nanoscale materials and over 60 types of CNTs and fibers. EPA has encountered challenges when assessing CNTs and fibers, due to several issues:

- No nomenclature system has been developed for variations in structure or chirality.
- Petitioners often submit insufficient data regarding relevant CNT properties.

- The test methods used for gathering the submitted data are unclear.
- Test results with which EPA is familiar may be inappropriate for CNTs.
- It is unknown how the chemical–structural and material characterization properties of better-known materials correlate with those of CNTs.

Where data are lacking, under TSCA, EPA uses a bounding scenario that assumes that all CNTs are released into the environment, are persistent, bioaccumulate, and are highly mobile. Due to the uncertainty of the relevance of both hazard and exposure data, EPA has considered the human health effects of CNTs to be a potential unreasonable risk. Generation of additional data would be required if a company wanted to manufacture CNTs without the current restrictions found in previously issued consent orders.

OECD plays a role in developing nanomaterial guidance documents and test guidelines [*115*]; the Canada–U.S. Regulatory Cooperation Council process is aimed at aligning the regulatory environment for nanomaterials between Canada and the United States [*117*]; and EPA is identifying research needs and collaborating with other agencies to develop data relevant to assessing the risks of ENMs.

Summary of Co-Chair Case Presentation—Mr. Reibstein

Lack of clarity in the regulatory environment is a detriment to industry as well as a failure to address the risks posed by nanotechnology. Clear regulations developed with the active engagement of knowledgeable practitioners would have a positive economic impact by reducing business risks. An effort should be made to avoid inherent toxicity at the early design stage, to understand risks presented by nanotechnology throughout the product life cycle, and to use democratic processes of deliberation, disclosure, and consensus-seeking among stakeholders. The Massachusetts Office of Technical Assistance and Technology has prepared a guidance document that describes these and other considerations for the safe development of nanotechnology [*118*].

Vignette Discussion

Participants first discussed decisions faced by the regulatory community when determining what type and quantity of information are required before regulatory action can be taken, or if it is appropriate to take action at all. For instance, some participants noted that it first must be determined whether a product actually contains nanomaterials. One comment was that, unfortunately, data on nanomaterial content across business sectors are inconsistent, often reflected by the incomplete transfer of material information across the supply chain (e.g., information transfer through incomplete or inaccurate SDSs).

In discussing risk assessment, some participants mentioned that the OECD nanomaterial guidance documents and test guidelines [*115*] are useful. Others noted that the regulatory structure for pre-market testing is more developed than that for the post-market review of nanotechnology-enabled products.

Breakout participants made the following suggestions concerning how NNI agencies can assist the nanotechnology risk management process:

- Collaboration between the business and the regulatory communities is needed to ensure transparency, avoid ambiguity, and lessen market uncertainty and impacts for industry.
- The NNI could help to facilitate this collaboration for good stewardship of nanotechnology by providing a framework for reasonable and responsible development.
- This framework could be specific for each nanotechnology sector or application.
- Some participants voiced the need for:

- More government–business liaison programs and public–private partnerships (PPPs) to develop guidance materials.
- A national advisory committee to facilitate negotiated rulemaking with Federal agencies.
- Programs that support industry consultation and public engagement throughout the entire regulatory process.
- A program to help start-ups in their evaluation of risk.
- Free assistance and resources for industry and business.

The Nanomanufacturing Community

Co-Chairs:
Craig Bandes, Pixelligent Technologies
Ahmed Busnaina, PhD, Northeastern University

Case Presentations

Summary of Co-Chair Case Presentation—Mr. Bandes

Pixelligent is a manufacturer of ZrO_2 nanocrystal dispersions for electronics, semiconductors, and industrial markets. Industry leaders must often decide how and where to invest with imperfect information. Such business decisions are standard for industry players; however, the nanotechnology market presents an additional challenge due to lack of clarity in the regulatory framework. Industry and regulatory agencies must work together to create clear regulatory requirements that are informed by the needs of all stakeholders. Entrepreneurs in this emerging market already face many challenges, such as finding investors and obtaining the necessary capital. An unclear regulatory framework adds to these challenges and could prevent the successful commercialization of emerging technologies.

Summary of Co-Chair Case Presentation—Dr. Busnaina

Northeastern University's Center for High-Rate Nanomanufacturing is developing a variety of technologies and applications related to advanced nanomanufacturing, including nanoscale templating and offset printing. It collaborates with a number of industrial partners and with NIOSH on worker safety. In order to address exposure concerns related to its manufacturing processes, the Northeastern research team members worked on high-rate toxicity testing and exposure assessment using a variety of techniques. They developed an EHS consortium and helped implement exposure and control evaluations in several company and research laboratories. This work contributed to a NIOSH safe practices document for ENMs [*119*].

In addition to EHS risks, business and market risks are critical considerations for developers of emerging technologies. For example, is there an existing infrastructure that supports their innovation? Researchers may have to develop specific applications for market acceptance. When smaller R&D projects aim to have their technology implemented at a commercial scale, it is often a "full-time job" to obtain the number of patents necessary to gain investment interest from larger companies.

Vignette Discussion

Comments offered by session participants included the following:

- As for all businesses, nanomanufacturing decisions are driven by a risk–benefit analysis; any scale up and increase in volume must correlate with increased profitability.
- Investment risks, as well as market potential, shelf life, and future processability, are also important.

- New precautions may be required to ensure worker and customer safety, even when there is a lack of data addressing such concerns.
- Regulatory testing guidelines, data and reporting requirements, and the potential failure of the regulatory framework to distinguish between nanomaterials of dissimilar inherent hazards, all present business risks. When regulatory guidelines are unclear, nanomanufacturers must decide whether to spend resources on legal advice.
- Agency–industry collaborations can be helpful, for example, the NIOSH guidance documents and field visits [*114*].
- Collaborations have not always facilitated a clear understanding by industry of applicable regulatory guidelines and how to meet them. To address this, the NNI could facilitate meetings between industry and regulatory agencies or agency visits to industry sites in order to support discussion of regulatory issues.
- Transparency is important; the reasoning behind regulatory decisions could be made available to industry actors.

The Small Business Community

Co-Chairs:
Doyle Edwards, Brewer Science, Inc.
Richard Pleus, PhD, Intertox, Inc.

Vignette Discussion

The group focused the majority of its discussion on the Nanoparticle X vignette. Participants offered a variety of comments, including the following:

- Small businesses would like a clear regulatory path or roadmap. Currently, the regulatory hurdles and associated costs and tasks for nanotechnology business development are not clear to start-up companies, compared to the known process of introducing new drugs and medical devices to commerce. A clearer path will allow investors to plan.
- Risk-based decision making is a positive approach to understanding possible company-wide EHS risks. Additionally, could a small business somehow use data from an ENM already on the market? Examples include cost sharing or fees for use of data.
- EHS data sets for analogous ENMs can help businesses predict worker exposure during manufacturing or potential environmental impacts.
- A central repository of ENM test results and application data could facilitate innovation.
- Businesses may consider foreign manufacturing locations that offer relaxed regulatory requirements but less focus on safety, thereby putting workers at greater risk.
- Harmonizing domestic and international regulatory and safety guidance may facilitate global export and import markets.

Participant comments on the tools that are available for risk management included the following:

- NIOSH processes for evaluating occupational hazards are a helpful platform for industry.
- Exposure could be contained with classical “engineering” controls; employees could be educated and protected using SDSs and other occupational safety tools with, at most, slight modification.
- For understanding the physico-chemical properties of ENMs as they relate to assessing EHS risk, the Nanotechnology Characterization Lab, managed under the National Cancer Institute of the NIH [*120*], could also provide fundamental information on ENMs utilized in industry settings.

Some participants commented on limitations of available tools:

- It is often difficult to ensure that engineering and education tools for ENM risk management are being used adequately, all the way down to the "worker level."
- Engineering controls are subject to some uncertainty because these tools are not always tested for effectiveness.
- Efforts undertaken at the Nanotechnology Characterization Laboratory are limited to biomedical projects (i.e., to meet requirements for FDA review).
- Small businesses often lack the support needed to translate risk-based information and to provide the appropriate level of guidance to workers (i.e., the type of support that would be given by an industrial hygienist).

The Financial Risk Community

Co-Chairs:
Clayton Shoup, M.A., C.I.H., C.S.P., Zurich North America
Martha Marrapese, JD, Keller and Heckman LLP

Case Presentations

The co-chairs indicated that insurance companies recognize the importance of nanotechnology in the marketplace; these companies can facilitate effective risk management for industry by extending financial capital and risk management resources. However, availability of consistent, transparent, and reliable toxicity research data and standards affects the ability of an insurer to effectively provide this service.

Summary of Co-Chair Case Presentation—Mr. Shoup

The hypothetical case study presented involved a company that manufactures socks with a nanosilver coating. In order to assess the fees for insuring such a company, Zurich North America would use a proprietary nanotechnology risk assessment tool called the Zurich Nanotechnology Exposure Protocol (ZNEP™) [*121*]. The ZNEP™ protocol, developed in 2008, assesses coverage costs based on a variety of factors, including nanomaterial characteristics; the manufacturing processes used to develop the product or material; the control measures being used; the final form or use of the developed product; and scientific and regulatory information such as risk and toxicity studies, information on EHS best practices, and EHS regulatory data (see Figure 7.3). The ZNEP algorithm is used to develop underwriting intelligence to produce an individual risk rating. The gathered information is also used to provide risk management support to the company. This support could include assisting in the development of best practices and helping to facilitate risk communication.

Vignette Discussion

Some representatives from the insurance industry discussed how they first must determine whether the business causes some form of exposure to nanotechnology; if so, they then determine if and how to cover the business (fully insure, offer supplemental coverage, etc.) and the cost for that coverage. Underwriting processes are the primary tools used by the financial risk community for assessing risk. Collective "think tank"-style analyses and processes are among the methods utilized for underwriting to ensure consistency in decision making. Underwriting intelligence protocols and models can yield individual risk ratings, insurance product specifics, and ideas for risk management and mitigation support by evaluating the following factors:

- Material characteristics.
- Toxicology data.
- Existing regulations.
- The manufacturing process used.
- The final form and use of the product.
- The control methods used by the company.

Additional comments offered by breakout session participants included the following:

- The primary limitation for underwriting in the nanotechnology sector is the lack of comprehensive risk-based data. Nondisclosures from businesses can limit access to key information, and regulatory uncertainty can limit the accuracy of the underwriting process. Additionally, data are only validated after they have been compiled over many years.
- A "big-picture life cycle perspective" should be adopted when gathering data for risk assessment because insurance companies often provide coverage for a product throughout its life cycle. This approach is most effective when insurance companies have access to EHS data, information on best practices and good product design, and clear regulations, lessening uncertainty and thereby improving premiums and facilitating renewals.
- Insurance companies also often gain information by consulting the Insurance Services Office [*122*] (which can gather data and recommend premiums) and through claims investigations. Therefore, existence of regulations, standards, or best practices throughout the life cycle of a product can help to resolve uncertainty and lead to more accurate decisions.

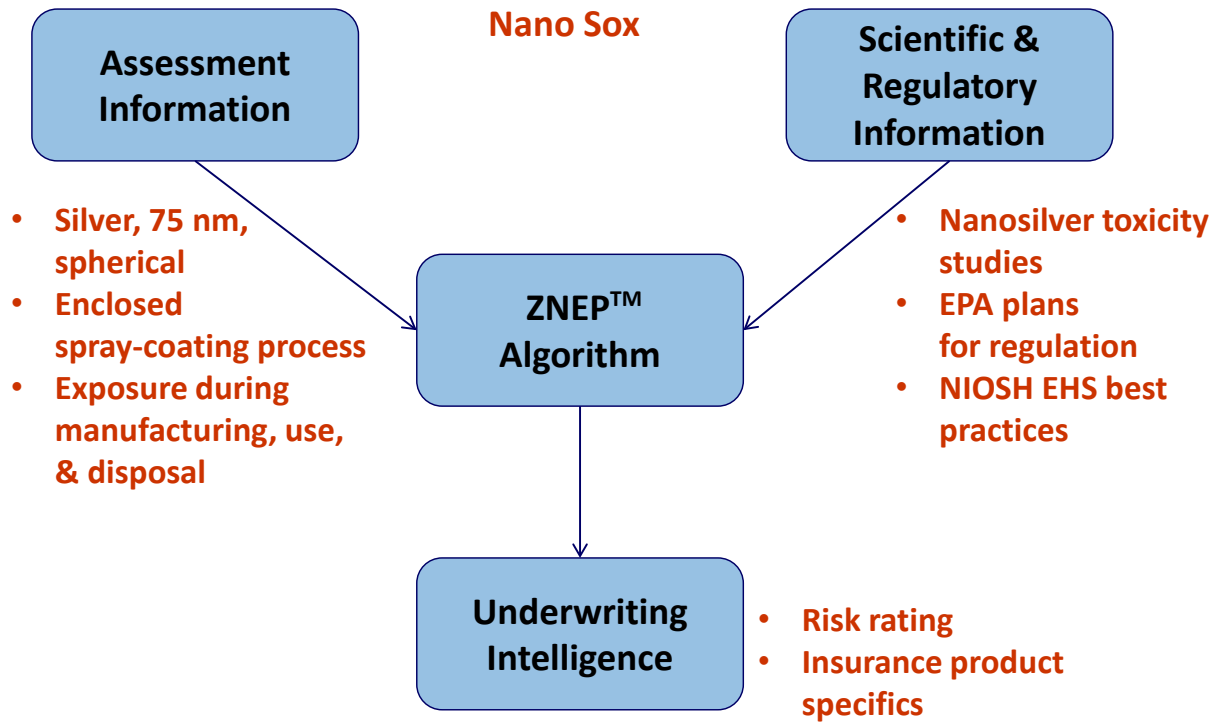

Figure 7.3. The Zurich Nanotechnology Exposure Protocol (ZNEP™), the nanotechnology risk assessment tool used by Zurich North America. Items in red text represent exemplar inputs for an evaluation of "Nano Sox." (Figure courtesy of Zurich North America.)

Participants provided some suggestions on how the NNI could improve risk-based decision making, including the following:

- Providing forums for discussion among stakeholders helps to inform the insurance community's understanding of nanotechnology-related risks. In addition to the insurance industry, other financial stakeholders (such as investors) could be involved in this dialogue, allowing the different financial stakeholder groups to understand the drivers and needs of other communities.
- More complete information on EHS risks is needed, including data addressing the long-term effects of nanotechnology applications.
- Consistent and transparent methodologies and data reporting methods should be developed.
- There is a need for clear and consistent standards and regulations, which will add certainty to the nanotechnology landscape. Regulatory alignment across agencies (i.e., OSHA, FDA, and EPA) and governments (e.g., the United States, Canada, and the European Union) is also important.

Other Public Communities

Co-Chairs:
David Berube, PhD, North Carolina State University
Charles Geraci, PhD, National Institute for Occupational Safety and Health

Case Presentations

Summary of Co-Chair Case Presentation—Dr. Berube

"Magic Nano" was an aerosol sealant used in bathrooms that was marketed in Germany. In 2006, reports that users of the product had experienced respiratory problems emerged, and six Germans were hospitalized after using the product. However, an investigation revealed that "Magic Nano" did not actually contain engineered nanoparticles. "Magic Nano" is but one example of a product that has used the "nano" prefix to suggest greater product value, even though the product does not actually contain ENMs [*123*].

Summary of Co-Chair Case Presentation—Dr. Geraci

In one case, workers in China experienced adverse and, in certain cases, fatal health effects in an environment containing airborne nanomaterials [*124*]. However, without exposure data and because of other potential causes for the workers' illness, the link between airborne nanoparticles and the workers' disease was inconclusive [*125*].

Vignette Discussion

Participants offered a variety of comments, including the following:

- The public plays a fundamental role in deciding what constitutes acceptable risk with regard to nanotechnology.
- Information on the effects of both acute and chronic nanomaterial exposure is needed to achieve an understanding of these potential hazards.
- Advice on prudent protective measures, tailored to different public groups encountering exposure in different contexts, is critical.
- The public also needs information regarding the quality of information conveyed in advertisements from marketers.

- A mechanism for the dissemination of comprehensible risk-based information to the public should be developed.
- An understanding of the public's threshold for information could also help to avoid information overload and an unnecessary expenditure of resources.
- If members of the public do not trust the source of information, they will not incorporate that information into their decision making. Given the importance of trust, responsible governance is critical. The behavior of private companies can also greatly affect public trust.
- Attitudinal and behavioral data that address how members of the public engage in reasoned action or planned behavior can help decision makers to anticipate public responses.
- Information regarding the distribution of risks across groups or classes should be obtained because this information is necessary to assess the equity with which risks and benefits are being distributed or imposed.
- Social science research can also be used to shed light on the public's attitudes and perceptions of nanotechnology-related risks.
- Given the public's desire to be informed, uncertainty should be communicated to the public whenever possible. The level of complexity and specificity of this communication should be determined by the audience's ability to comprehend this information.

Participants discussed the various existing sources of information on nanotechnology-related risks, including media, Federal Government agencies (such as NIOSH, EPA, FDA, and CPSC), NGOs, and other stakeholder groups. Some participants identified media inaccuracies, the varying levels of trust held by government agencies, and the style of communication used by knowledgeable experts (which is not always ideal for communicating with the public) as limitations of these available sources. Others commented that the public lacks a "one-stop shop, go-to" place for information on the risks of nanotechnology; therefore, members of the public may struggle to find the appropriate sources of information.

Suggestions offered by participants for the NNI to assist public risk-based decision making included the following:

- Support a national center that targets different stakeholder audiences and educates these audiences so that they may engage in informed risk-based decision making.
- Provide ongoing, adequate support for risk communication between multiple audiences and stakeholder groups.
- Support a research center that joins government agencies and other stakeholder groups in collaborative risk assessment projects.

The NGO Community

Co-Chairs:

Terry Gordon, PhD, New York University School of Medicine and the American Conference of Governmental Industrial Hygienists

Carolyn Cairns, MPH, Independent consultant in Environmental Health, Sustainability, and Product Safety Science

Case Presentation

Summary of Co-Chair Case Presentation—Dr. Gordon

Various NGOs have made efforts to develop environmental exposure threshold limit values (TLVs) and occupational exposure limits for nanoparticles. Examples of NGOs that work to set OELs include the American Conference of Governmental Industrial Hygienists (ACGIH) TLV Committee [*126*], Germany's Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area [*127*], the Occupational Alliance for Risk Science (OARS) managed by the Toxicology Excellence for Risk Assessment group [*128*], and the Scientific Committee on Occupational Exposure Limits of the European Commission [*129*].

The process of setting OELs requires a significant amount of peer-reviewed data, such as human or animal studies, data to determine no-observed-adverse-effect levels (NOAELs), and reliable size data to compare materials. Other than ZnO and TiO_2, there are too few "nano" substances with sufficient data sets to set OELs. Therefore, the ACGIH TLV committee has begun to experiment with using benchmark materials for setting OELs when data are limited. However, extrapolating from a benchmark dose introduces significant uncertainty, and there is currently no reliable substitute for *in vivo* testing.

Vignette Discussion

Breakout participants addressed the issues presented in the vignette by considering a hypothetical example of nanoparticles in paints, coatings, and potentially, food packaging. Since some participants wanted a real-world example, the discussion ended up focusing on the use of nanoparticles in commercial sunscreens. The following risk-based information was suggested by some NGO-affiliated participants as necessary for making decisions in this context:

- Information on which sunscreens contain nanomaterials.
- Data on what makes the "nano ingredients" in commercial sunscreens toxicologically or functionally different from conventional ingredients.
- Analytical methods and standard nomenclatures to characterize and identify nanomaterials in sunscreens.
- Data on the performance of nanotechnology-enabled sunscreens (i.e., how do sunscreens containing nanoparticles compare with conventional sunscreens with respect to sun damage protection?).

Participants suggested some potential information needs:

- Verified information on which commercial products contain ENMs.
- Data on the environmental fate of ENMs, their impact on biological systems, and their transformational effects under environmental conditions.

- Published studies investigating the safety of actual commercial products, as opposed to discrete ingredients or simulated products.
- Data on the environmental and health effects of ENM aggregation or agglomeration.

Some breakout session participants suggested that premarket safety testing of final products (as opposed to just ingredients) or implementation of a meaningful practice of public disclosure for ENM use in consumer products could help to address these substantial data gaps. Suggestions for moving nanotechnology risk management practice forward included the following:

- The existing EHS data on ENMs should be organized and made easily accessible.
- A standard set of toxicity testing methods for ENMs could be developed and promoted.
- Studies should be supported to determine the predictive value of *in vitro* testing methods for assessing *in vivo* health effects.
- Studies should be supported that address the risks presented by ENMs in various exposure scenarios and in various stages of the product life cycle.
- Studies should be supported that address the presence or absence of ENMs in consumer products, the development of methods to characterize potential exposure that could result from the ENMs as presented in these products, and the effects of such exposure.
- A future workshop could gather multiple stakeholder groups to determine how to achieve meaningful disclosure of ENM use in consumer products and in occupational settings.
- An inventory could be developed that lists the presence of ENMs in consumer products and in occupational settings.
- Involvement of the Agency for Toxic Substances and Disease Registry (ATSDR) could be supported in the communication and management of the risks presented by ENMs.

8. Roundtables

Parallel roundtable sessions were convened after the breakout sessions. These moderated sessions provided participants with an opportunity to voice questions or discuss issues that had not been the topic of the previous structured discussions. The roundtable discussions are summarized below.

Roundtable 1: The Needs and Perspectives of Emerging Business

Moderator: Jay West, American Chemistry Council

Emerging businesses compartmentalize their risks (regulatory risks, market risks, etc.) and then determine whether a specific risk is acceptable. These decisions are based on a risk–benefit analysis; risks are inherent in many products, and all businesses accept some amount of risk, regardless of the business context. However, participants offered comments on several specific challenges for emerging businesses involved in nanotechnology:

- There is no "roadmap" for an emerging business producing nanotechnology-enabled products, as there is for drug development [*130*] or emerging technologies in the semiconductor industry.
- There is not enough communication between agencies and businesses regarding regulatory requirements and best practices. Small nanomanufacturing companies encounter difficulties when trying to do business with larger industries as a result of this lack of regulatory clarity, thereby impeding industry collaboration.
- "User-friendly" information relating to the risks of nanotechnology is scarce. Often, the available data are not summarized and simplified, making the data difficult to use for businesses that lack specialized technical expertise.
- Some companies may avoid participation in meetings such as this workshop, to minimize the perception that their "nano" activities represent risk; the NNI could address this by increasing its outreach to small businesses.

Roundtable participants made several suggestions for assisting the emerging-business community, including the following:

- **Create a repository of "user-friendly" information on nanotechnology risk.** For example, the "Good Nano Guide" [*98*] was cited as one helpful resource that is available. The repository could also include Federal agency contact details so that users can receive clarification, if necessary.
- **Provide concrete guidance for emerging businesses relating to realistic scenarios.** Guidance for introducing new products could also be provided. In particular, "step-by-step" guidance for meeting the regulatory requirements of OSHA and EPA is needed. These roadmaps would be pivotal for reducing business uncertainty and would assist small businesses in their attempt to engage with larger industries.
- **Improve methods for outreach or communicating with the small business community.** For example, the Small Business Innovation Research and Small Business Technology Transfer (SBIR/STTR) programs [*131*] were suggested as vehicles to engage with small businesses. These programs could provide information that would direct businesses to EHS resources. Agencies participating in the NNI could also share their best practices for engaging small businesses.

- **Make liaisons available to small businesses with regulatory agencies and agencies participating in the NNI through a defined procedure.** EHS subject-matter experts in Federal agencies could act as liaisons with the small business community. For example, NIOSH engages in productive communication with businesses, and NIOSH field teams help to address some of the practical and financial barriers that the businesses face [*99*]. CPSC also has a small collaborative segment that helps industry actors to develop methods for testing product safety [*132*], although this service may not be applicable to nanotechnology companies creating products that are not final consumer products. Creation of liaison teams from regulatory agencies such as EPA would be beneficial to the small business community.

Roundtable 2: A Sector-Based Approach: Perspectives from the Pharmaceutical Industry

Moderators:
Frank Malinoski, PhD, Liquidia Technologies, Inc.
Lawrence Tamarkin, PhD, CytImmune Sciences, Inc.

The roundtable began with presentations by the moderators on Liquidia's particle replication in non-wetting templates (PRINT) technology for vaccine manufacturing, and on CytImmune's nanotechnology-enabled drug delivery system, Aurimune™ [*133*].

In the ensuing discussion, moderators and roundtable participants offered a variety of comments, including the following:

- Specific technical challenges need to be addressed when characterizing complex nanomedicines and when manufacturing these drugs at the commercial scale.
- Given the large investment that is required to bring a drug to market, investing in nanotechnology-enabled drug development may be perceived as a significant business risk, but this risk is no greater than traditional new drug entities.
- The U.S. regulatory framework is sufficiently comprehensive to accommodate and support the development of nanomedicines and allows for specific considerations on a case-by-case basis. In particular, the Food and Drug Administration guidelines on Pharmaceutical Development [*130*], Quality Risk Management [*134*], Pharmaceutical Quality System [*135*], and the principles of Quality by Design (QbD) [*130*] all provide a valuable framework for nanomedicine development.
- The efforts of the National Cancer Institute (NCI) at the Nanotechnology Characterization Laboratory (NCL) [*136*] have also helped move nanomedicine development forward. By characterizing nanomedicines submitted by industry, this resource provides valuable third-party validation and characterization of nanomaterials being developed for use in medical products. Such assurance is vital for small businesses.
- The NCI Translation of Nanotechnology in Cancer (TONIC) group has assisted in the development of nanomedicines for cancer treatment by encouraging collaborative industry and government agency efforts [*137*].

Various suggestions were offered regarding how NNI support can help to move the field of nanomedicine forward:

- **Continue to support independent third-party validations of data**, such as the efforts taking place at NCL.

- **Continue to support collaborative endeavors between industry and government agencies**, such as those of the TONIC group. Industry–agency alliances may be helpful in other nanotechnology sectors as well.
- **Support the education of pharmaceutical companies and the public on the benefits of nanomedicines.** Ultimately, pharmaceutical companies determine which drugs will be developed through their investment decisions. Educating the public on the benefits of nanomedicines will help to ensure a market for these drugs, thereby encouraging industry investment.
- **Continue to support FDA's regulatory efforts** to ensure that these efforts keep pace with the scientific and technical developments occurring in the pharmaceutical industry.

Roundtable 3: Public Risk Perception and Communication

Moderators:
Barbara Herr Harthorn, PhD, University of California, Santa Barbara
David Andrews, PhD, Environmental Working Group

This roundtable began with case study presentations by the moderators. Dr. Andrews discussed the seventh annual review of sunscreens by the Environmental Working Group (EWG) [*138*], which evaluated the modeled efficacy and the health hazards associated with the listed ingredients of nearly 1400 products. The evaluation of health hazards was based on a review of nearly 60 industry, academic, and government regulatory and toxicity publications and databases, as well as the peer-reviewed literature. When conducting the toxicity review of nanomaterials in sunscreens, a primary focus was exposure via dermal absorption. The literature review revealed minimal evidence of dermal penetration by ENMs at any size scale, and the reviewers ultimately recommended sunscreens containing ZnO and TiO_2 nanoparticles as viable options for consumers seeking sun protection. Products with ZnO and TiO_2 ranked high on the list of recommended products because of their efficacy in providing ultraviolet A (UVA) as well as ultraviolet B (UVB) protection with minimal concerns in regard to toxicity. The report also recommended that powders and lip products containing TiO_2 nanoparticles be avoided; this precautionary recommendation was based on the proximity to the mouth and based largely on a lack of information. There were also concerns regarding mineral structure, particularly with respect to TiO_2, because the anatase crystal phase of this material has been shown to be more reactive than other forms.

Dr. Harthorn discussed effective methods to engage the public and to ensure that decisions based on empirical evidence about the societal as well as technical aspects are made with respect to nanotechnology. She noted that information such as the sunscreen data should be presented in a way that is easily understandable by members of the general public since they may not readily identify technical inaccuracies, misleading information, or gaps in the data.

The roundtable moderators and other participants offered suggestions for improving public risk perception and communication, including the following:

- **Nanomaterials should be treated as if they are new chemicals**, and research should be done in order to determine which nanomaterials pose EHS risks and which do not.
- **An authoritative, trusted, "go-to" source of information is needed.** For instance, a website could be created that contains centralized, synthesized information about nanotechnology for consumers. GreenFacts [*139*] was identified as an example of a resource that successfully

communicates EHS information to a lay audience. Safety data sheets are needed that adequately differentiate nanoscale materials.

- **Best practices should be developed for engaging with diverse audiences and communicating information about nanotechnology.** For instance, forms of certification and labeling of nanotechnology-enabled products should be encouraged. However, labeling may present other issues: labeling could cause distrust simply due to the existence of the label, and labels may not be an effective means to communicate information. In particular, labeling a product as "nano" may not address the public's primary concern, which is simply to know whether these nanotechnology-enabled products are safe.

9. Recurring Themes

The NNI R3 Workshop was organized to assess the state of practice and tools for risk assessment and management, how sector-specific perspectives may influence these practices, and ways that NNI agencies can assist stakeholders in the responsible development of nanotechnology. This workshop was designed to gather data from a wide range of stakeholders in a "top-down" fashion by focusing on identifying types of decisions and decision-maker needs that guide nanotechnology risk assessment and risk management.

State of Practice and Available Tools

Few nanomaterials have been well characterized, and even those evaluated may not have been assessed for each part of the life cycle, especially as they are actually functionalized in the final technology or product. Therefore, much of the state of practice in risk management for nanotechnology presented at the workshop involved dealing with uncertainty due to the limited amount of data. More than one presenter stressed, however, that even with quantitative data, valuations of risk cannot be defined objectively without considering stakeholder values. This necessitates a dialogue between risk managers and other stakeholders early and often in the risk management process. The ability to act more swiftly using incomplete or qualitative data in a protective manner was encouraged. Since both qualitative- and quantitative-based risk management practices involve subjective valuations of risk (e.g., the relative value of reduced longevity of people in different age classes), assumptions and valuations should be made transparent and explicit. Decision analysis was mentioned as a way to standardize and make more explicit this decision-making process.

Stakeholders presented several tools in use to assess risk in the face of incomplete data, including life cycle analysis (LCA), screening-level risk assessment tools (e.g., control banding), alternative analysis tools (e.g., multicriteria decision analysis), and decision analysis tools (e.g., value of information analysis). Life cycle analysis for evidence-based nanotechnology risk assessment was a practice common across stakeholder groups. This type of analysis can be populated with characterization and EHS data from databases like the Nanomaterial Registry [*63*] and can help focus future data collection efforts.

Grouping materials with similar function, physico-chemical similarity, or exposure outcomes was presented as a way to deal with missing data using a method called "control banding." This method incorporates Lawrence Livermore probability and risk severity scores [*55*]. Comparative risk assessment (also called an "alternatives analysis"), instead of the classical risk model of identify, quantify, and control, is where functional, non-nanoscale alternatives are compared with the subject of assessment. GreenScreen [*87*] was offered as a tool to facilitate alternatives analysis by providing a screening measure that uses existing data along with substitute values for missing data. These substitute data have been evaluated through systematic review by certified profilers to verify that the substitution can be performed scientifically. Value-of-information analysis was cited as a tool to "quantify…the potential benefit of additional information in the face of uncertainty" [*105*]. Structured decision making was discussed as a way to deal with qualitative data and to standardize the risk management process.

The need for more widely used standards for testing methods, exposure thresholds, and procedural guidelines was mentioned repeatedly. Several resources in this area were identified by participants:

- International documents (ASTM [*57*] and ISO [*58*]).
- U.S. Government documents:
  - NIST standard reference materials [*116*].
  - FDA guidelines on:
    - Pharmaceutical Development [*130*].
    - Quality Risk Management [*134*].
    - Pharmaceutical Quality System [*135*].
    - The principles of Quality by Design [*130*].
  - OSHA OELs and SDSs.
  - NIOSH guidance documents [*114*].

Additionally, members of the financial risk community (i.e., insurance industry) stated that they gain information by consulting the Insurance Services Office [*122*] (which can gather data and recommend premiums) and through claims investigations. The ACGIH Threshold Limit Values (TLV) Committee [*126*] is also known to set occupational exposure limits.

A complete list of tools and standards mentioned can be found in Appendix D. Additionally, Table 9.1 synthesizes the topics that were discussed by the participants in the general and breakout sessions that took place during the course of the R3 Workshop.

Stakeholder Perspectives on Risk

The public plays a fundamental role in deciding what constitutes acceptable risk with regard to nanotechnology. As highlighted by the keynote speakers, stakeholder perceptions are complex and require expert analysis to understand potentially subtle or obscure ethical complexities; empirical evidence indicates that using an intuitive understanding of "risk" to respond to societal needs is faulty. Stakeholder values should be integrated early on into the risk management process since effective risk communication and management will help to align actual risk and perceived risk.

Although the stakeholder perspectives varied somewhat, most groups represented at the workshop expressed the desire for more information on the potential hazards of and exposure to nanotechnology. Research shows that technical risk data alone will not affect decisions consistently; judgments by different stakeholders with varying biases, values, and stances can affect how consumers, regulators, developers, and insurers behave [*33*]. Even when available, decision makers may not be clear what weight or value is appropriate to place on certain data when setting policy. Formal decision analytical tools can help in placing these weights and values in a transparent way. For the business community, data gaps and public perceptions of risk are both important in terms of responsible development, regulatory compliance, and market acceptance. Overall, better outcomes will result if these issues are explicitly addressed.

Suggestions to NNI Agencies

Workshop participants were asked to suggest ways in which NNI agencies can best support risk-based decision making. Notable suggestions can be grouped broadly into three categories: communication resources, decision tools and data resources, and standardization and guidance resources.

Facilitate Communication

Several suggestions to the NNI agencies centered on facilitating opportunities for better communication between the government and the private sector, and providing fora for continued communication among stakeholders.

Table 9.1. Synthesis of topics discussed by breakout session and group

	DAY 1 BREAKOUT SESSIONS			DAY 2 BREAKOUT SESSIONS						
	Occupational Risk	Product Life Cycle	Environmental Life Cycle	Research Community	Regulatory Community	Nano-manufacturing	Small Business	Financial Risk	Other Public	NGO
Methods/Tools for Detection and/or Characterization of ENMs	✓	✓		✓				✓		✓
Toxicology Studies on ENMs	✓	✓	✓					✓	✓	✓
Repository of Information	✓	✓	✓	✓			✓	✓	✓	✓
Models for Exposure	✓	✓	✓	✓						✓
Transparent Reporting of ENM Presence Across the Supply Chain	✓	✓		✓					✓	✓
Communication and Decision Tools	✓		✓	✓	✓	✓	✓	✓	✓	✓
Data Quality		✓	✓	✓				✓		✓
A Clear Roadmap or Framework for Regulatory Compliance					✓	✓	✓			
Addressing EHS Issues at an Early Stage			✓	✓						✓
Improved Access to and Investigation of Restricted Information	✓	✓	✓					✓		
Standards and Guidances for Risk Assessment and Management	✓	✓	✓		✓	✓	✓	✓		✓

Improve Government–Business Communication

It was suggested that the NNI support more government–business liaison programs. Nanotechnology developers expressed a desire for assistance from the NNI in interfacing with government organizations, especially when dealing with sensitive confidential business information or intellectual property. Such data would also be useful to academic researchers studying hazards and exposure. It was suggested that NNI agencies could investigate ways to identify common issues and trends reflected in this information, while still maintaining its confidential nature. It was also suggested that the Federal NNI agencies work with State governments to help develop integrated and consistent approaches for risk management. Finally, a directory of agency decision makers and points of contact was desired.[9]

Continue Support for Stakeholder Workshops

Additional stakeholder workshops to facilitate responsible development of nanotechnology were suggested, along with meetings with Federal and non-Federal stakeholder groups (such as manufacturers and small businesses) to discuss nanotechnology-related risk management. Specific workshops suggested included the following:

- Multiple stakeholder groups to determine how to achieve meaningful disclosure of ENM use in consumer products and in occupational settings.
- The research and insurance communities to help inform risk-based decisions in underwriting.
- Industry and government to develop a regulatory framework.

Provide Decision Tools and Data Resources

The most often heard suggestions for the NNI agencies were to provide an authoritative point source of information, tools, and resources, and to continue to support risk communication between stakeholder groups.

Create an Independent Risk Management Center and/or a Central Repository for Exposure and Hazard Information Related to Nanotechnology

More than one participant suggested that the NNI agencies could support an independent risk management resource center. Such a center would be a repository for support and information, could anticipate problems and pool lessons learned, and could facilitate independent third-party validations of data such as the efforts taking place at the NCL.

As a variation on that theme, it was suggested that the NNI host a central repository for exposure and hazard information related to nanotechnology. The need for a trusted, central repository of information related to potential risks of nanotechnology was expressed. This “one-stop-shop” could host links to databases and other resources such as the following:

- Existing nanoEHS information on nanotechnology-enabled products.
- OSHA SDSs.
- Difficult-to-publish but useful data (“negative results”).
- Standards relevant to nanomaterials.
- Test methods.

[9] Contact information for Federal decision makers (www.nano.gov/partners), regional, State, and local resources (www.nano.gov/initiatives/commercial/state-local), industry collaborators (www.nano.gov/initiatives/commercial/industry-collaborations), and more can be found at www.nano.gov.

- Occupational exposure limits.
- Material physico-chemical characteristics and EHS data (Nanomaterials Registry).
- Guidance documents from FDA, OECD, NIOSH, and ACGIH.
- Risk management tools.

Provide Standards and Guidances

The need for examples of best practices in the form of standards and guidance resources was mentioned throughout the workshop (see list above). Specifically, such documents can help small businesses in the responsible development of nanotechnology.

Provide Guidance for Small Businesses

Representatives of the small business community stated that they could use assistance from the NNI agencies in interpreting and navigating the regulatory process with regard to nanomaterials. Some suggestions were to offer free assistance and resources (though a fee could be charged similar to the Prescription Drug User Fee Act [*14*]), make use of SBIR/STTR programs [*131*], develop a program to help start-ups in their evaluation of risk (i.e., the type of support that would be given by an industrial hygienist), develop a "roadmap" or "framework" to facilitate the development of nanotechnology-enabled applications through the regulatory process, and support more public–private partnerships and collaborative endeavors between industry and government.

The Path Forward

The R3 workshop successfully brought together a wide range of stakeholders who presented a variety of methods and tools that can be used to evaluate the potential risks of nanomaterials across the life cycle. Risk assessors, including professionals from small companies, environmental groups, occupational health and safety organizations, and insurance companies, outlined the criteria and approaches that they currently use for nanomaterial evaluations. Although still in the nascent stages of nanotechnology risk assessment and management, the participants demonstrated that a combination of existing tools and data can be used to support science-based decisions regarding implications from the use of nanomaterials in a range of scenarios. Integration of risk assessment and management requires supplementing traditional quantitative risk assessment tools with emerging methods such as life cycle and decision analysis. To support the sustainable development of nanotechnology, the risk community must continue this dialogue. Such collaborative efforts will help improve existing methods and develop new communication approaches that provide a better understanding of potential environmental and health implications of nanotechnology-enabled products.

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Appendix A. Workshop Agenda[10]

2013 NNI Workshop on Stakeholder Perspectives on Perception, Assessment, and Management of the Potential Risks of Nanotechnology

Tuesday September 10, 2013

8:30 – 8:35	**Introductions** **Igor Linkov** (Department of Defense), **Treye Thomas** (Consumer Product Safety Commission), **Jeff Steevens** (Department of Defense)
8:35 – 8:50	**Welcome, NNI Overview, and Charge to Participants [PDF]** **Altaf Carim** (Office of Science and Technology Policy)
8:50 – 9:00	**Activities since the 2010 NNI Capstone Meeting and Expectations** **Treye Thomas** (Consumer Product Safety Commission)
SESSION 1:	**A Snapshot on the Perception, Assessment, and Management of the Potential Risks of Nanotechnology** Moderator: **Mark Wiesner** (Duke University)
9:00 – 9:20	**A Perspective from Industry [PDF]** **Stephen Gibbons** (Brewer Science, Inc.)
9:20 – 9:40	**A Perspective from the Consumer Community [PDF]** **Michael Hansen** (Consumers Union)
9:40 – 10:00	**A Perspective from the Labor Community [PDF]** **Darius Sivin** (The International Union, United Automobile, Aerospace and Agricultural Implement Workers of America)
10:20 – 10:40	**A Perspective from the Standards Community [PDF]** **Ajit Jillavenkatesa** (National Institute of Standards and Technology)
10:40 – 11:00	**A Perspective on Regulations [PDF]** **Timothy F. Malloy** (University of California, Los Angeles)
11:00 – 11:20	**A Perspective from the NGO Community [PDF]** **Jennifer Sass** (Natural Resources Defense Council)
11:20 – 11:50	**Discussion with Panel of Morning Speakers**
11:50 – 12:00	**Charge to Breakout Participants** **Jeff Steevens** (Department of Defense)

[10] NOTE: The original full agenda, including times for coffee and lunch breaks, as well as the copies of the presentation slides, may be found at the NNI workshop webpage, www.nano.gov/R3workshop. This version notes the substantive activities only. Additionally, a webcast of most presentations is available at www.tvworldwide.com/events/nnco/130910.

SESSION 2: **BREAKOUT SESSIONS (PART 1)**

13:00 – 16:00 **PARALLEL BREAKOUT SESSIONS BY TYPE OF DECISION**

Group 1: Occupational Risk Analysis and Decision Making
Chairs: **Paul A. Schulte** (National Institute for Occupational Safety and Health)
Bruce Lippy (CPWR—The Center for Construction Research and Training)

Group 2: Commercial Product Life Cycle Stage
Chairs: **Rick Canady** (International Life Science Institute)
Todd Kuiken (Woodrow Wilson International Center for Scholars)

Group 3: Environmental Life Cycle Implications
Chairs: **Tom Seager** (Arizona State University)
Matthew Hull (Virginia Tech)

SESSION 3: **REPORT BACK AND SYNTHESIS CONVERSATION**

Moderators: **Treye Thomas** (Consumer Product Safety Commission)
Christine Hendren (Duke University)

16:30 – 17:00 **Summary of Breakout Sessions**

Breakout Session Co-Chairs

17:00 – 17:15 **Discussion and Public Comments**

Wednesday September 11, 2013

8:30 – 8:45 **Recap of Day 1 and Instructions for Day 2 [PDF]**

Igor Linkov (Department of Defense)

SESSION 4: **Keynote: Perspectives on Risk Analysis**

Moderator: **Igor Linkov** (Department of Defense)

8:45 – 9:15 **Broader Review and Perspectives on Risk Analysis [PDF]**

Baruch Fischhoff (Carnegie Mellon University)

9:15 – 9:45 **Nanotechnology Multi-Stakeholder Risk Perception: Implications for Risk Analysis, Management, and Communication [PDF]**

Barbara Herr Harthorn (University of California, Santa Barbara)

SESSION 5: **BREAKOUT SESSIONS (PART 2)**

10:15 – 12:15 **Parallel Breakout Sessions by Type of Decision Maker**

Group 1: The Research Community
Chairs: **Christie Sayes** (Research Triangle Institute)
Jackie Isaacs (Northeastern University)

Group 2: The Regulatory Community
Chairs: **Rick Reibstein** (Massachusetts OTA)
Janet Carter (Occupational Safety and Health Administration)
Jim Alwood (Environmental Protection Agency)

Group 3: The Nanomanufacturing Community
Chairs: **Ahmed Busnaina** (Northeastern University)
Craig Bandes (Pixelligent Technologies)

Group 4: The Small Business Community
Chairs: **Doyle Edwards** (Brewer Science, Inc.)
Rick Pleus (Intertox, Inc.)

Group 5: The Financial Risk Community
Chairs: **Martha Marrapese** (Keller Heckman LLP)
Clayton Shoup (Zurich North America)

Group 6: Other Public Communities
Chairs: **David Berube** (North Carolina State University)
Charles Geraci (National Institute for Occupational Safety and Health)

Group 7: The NGO Community
Chairs: **Terry Gordon** (American Conference of Governmental Industrial Hygienists, NYU School of Medicine)
Carolyn Cairns (Independent Consultant)

SESSION 7: REPORT BACK AND SYNTHESIS CONVERSATION

Moderators: **Jeff Steevens** (Department of Defense)
Carolyn Cairns (Independent Consultant)

12:15 – 13:00 **Summary of Breakout Sessions**

Breakout Session Co-Chairs

SESSION 8: PARALLEL ROUNDTABLE SESSIONS & CONCLUDING REMARKS

14:00 – 16:00 **Roundtable Discussion Groups:**

Group 1: Needs and Perspectives of Emerging Business

Moderator: **Jay West** (American Chemistry Council)

Group 2: A Sector-Based Approach: Perspectives from the Pharmaceutical Industry

Moderators: **Frank Malinoski** (Liquidia Technologies, Inc.)
Lawrence Tamarkin (CytImmune Sciences, Inc.)

Group 3: Public Risk Perception and Communication

Moderators: **Barbara Herr Harthorn** (University of California, Santa Barbara)
David Andrews (Environmental Working Group)

16:30 – 17:00 **Summary and Discussion of Roundtable Sessions**

Moderator: **Jeff Steevens** (Department of Defense)

17:00 – 17:15 **Discussion and Public Comments**

17:15 – 17:30 **Concluding Remarks**
Igor Linkov, Risk and Decision Science Focus Area Lead, U.S. Army Engineer Research and Development Center, Department of Defense

Appendix B. Workshop Participants[11]

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[11] NOTE: Participants' affiliations are as of the date of the workshop.

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Appendix C. List of Acronyms

ACGIH	American Conference of Governmental Industrial Hygienists
ANSI	American National Standards Institute
ASTM	American Society for Testing and Materials
ATSDR	Agency for Toxic Substances and Disease Registry
CBI	confidential business information
CHA	Chemical Hazard Assessment
CNS	Center for Nanotechnology in Society
CNT	carbon nanotube
CoT	Committee on Technology [NSTC]
CPSC	Consumer Product Safety Commission
CPWR	Center for Construction Research and Training
DOD	Department of Defense
DTSC	Department of Toxic Substances Control [California]
EHS	environment(al), health, and safety
ELISA	enzyme-linked immunosorbent assay
ENM	engineered nanomaterial
EPA	Environmental Protection Agency
EU	European Union
EC	European Commission
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
GRAS	Generally Recognized As Safe
ILSI	International Life Sciences Institute
IP	intellectual property
ISO	International Organization for Standardization
MSDS	material safety data sheet
nanoEHS	nanotechnology-related environmental, health, and safety
NAS	National Academy of Sciences
NCI	National Cancer Institute [NIH]
NCL	Nanotechnology Characterization Laboratory [NIH/NCI]
NEHI	Nanotechnology Environmental and Health Implications Working Group [NSET]
NGO	nongovernmental organization
NIOSH	National Institute of Occupational Safety and Health

NIST	National Institute of Standards and Technology
NMSP	Nanoscale Materials Stewardship Program [EPA]
NNCO	National Nanotechnology Coordination Office
NNI	National Nanotechnology Initiative
NRC	National Research Council of the National Academies
NRDC	Natural Resources Defense Council
NSET	Nanoscale Science, Engineering, and Technology Subcommittee [NSTC]
NSF	National Science Foundation
NSTC	National Science and Technology Council
NYU	New York University
OARS	Occupational Alliance for Risk Science
OECD	Organisation for Economic Co-operation and Development
OEL	Occupational Exposure Limit
OSHA	Occupational Safety and Health Administration
PBT	persistent, bioaccumulative, and toxic
PNAS	*Proceedings of the National Academy of Sciences*
PPP	public–private partnership
QbD	quality by design
QSAR	quantitative structure–activity relationship
R3	risk assessment, risk management, and risk communication
R&D	research and development
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals Act [EU]
SBIR/STTR	Small Business Innovation Research/Small Business Technology Transfer
SCOEL	Scientific Committee on Occupational Exposure Limits [EC]
SDM	structured decision making
SDS	safety data sheet [formerly MSDS]
SNUR	Significant New Use Rule [EPA]
TLV	threshold limit value
TONIC	Translation of Nanotechnology in Cancer [NCI]
TSCA	Toxic Substances Control Act
UAW	United Automobile Workers
UCLA	University of California, Los Angeles
UCSB	University of California, Santa Barbara
UVA	Ultraviolet A
UVB	Ultraviolet B

Appendix D. Available Tools and Information Repositories

U.S. Government[12]

DOD

- US Army NanoExPERT Tool Box [*140*].

DOE

- "Control Banding Nanotool" (Figure 6.1 on p. 27), which incorporates Lawrence Livermore probability and risk severity scores for risk assessment in the face of incomplete information and uncertainty [*55*].

EPA

- 2012 RTI study funded by EPA on methods for prioritizing research areas on hypothetical use of multiwalled CNTs in upholstery fabric based on stakeholder input [*113*].

FDA

- Pre-submission consultation with the FDA [*141*].
- Guidance documents [*104*]. Specifically mentioned:
  - Pharmaceutical Development [*130*].
  - Quality Risk Management [*134*].
  - Pharmaceutical Quality System [*135*].
  - Principles of Quality by Design [*130*].

NIH

- Nanotechnology Characterization Laboratory [*136*] materials testing and fundamental information on ENMs related to cancer (NIH/NCI).
- The NCI Translation of Nanotechnology in Cancer group has assisted in the development of nanomedicines for cancer treatment by encouraging collaborative industry and government agency efforts [*137*].
- National Center for Biotechnology Information PubMed database of research studies [*103*].

NIOSH

- Nanotechnology Field Studies Effort [*99*].
- Guidance documents:
  - *Workplace Safety & Health Topics: Nanotechnology* [*114*].
  - *General Safe Practices for Working with Engineered Nanomaterials in Research Laboratories* [*119*].

NIST

- NIST standard reference materials [*116*].

[12] The references in this list may be found in Chapter 10 (References).

NNCO

- Industry and State Liaison point of contact (Dr. Michael Kiley, mkiley@nnco.nano.gov, 703.292.4399).
- Contact information for Federal decision makers (www.nano.gov/partners).
- List of regional, State, and local resources (www.nano.gov/initiatives/commercial/state-local).
- Resources for business development and technology transfer (www.nano.gov/businessdevelopment).
- A FAQ page for nanotechnology business development (www.nano.gov/bizfaqs).
- Information on opportunities for collaboration and funding (www.nano.gov/collaborationsandfunding), including a list of open contests and challenges (www.nano.gov/ContestsAndChallenges).
- A database of publications and resources including budgets, strategic documents, workshop reports (www.nano.gov/publications-resources).
- List of NNI Environmental, Health, & Safety-Related Documents (www.nano.gov/EHSdocuments).
- Information on Federal Legislation and Congressional Events (www.nano.gov/you/government-legislation).

OSHA

- A database is in development for identifying the potential hazards posed by nanomaterials (see p. 36).
- Safety data sheets (SDSs, formerly known as MSDSs).

International

- TEMAS—The Swiss Precautionary Matrix for Synthetic Nanomaterials is a tool "made to support all interest groups having a responsibility for the safety of workers, consumers or the environment" [*109*].
- Publications from Germany's Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area [*127*].
- NanoRiskCat, a risk categorization framework developed in Denmark, is "able to identify, categorize and rank exposures and effects of nanomaterials used in consumer products based on data available in the peer-reviewed scientific literature and other regulatory relevant sources of information and data" [*110*].
- The European Registration, Evaluation, Authorisation, and Restriction of Chemicals program approach to nanomaterials, initiated through European legislation [*89*].
- Publications from the Scientific Committee on Occupational Exposure Limits of the European Commission [*129*].
- Documentation from the International Organization for Standardization [*58*] and its online browsing platform [*62*].
- Publications from the Organisation for Economic Co-operation and Development addressing the safety of ENMs [*115*].

State and Local

- Contact information for State, regional, and local resources on nano.gov (see NNCO on p. 73).
- California's Safer Consumer Products Regulation "alternatives assessment" [*81*].
- Guidance from the Massachusetts Office of Technical Assistance and Technology on the safe development of nanotechnology [*118*].

Private

- List of industry collaborators on nano.gov (see NNCO on p. 73).
- Documentation from the American Society for Testing and Materials [*57*].
- Dr. Tom Seager's life cycle assessment framework that assesses the EHS implications of a technology when data are sparse (see Figure 6.4 on p. 32).
- Germany's Federal Institute for Materials Research and Testing Nanoscale Reference Materials [*64*] website.
- GreenFacts [*139*] as an example of a resource that communicates EHS information to a lay audience.
- GreenScreen [*87*] can be used to screen and communicate hazard information on specific classes of nanomaterials.
- Nano GO Consortium standardized methods for assessing the health and safety of engineered nanomaterials [*97*].
- Nanomaterial Registry [*63*].
- Nanotechnology Standards Database, sponsored by the American National Standards Institute (ANSI) Nanotechnology Standards Panel [*61*].
- National Academy of Engineering (NAE) and National Academy of Sciences reports.
- Occupational Exposure Limits from the American Conference of Governmental Industrial Hygienists TLV Committee [*126*].
- Safe-and-Green-Nano List, an open-source online information clearinghouse for information on the safe development of nanomanufacturing and the potential for greener products through nanoscience [*142*].
- Structured Decision Making tool under development at CNS-UCSB: A nanotechnology risk screening tool [*33*] for structured decision making to account for motivated cognition.
- The "Good Nano Guide," serving as an "Internet-based collaboration platform specially designed to enhance the ability of experts to exchange ideas on how best to handle nanomaterials in an occupational setting" [*98*].
- The Insurance Services Office [*122*].
- The Occupational Alliance for Risk Science of Toxicology Excellence for Risk Assessment [*128*].
- The proprietary nanotechnology risk assessment tool called the Zurich Nanotechnology Exposure Protocol [*121*].
- The publications database [*102*] available at nanoHUB.

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