Bridging NanoEHS Research Efforts: A Joint U.S.–EU Workshop

March 11–12, 2011

Workshop Proceedings

This document is the report of the United States–European Union Joint Workshop on Bridging Nanotechnology Environmental, Health, and Safety ("nanoEHS") Research Efforts, held March 11–12, 2011, in Washington, DC. The workshop was sponsored by the Federal agencies participating in the U.S. National Nanotechnology Initiative, the European Commission, and the American Association for the Advancement of Science BILAT-USA program. The workshop brought together U.S. and EU scientists engaged in nanotechnology environmental, health, and safety research to identify areas of shared nanoEHS interest and mechanisms for collaboration to advance the science.

This report is not a consensus document but rather is intended to reflect the diverse views, expertise, and deliberations of the workshop participants.

The report was designed, assembled, and edited by staff of the U.S. National Nanotechnology Coordination Office.

Published in the United States of America and in the European Union, 2012.

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Executive Summary

Nanomaterials are increasing in complexity and number, and the responsible development of nanotechnology-enabled (nano-enabled) commercial products is proving challenging because many near- and long-term environmental, health, and safety (nanoEHS) questions—such as the potential toxicity of some nanoscale materials—are incompletely answered. The United States and the European Union share the need to address these questions with the best available science and to engage with international partners to exchange information, develop best practices, and leverage limited resources.

To these ends, the United States and the European Union jointly hosted a workshop, *U.S.–EU: Bridging NanoEHS Research Efforts*, on March 10–11, 2011, in Washington, DC. This workshop brought together researchers, industry representatives, public health stakeholders, and regulatory scientists from Europe and the United States. The primary goals of the workshop were to engage in an active discussion about EHS questions for nano-enabled products, encourage joint programs of work that could leverage research assets and resources, and identify mechanisms to expand collaboration.

The structure of this report reflects the program of the workshop, which was broadly divided into four parts: Understanding U.S. and EU Perspectives and Programs; Data Needs for Regulatory Decision Making; Tackling the Challenges of Producing Reliable and Reproducible Data for Nanomaterials Assessment and Risk Management; and Collaborative Mechanisms for Joint Work.

Understanding U.S. and EU Perspectives and Programs

The opening session of the workshop provided context for discussing the complex topic of nanoEHS research through presentations of stakeholder perspectives on various aspects of nanoEHS research and of national and international nanoEHS programs. Representatives from the U.S. Government and the European Commission recognized the potential of nanotechnology to address societal challenges and to spur economic growth, while emphasizing the need to develop nanotechnology responsibly. The speakers further highlighted the value of shared priorities, joint projects, and collaboration in maturing the field. Research strategies in the United States, the European Union, and the EU member states support nanoEHS research with an emphasis on life cycle analysis of nano-enabled products. Speakers from the Organisation for Economic Co-operation and Development (OECD) and the International Organization for Standardization (ISO) discussed how international efforts aid in the responsible development of nano-enabled products and nanoEHS research by fostering international cooperation, pooling expertise, and developing standards.

Representatives from industry described the role that publicly funded, safety-related projects involving partners from industry, academia, and authorities play in complementing companies' internal nanoEHS research activities. Generally, industries participate in publicly funded research projects that would be unaffordable for a single company. This participation also creates public confidence in the research results. Additionally, an industry speaker voiced the

need for regulations that are science-based to encourage responsible development of innovative products. Finally, a presentation from a U.S.-based nongovernmental organization underscored the urgency of coordinating research around the central objective of effectively characterizing exposures associated with nanomaterials already in or entering the chain of commerce.

Data Needs for Regulatory Decision Making

An introductory talk set the stage for two subsequent breakout sessions on this topic by presenting an overview of regulatory data gaps and noting that although the data are incomplete, important trends are starting to emerge that indicate a short-term ecotoxicity of nanomaterials.

Presentations in the *Human Health Data Needs* breakout session highlighted the need for standardized exposure scenarios, chronic toxicity data, and personal monitoring of worker exposures. The central research needs that emerged during the discussion were nanomaterial characterization, reference nanomaterials, endpoint selection, exposure considerations, and the need for integrated and complete health effects databases within the broader context of EHS datasets.

Presentations in the *Environment Data Needs* breakout session demonstrated the complexity of nanomaterials hazards assessment in the environment. This complexity is illustrated by the diverse mechanisms by which nanoparticles (NPs) might harm cells and the multiple fates NPs might have in the environment. Based on a list of regulatory challenges identified during the discussion, three data and research needs were highlighted: source characterization, susceptibility, and integration of existing information with actions based on recommendations.

After the breakout sessions, a panel of U.S. and EU regulators discussed the research needs that were identified in the breakout sessions. Panelists agreed with the themes that had emerged during the breakout sessions, and they identified additional needs for standardizing sample preparation, measuring relevant exposure, and evaluating the effects of the matrix material. The panelists identified nanoEHS research goals common to both human health and the environment, and they emphasized the need to prioritize research toward these cross-cutting goals and the need for collaboration among experts in human health and the environment. Finally, they noted that improved communication among industry, researchers, and policymakers is essential for progress in research on and regulation of nanomaterials.

Tackling the Challenges of Producing Reliable and Reproducible Data for Nanomaterials Assessment and Risk Management

This segment of the workshop consisted of six breakout sessions divided into two general topic areas: *Human Health and Ecological Effects*, and *Measuring Exposures and Fate of Nanoparticles in the Workplace and the Environment*. While the three *Human Health and Ecological Effects* breakout sessions ranged in specific focus from surface modifications of nanomaterials to dose–response data, the state of the science that emerged from the discussions suggests that standardized reference materials are needed; definition and understanding the novel properties of nanomaterials continues; pristine nanoparticles, whether aggregated/agglomerated or not, are unlikely to exist in the environment or in the body; the

surface coating on a nanoparticle affects many biological processes; and all three currently reported dose metrics—mass, particle size, and particle number—should be reported when possible.

The three breakout sessions on *Measuring Exposures and Fate of Nanoparticles in the Workplace and the Environment* focused on model nanoparticles, environmental media, and general population exposures. Participants in the breakout session on model NPs agreed that model NPs are useful in life cycle analysis, as reference materials, in release models and exposure assessment, and in distinguishing engineered nanomaterials (ENMs) from background nanomaterials. The breakout groups on environmental media and on general population exposure both identified the need to anticipate possible transformations that may take place as nanomaterials flow through synthesis, manufacture, commerce, and into the environment, and the need for an appropriate framework for accurate modeling that reflects potential transformations, surface mechanisms, and aggregation properties. They also underscored the need to relate potential nanomaterial releases from products to actual human exposures.

In a plenary session on *Industrial Risk Management Considerations for Worker Protection*, speakers gave an overview of additional research needs for providing worker safety, which include technologies that can distinguish between engineered nanomaterials and background nanomaterials, standardized sampling, realistic release scenarios, and life cycle analysis. It was also proposed that control banding concepts could be applied to nanoEHS research. Finally, it was emphasized that risk managers should be cautious no matter what their experience level because nanotechnology is a new field in which even experts have a lot to learn.

Mechanisms for Collaborative Work

Collaboration between the European Union and the United States in nanotechnology-related EHS research is expected to deliver faster and more integrated progress in issues of high societal value. Both sides commit significant resources in their separate public programs to support safety-oriented research and networking activities. Bridging these networks is a first priority, and multiple mechanisms may help create these bridges. BILAT-USA and Link2US are initiatives that currently exist for funding research projects that can support transatlantic dialogue among nanoEHS researchers. Communities of Research (CORs) are being developed to provide a communication platform for specific research themes, for example, materials, hazards, exposure, and risk control, and to obtain maximum collaboration with minimal budgets. Finally, an annual workshop will provide the possibility of face-to-face meetings among researchers and a venue to continue and mature the U.S.–EU nanoEHS dialogue.

1. Introduction

Nanomaterials are increasing in complexity, and nanotechnology-enabled (nano-enabled) commercial products are under research and development with many near- and long-term environmental, health, and safety (EHS) questions—such as the potential toxicity of some nanomaterials—incompletely answered. In order to capture and understand the breadth of nanoEHS research that is currently under way, leverage the work being done, and target future research needs efficiently, the United States and European Union jointly hosted a workshop, *U.S.–EU: Bridging NanoEHS Research Efforts*, on March 10–11, 2011, in Washington DC.

The primary goals of the workshop were to

- Engage in an active discussion about environmental, health, and safety questions for nano-enabled products
- Encourage joint programs of work that can leverage each other's resources
- Establish Communities of Research (using the Communities of Practice model), including identification of key U.S. and EU points of contact, establishment of interest groups, and identification of themes and key U.S. and EU funding sources for near-term and future collaborations

The workshop planning team was co-chaired for the European Union by the Directorate-General for Research and Innovation of the European Commission and for the United States by the Environmental Protection Agency (EPA), the Department of State, and the National Nanotechnology Coordination Office (on behalf of the Nanoscale Science, Engineering, and Technology Subcommittee of the National Science and Technology Council's Committee on Technology and its Nanotechnology Environmental and Health Implications Working Group). More than 200 scientists and other stakeholders representing academia, industry, nongovernmental organizations (NGOs), public health stakeholders, and the U.S. and European governments attended the workshop.

The first day of the workshop opened with plenary presentations that provided the perspectives of the various stakeholders, including governments, NGOs, and industry interested in nanoEHS research and regulation. The second session of the day focused on data needs for regulatory decision making. An overview of the general components of U.S. and EU regulatory decision making and data needs set the stage for two concurrent breakout sessions that explored human health and environmental data needs. The day closed with a panel discussion in which U.S. and EU regulators discussed their perspectives on the research needs that were identified in the breakout sessions.

The second morning of the workshop was devoted to tackling the challenges of producing reliable and reproducible data for nanomaterials assessment and risk management. Six concurrent breakout sessions—divided into two general topic areas: *Human Health and Ecological Effects*, and *Measuring Exposures and Fate of Nanoparticles in the Workplace and the Environment*—were held to address specific aspects of this topic:

Human Health and Ecological Effects

1. When do unique properties—with risk assessment implications—arise for specific nanomaterials?
2. How do surface modifications and chemical transformations affect toxicity?
3. What metrics are most scientifically accurate when relating dose to response in toxicity assessments? How are dose–response data best extended to determining occupational exposure limits and environmentally relevant concentrations?

Measuring Exposures and Fate of Nanoparticles in the Workplace and the Environment

4. How relevant are model nanoparticles to understanding exposure in the workplace? How relevant are they to recommending industrial hygiene practices?
5. What are the critical parameters and data needs for understanding the behavior of nanoparticles in environmental media?
6. What are the critical parameters and data needs relevant to understanding the behavior of nanoparticles in consumer and general population exposures?

The afternoon of the second day began with a plenary session on industrial risk management considerations for worker protection, and the workshop closed with a session on "Getting It Done Together," which focused on establishing scientific themes and mechanisms for ongoing interactions and next steps to grow U.S.–EU research collaborations.

This report summarizes the principal conclusions of the presentations and discussions that took place during the *U.S.–EU: Bridging NanoEHS Research Efforts* workshop. Additional materials related to the workshop, such as speaker presentations, are available online: http://us-eu.org/.

The structure of this document generally reflects the organization of the workshop. Section 2 summarizes the perspectives of the various stakeholders in the nanoEHS research and regulatory processes in both the European Union and the United States. Section 3 gives an overview of *Data Needs for Regulatory Decision Making*, followed by a summary of the breakout sessions on *Human Health Data Needs* and *Environmental Data Needs*, and a summary of the regulatory panel discussion. Section 4 presents the findings from each of the six breakout groups on *Tackling the Challenges of Producing Reliable and Reproducible Data for Nanomaterials Assessment and Risk Management*; it is divided into the general topic areas of *Human Health and Ecological Effects*, and *Measuring Exposures and Fate of Nanoparticles in the Workplace and the Environment*. Section 5 describes *Industrial Risk Management Considerations for Worker Protection* that were explored in the workshop, and Section 6 describes the workshop's discussions on *Establishing Scientific Themes and Mechanisms for Ongoing Interaction* and *Growing the Effort*. Appendix A gives the full workshop agenda, Appendix B lists the workshop participants, and Appendix C provides titles and links for the speaker presentations. Appendices D, E, and F provide the discussion templates for the breakout groups, the post-workshop survey form, and a list of the abbreviations and acronyms used in this report.

2. Opening Comments and Understanding U.S. and EU Perspectives and Programs

Introduction

The opening session of the workshop provided context for later discussions on the complex topic of nanoEHS research through presentations on stakeholder perspectives and on U.S. and EU national and international nanoEHS programs. Speakers described the research plans of the European Commission (EC), examples of nanoEHS research programs in European nations, the research strategy and select research activities in the United States, the coordinating role of international organizations, and perspectives of industry and a nongovernmental organization.

Welcoming Remarks

Daniel Clune, U.S. Department of State

Mr. Daniel Clune welcomed all participants to the workshop and commended the significance of the meeting. He acknowledged that nanotechnology will be a major contributor to both the U.S. and European economies while emphasizing that it is essential to collectively consider the potential impact of nanotechnology and specific nanomaterials on humans and the environment. Mr. Clune described several of the mechanisms through which the United States engages with international partners on nanoEHS issues, including multilateral fora and bilateral meetings, noting that perhaps the most important U.S.–international collaboration on EHS research is with the European Union. This was acknowledged at the U.S.–EU Joint Consultative Group Meeting in May 2010, and this workshop is a direct outcome of those discussions. The Transatlantic Economic Council encourages researcher exchanges to support commonly agreed-on, science-based approaches to regulation, while the European Commission–United States High-Level Regulatory Cooperation Forum has specifically called for both sides to "look at the best available science on nanotechnology and to continue to share best practices and research" in support of risk-based approaches.[1] The Forum's recommendations are well aligned with the objectives of this workshop.

Herbert von Bose, European Commission

Mr. Herbert von Bose thanked Mr. Clune for the warm welcome and, speaking on behalf of the European Commission, he expressed the EC interest in close and fruitful cooperation. This spirit was already expressed by Commissioner Máire Geoghegan-Quinn on her visit to the United States in 2010. The United States is a main strategic partner for Europe, and both partners consider research and innovation to be key priorities for economic recovery and job creation. The European Commission would like to continue supporting a platform for cooperation inside the U.S.–EU Science and Technology agreement, and it is incumbent upon the research community to make it work. Although the two teams know each other well and cooperate

[1] European Commission–United States High-Level Regulatory Cooperation Forum, *Report of the 9th Meeting, Washington DC, 16 December 2010* (http://whitehouse.gov/sites/default/files/omb/oira/irc/hlrcf_summary_report_december_2010.pdf), 8.

already to some degree, it is crucial for the field of nanotechnology safety that more collaboration be developed. Mr. von Bose expressed confidence that the U.S. and EU teams will establish the cooperation needed for implementing their complementary innovation objectives.

Purpose and Goals

Sally Tinkle, U.S. National Nanotechnology Coordination Office

Dr. Sally Tinkle described the goals of the workshop in relation to the strategic priorities of the United States and the European Union. She noted that the workshop addressed recommendations in the United States by the President's Council of Advisors on Science and Technology and the 2011 National Nanotechnology Initiative (NNI) EHS Research Strategy that have encouraged expanding international cooperation on nanoEHS issues. In the EU, the focus of this workshop aligns with strategic priorities in the European strategy and Action Plan on Nanotechnology that call for international cooperation. Based on these recommendations, the primary goals of the workshop were to

- Engage in an active bilateral discussion about environmental, health, and safety questions for nano-enabled products
- Encourage joint programs of work that will leverage resources
- Identify mechanisms to expand collaboration, including identifying key U.S. and EU points of contact, establishing interest groups, and identifying themes and U.S. and EU funding sources for near-term and future collaborations

Research-to-Regulation Transition Needs

Elke Anklam, European Commission, Institute for Health and Consumer Protection

Dr. Elke Anklam highlighted the role of the European Commission's Joint Research Centre (JRC) in providing support to the Commission's General Directorates for the conception and implementation of regulation. She outlined the European approach to deal with nanotechnology-related issues in consumer products legislation and addressed urgent research needs to close existing knowledge gaps for the appropriate consideration of nanomaterials in consumer products, cosmetics and food in particular.

Overview of EC Nano-EHS Research Plans

Georgios Katalagarianakis, European Commission Directorate-General for Research and Innovation (DG R&I)

Dr. Georgios Katalagarianakis outlined the main objective of the "Europe 2020" strategy: smart, sustainable, and inclusive growth. Research and innovation have been identified as key means for driving European social and economic prosperity as well as for achieving environmental sustainability. The Green Paper on the European Union's research and innovation policy places a major emphasis on securing strong positions in key enabling technologies such as information and communications technology, nanotechnology, advanced materials, manufacturing, space technology, and biotechnology, and underlines their significance to Europe's competitiveness

and its ability to provide the innovative goods and services essential for meeting global challenges.[2]

Dr. Katalagarianakis stated that, in particular, nanotechnology offers substantial possibilities for improving the competitive position of the EU and for responding to key societal challenges. Nanotechnology is referred to as the new "general purpose technology," a springboard for long-term productivity increases, economic growth, and a means of addressing grand challenges. Manufactured nanomaterials are expected to yield significant innovation, hence providing a new competitive edge to European industry and strong benefits for the society in a very wide range of applications from medicine to agriculture, from biology to electronics. The new technology applications not only should be safe themselves but should also offer substantial improvements in human health and environment protection.

Mindful of the safety aspects of these emerging technologies, the European Commission actively promotes and supports research and development as well as innovation in this area. Ensuring the safe development of nanotechnologies, through a sound understanding of their potential impact on health or on the environment and through the development of tools for exposure monitoring, risk assessment, and risk management, is a key factor to fully harvest the benefits from their deployment.

Research efforts in the European Union have achieved significant technological progress both in the technology and in its safety management. Several research projects are either completed or running that represent a total EU research and technological development investment of €112 million from the NMP[3] and other programs under the 6th Framework Programme (11 projects, €30 million) and the 7th Framework Programme (25 projects, €82 million). New projects supported by about €29 million of EU funding were to be launched in 2011. These projects, together with a significant number of projects supported by government resources in the EU member states and the 7th Framework Programme (FP7) associated states, and other projects addressing safety as side objective, represent the valuable efforts of the EU scientific and industrial research community for progress in all aspects of nanotechnology-related safety issues (nanosafety).

Dr. Katalagarianakis pointed out that synergy among these projects, collaboration to maximize impact, policy elaboration, planning of future actions, and international cooperation are the main aims of the NanoSafety cluster (http://www.nanosafetycluster.eu), a projects-based stakeholders' open forum. He closed by emphasizing that the ultimate goal of the NanoSafety cluster and a U.S.–EU collaboration is to ensure safe handling of nanomaterials and safety of nanotechnology-based products and nanotechnologies in their entire supply chain—including use and final disposal or recycling—by establishing a new safety culture and developing and implementing a complete system of methods, techniques, and equipment; a competent scientific and technical community; and a portfolio of measures to promote a total safety

[2] European Commission. *Green Paper. From Challenges to Opportunities: Towards a Common Strategic Framework for EU Research and Innovation Funding,* 2011; http://ec.europa.eu/research/horizon2020/index_en.cfm?pg=documents.

[3] *NMP* stands for *nanotechnology and nanosciences, knowledge-based multifunctional materials, and new production processes and devices* in EU 6th and 7th Framework Programmes for scientific and technological R&D policies and programs.

paradigm and to inform the general public about safety management of the technologies utilizing engineered nanoparticles.

Overview of the U.S. 2011 EHS Research Strategy

Sally Tinkle, U.S. National Nanotechnology Coordination Office

Dr. Sally Tinkle began her presentation with an overview of the NNI, which was launched by the U.S. Government in 2000 in recognition of the potential for nanotechnology to create scientific and technological breakthroughs that enhance national security, strengthen the economy, and improve societal well-being. The NNI is a multidisciplinary effort in which 25 Federal agencies,[4] with responsibilities ranging from basic research funding to application and regulation, collaborate to promote the safe and efficient development and deployment of nanotechnology. The NNI has four primary goals, as described in the 2011 *NNI Strategic Plan*:[5] (1) to advance a world-class nanotechnology R&D program; (2) to foster the transfer of new technologies into products for commercial and public benefit; (3) to develop and sustain educational resources, a skilled workforce, and the supporting infrastructure and tools to advance nanotechnology; and (4) to support responsible development of nanotechnology.

Dr. Tinkle continued by describing the U.S. nanoEHS strategy in the framework of the NNI. EHS research is an integral part of all four NNI goals, although the goal of responsible development is particularly dependent upon EHS research. As such, the NNI member agencies collaborated to produce the 2011 *NNI Environmental, Health, and Safety Research Strategy* that is intended to provide guidance to Federal agencies that support or rely on nanoEHS research. The NNI EHS research strategy was crafted with the following goals: protect public health and the environment; employ science-based risk analysis and risk management; and foster technological advancements that benefit society.

Dr. Tinkle highlighted the fact that the concepts of risk assessment and product life cycle analyses are central to the 2011 NNI EHS Research Strategy. When assessing risk, the potential hazard of a nanomaterial and the potential exposure of humans and/or the environment to the nanomaterial are the primary considerations. This assessment of hazard and exposure allows for the comparison of nanomaterials and other substances, the comparison of different types of nanomaterials, or the evaluation of a single nanomaterial.

She went on to note that NNI stakeholders have determined that a comprehensive risk assessment strategy should also include an evaluation of the risk across the product life cycle from the production of the raw materials to the disposal of the product after use. Integrating the product life cycle stages with the risk assessment paradigm enables the identification and prioritization of crucial nanoEHS research needs in six categories: (1) Nanomaterial Measurement Infrastructure; (2) Human Exposure Assessment; (3) Human Health; (4) Environment; (5) Risk Assessment; and (6) Predictive Modeling. The 2011 NNI EHS Research Strategy incorporates, for the first time, a research emphasis on predictive modeling and informatics, which can aid in improving data, validating theories, and augmenting collaboration.

[4] There are 26 U.S. Federal agencies involved in the NNI as of 2012.

[5] This and other U.S. NNI publications may be found at http://nano.gov/publications-resources.

Finally, issues of ethical, legal, and societal implications (ELSI) of nanotechnology are woven throughout the research strategy.

The NNI agencies will need to work together in a focused and collaborative manner to achieve the goals of the NNI EHS research strategy. This effort is primarily coordinated through the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the U.S. National Science and Technology Council's Committee on Technology and its Nanotechnology Environmental and Health Implications Working Group. These groups have identified the following guidelines to aid agencies in their strategic planning: prioritize which nanomaterials to research; establish standard measurements, terminology, and nomenclature; maximize data quality; stratify knowledge for risk assessment; partner to achieve the NNI EHS research goals; and engage internationally. For example, the NNI EHS research strategy proposed dual criteria for prioritizing selection of ENMs for research: nanomaterials that may provide a major contribution to the ENM research knowledge base or nanomaterials and nanotechnology-enabled products that may pose a safety concern to humans and the environment.

The nanoEHS research strategy summarized above is in alignment with the goals and objectives in the 2011 NNI Strategic Plan. The collaborative U.S.–EU effort will help to realize the vision of a future in which nanotechnology provides maximum benefit to the environment and to human social and economic well-being.

OECD WPMN: Latest Developments and Outlook

Alexander Pogany, Austrian Federal Ministry of Transport, Innovation and Technology (BMVIT)

Dr. Alexander Pogany gave an overview of the Organisation for Economic Co-operation and Development (OECD) Working Party on Manufactured Nanomaterials (WPMN), which was established in September 2006 to foster international cooperation in health and environmental safety-related aspects of manufactured nanomaterials (http://oecd.org/env/nanosafety). The OECD WPMN is also examining the applicability of existing test guidelines to nanomaterials and identifying risk assessment issues, alternative test methods, and exposure measurement and mitigation systems. In 2007, the WPMN launched the Sponsorship Programme for the Testing of Manufactured Nanomaterials. OECD member countries, as well as some nonmember economies and other stakeholders participating in the program, pool their expertise and fund the safety testing of specific manufactured nanomaterials. In launching the Sponsorship Programme, the WPMN agreed on a priority list of manufactured nanomaterials and a list of endpoints relevant for human health and environmental safety for which the manufactured nanomaterials should be tested.

Standardization for Nanosafety: ISO Plans and Perspective

Daniel Bernard, Arkema, Inc. (U.S.)

Dr. Daniel Bernard's presentation on the role of the International Organization for Standardization (ISO) in nanoEHS and nanotechnology was based on the idea that given this field's enormous potential for competitiveness in industry and benefits for society at large,

nanotechnology stakeholders have to ensure its development in a safe and responsible manner. Policies to this end are being proposed, developed, and approved at different levels by the various national and organizational members of the ISO through its Technical Committee 229 (Nanotechnologies). The ISO is committed to the development of high-quality health, safety, and environmental standards as one of the building blocks to ensure that products and systems are developed and commercialized in a safe, well-integrated, and responsible manner. This should improve occupational safety, consumer protection, and environmental protection by promoting best practices in the production, use, and disposal of nanomaterials, nanotechnology products, and nanotechnologically enabled systems. Standards will support characterization and exposure assessment of nanomaterials by developing

1. Methodologies for nanomaterial characterization in the manufactured form, before toxicity and eco-toxicity testing
2. Techniques for sampling and measuring workplace, consumer, and environmental exposure to nanomaterials
3. Methods to simulate exposures to nanomaterials

Dr. Bernard clarified that work on toxicology and screening is performed mainly within the framework of the OECD, and risk assessment is carried out mainly by national authorities.

Examples of EU National Efforts

Thomas A.J. Kuhlbusch, German Institute of Energy and Environmental Technology

Dr. Thomas Kuhlbusch began by speaking about NanoCare, a German initiative to develop a knowledge base to catalog the findings of innovative research in health aspects of synthetic nanomaterials. He explained that the aim of NanoCare is to pursue a comprehensive approach on exposure and hazard assessment for selected nanomaterials employed in industry. NanoCare started in 2006 and presented its results in a public scientific report in 2009.[6] Major nanotechnology-related industries, research institutions, and universities (16 partners overall) worked together through NanoCare to investigate the release of nanomaterials at workplaces and during processing, the biokinetics of nanomaterials, and the possible toxicological effects of nanomaterials *in vivo* and *in vitro*. Major outcomes included the involvement of the public in a discussion on nanosafety (*Bürgerdialoge*), the development and evaluation of devices and standard operating procedures to test nanomaterial release during processing, a finding of the higher sensitivity to nanomaterials of "fresh" macrophages compared to established cell lines, and the finding of a correlation between *in vivo* and *in vitro* health-related endpoints.

Dr. Kuhlbusch further described how the NanoGEM program started at the end of 2010, building on the findings of NanoCare. NanoGEM combines industry, research institutions, universities, and public bodies to work together on nanosafety for humans and on risk estimates. With 19 partners, NanoGEM is conducting research in the development of new *marked* nanomaterials comparable to industrial mass products such as TiO_2 and SiO_2. Marking of the materials is achieved by doping with europium or elemental silicon or including a core-

[6] Dechema e.V. and NanoCare Project Consortium, Germany. 2009. *NanoCare. Health related aspects of nanomaterials. Final scientific report;* http://www.nanopartikel.info/cms/lang/en/Projekte/NanoCare/NanoCare-Publikationen.

fluorescent material–shell structure. This allows the study of biokinetics in body fluids and cells due to the possibility of clear and simplified identification. Further on, 12 well-characterized materials will be employed and tested with regard to possible exposure and toxicological effects *in vivo* and *in vitro*. Special focus is on the coating of the materials and how this affects interactions with proteins, the biokinetics, the stability of the agglomerates, and possible health-related effects.

The information gathered and newly obtained within NanoGEM will be combined to derive a first risk estimate for the nanomaterials in view of worker and consumer safety as well as regulatory safety testing. In conclusion, Dr. Kuhlbusch related that major advances from NanoGEM are seen in the areas of nanomaterial release, exposure-related measurement strategies, nanomaterial and biological fluid interaction, biokinetics, new study methods, and health- and risk-related assessments.

Examples of U.S. Efforts: Nanotechnology Research in NIOSH

Vince Castranova, U.S. National Institute for Occupational Safety and Health (NIOSH)

Dr. Vince Castranova spoke about research on toxicological characteristics and workplace safety aspects of nanoparticles that began at NIOSH in 2004. He outlined the 10 critical topic areas in which the NIOSH Nanotechnology Research Center (NTRC) conducts research:[7]

1. Toxicology and Internal Dose
2. Measurement Methods
3. Exposure Assessment
4. Epidemiology and Surveillance
5. Risk Assessment
6. Engineering Controls and Personal Protective Equipment
7. Fire and Explosion Safety
8. Recommendations and Guidance
9. Communication and Information
10. Applications

Dr. Castranova noted that the NTRC has published a number of guidance documents and research reports concerning nanotechnology. These documents include a strategic plan for NIOSH nanotechnology research and a progress report of NTRC activities.[8] Other NTRC documents provide information on approaches to safe handling of nanoparticles in the workplace, interim guidance for medical screening and hazard surveillance for nanotechnology workers, and practical guidance for the nanoparticle emission assessment technique (NEAT). NIOSH has released a Current Intelligence Bulletin giving a recommended exposure limit (REL) for nanostructured TiO_2 and a draft document proposing a REL for carbon nanotubes. In

[7] See http://www.cdc.gov/niosh/topics/nanotech/.

[8] See http://www.cdc.gov/niosh/topics/nanotech/pubs.html, including the NIOSHTIC-2 searchable bibliographic database linked at the bottom of the page.

addition, NIOSH/NTRC offers publications concerning the effectiveness of filter media or local ventilation for controlling nanoparticles, as well as publications concerning the respiratory, cardiovascular, and central nervous system effects of pulmonary exposure to nanoparticles.

Research in Support of Consumer Protection Legislation

Hermann Stamm, Italian Institute for Health and Consumer Protection, EC Joint Research Centre Directorate-General (DG JRC)

Dr. Hermann Stamm's presentation gave an overview of the research needs for nanomaterials in consumer protection legislation, saying two main areas have to be addressed: (1) the safety and risk assessment of nanomaterials to assure their safe use in consumer products, and (2) the detection, quantification, and characterization of nanomaterials in complex matrices in view of labeling requirements, e.g., in the case of cosmetic products or food.

Then Dr. Stamm addressed the questions and needs for further research in these areas. He gave a short overview on current European regulations, where nanomaterials are explicitly considered or may need specific attention. He outlined research and policy support activities of the EU Joint Research Centre in the field of nanomaterials safety, covering also harmonization and standardization activities in international organizations (OECD, ISO). He emphasized the need for international cooperation for the development of harmonized test methods and standards in order to provide relevant data for risk assessors.

EU Industry: Safety Research as an Integral Part of the Industrial Innovation Strategy

Peter Kruger, Bayer

Dr. Peter Kruger explained that innovations along the industrial value chain consisting of research, development, and successful commercialization of products are driven by current challenges of the society. Nanotechnology-based innovations are commonly seen as highly relevant potential options for the most essential challenges, such as energy conversion, energy storage, efficient use of resources, climate protection, mobility, communication and information management, and affordable and efficient health care.

In order to deliver the benefits of nano-based innovations to serve society, Dr. Kruger emphasized that the safety of particular nanomaterials cannot be assumed in their specific intended applications along different stages of their life cycles. Within the chemical industry an intensive product stewardship program has been implemented to ensure the safety of chemical products within their value chains in general.

This product stewardship program is today also applied to nanomaterials and contains several key elements. One element is conduct of studies according to OECD guidelines for nanomaterials to explore, test, and evaluate potential exposure scenarios and biological interactions of a company's nanomaterials/nanoproducts in their intended applications throughout their life cycles to ensure the safety of workers, consumers, and the environment.

This also includes the element of developing special techniques, methodologies, and metrologies for the detection and characterization of nano-objects and nanomaterials.

Another key product stewardship element is a company's participation in publicly funded safety-related projects, with partners from industry and academia combining their broad expertise; this complements company internal activities to create a deeper understanding of general structure–activity/property relationships for specific classes of nanomaterials with respect to their biological interactions and exposure scenarios. The development of highly sophisticated nano-analytics also can be performed within publicly funded projects. Dr. Kruger noted that participation in publicly funded projects generally delivers broader results that would be unaffordable by a single company, and further, it creates greater public confidence in the results because of the participation of a wide variety of partners, such as companies, institutes, scientific organizations, and public authorities.

The element of product stewardship that supports work for globally harmonized standardization (ISO-, OECD-level) ensures that safety standards for the assessment of nanomaterials become comparable worldwide on a long time scale.

The product stewardship element of company participation in highly regarded professional associations helps ensure that companies across value chains develop and apply high-level global safety standards to avoid any type of nano-related incidents as much as possible, keeping also in mind that the poorest performer determines public perception.

Finally, there is the key product stewardship element of communication and dialog with stakeholders from society to explain and discuss potential benefits of nanomaterials; this goes along with the measures undertaken to ensure safety in all stages of the life cycle in intended applications. These elements are essential to create public understanding and acceptance for new materials and their applications.

Dr. Kruger gave the example of the Innovation Alliance Carbon Nanotubes (Inno.CNT; http://www.inno-cnt.de), consisting of 90 partners in 27 projects partly funded by the German government and working on technical and application projects for energy/environment, mobility, lightweight construction, and electronics, and simultaneously taking care of safety issues. The strength of this alliance demonstrates clearly that "safety research is an essential part of the innovation strategy" from the industrial perspective.

U.S. Industry: Defining Research Needs and Crop Protection Products

Wendelyn Jones, CropLife America

Dr. Wendelyn Jones described how nanotechnology has a range of beneficial applications, including in crop protection products, and its adoption could facilitate the development of a new set of tools to support modern agriculture. Crop protection products are effectively regulated under the U.S. Federal Insecticide, Fungicide, and Rodenticide Act to include human and environmental safety considerations. Dr. Jones emphasized the need for science-based proposals and actions by the U.S. EPA to support responsible and innovative product development. She stated that CropLife America and its member companies believe that the benefits of nanotechnology will only be realized if science is the primary driver in regulation.

Dr. Jones described a number of research needs in her talk, including tackling the problem of poor water solubility of hydrophobic chemicals affecting the bioavailability of chemicals, and determining dose metrics for nanotoxicity and whether nano-based crop protection chemicals can cross the blood–brain barrier. Nano-based crop protection products have potential benefits that include greater precision in pesticide/herbicide usage, reduced spray drift and surface runoff, better control/precision in release, reduced amounts needed, more efficient emulsification and encapsulation of active ingredients, and greater stability. She also stated that scientific discussions about environmental, health, and safety questions for nanomaterials should bridge geographies and governments.

U.S. NGO: Focus and Approach in Developing Plans

Carolyn Cairns, U.S. Consumers Union

Ms. Carolyn Cairns' presentation outlined the consumer perspective on the research needs to assess risks from nano-engineered materials. Her remarks emphasized the urgency of coordinating research around the central objective of charactering exposures associated with actual nanomaterials in or entering the chain of commerce. She discussed results from Consumer Reports' tests identifying nanoscale minerals in leading brands of sunscreens, as well as the need to develop analytical methods capable of identifying all other commercialized nanomaterials in the full set of product and biological matrices in which they are likely to be found.

3. Data Needs for Regulatory Decision Making

General Components of Regulatory Decision Making and Data Needs

Phil Sayre, U.S. Environmental Protection Agency

Dr. Phil Sayre of the U.S. EPA's Office of Pollution Prevention and Toxics (OPPT) reviewed U.S. "Experiences with Assessing the Risks of Nanomaterials, and Implications for Research" to set the stage for two subsequent breakout sessions on data needs for regulatory decision making. His talk described some of the data and data gaps encountered by OPPT and other U.S. regulatory agencies in order to indicate some areas in need of further research that could be relevant to U.S.–EU collaborative efforts. He addressed the regulatory authorities and associated data needs under some of EPA's own authorities and those of the U.S. Food and Drug Administration (FDA), Consumer Product Safety Commission (CPSC), Occupational Safety and Health Administration (OSHA), and Department of Agriculture (USDA).

Data needs are in part driven by the types of nanomaterials seen to date. With this in mind, Dr. Sayre noted that for industrial chemicals, as an example, over 100 total submissions have been reviewed under the Toxic Substances Control Act; approximately half of these submissions involved carbon-based nanomaterials, such as carbon nanotubes and nanofibers, with the next major class of materials being metal oxides and metals.[9] Key to many decisions on potential risks to human health and the environment is an accurate description of the nanomaterial under review: its physicochemical properties are often pivotal to reaching conclusions about potential hazards and fate. EPA reviewed its guidelines for ecotoxicity in 2009 and found that methods and approaches for preparing exposure media, as well as for measuring and characterizing nanomaterials, should be further developed.[10]

While ecotoxicity data and health effects data are still scarce, Dr. Sayre described important trends that are emerging on the overall shorter-term ecotoxicity of nanomaterials, and some chronic ecotoxicity data that had recently been published. He observed that health effects data on some nanomaterials indicate higher concerns for pulmonary effects, and subchronic inhalation toxicity data via this route are emerging, at least for carbon nanotubes. Exposure data on airborne concentrations of nanomaterials in the workplace are still very limited, and the same is true of general population and environmental exposures. However, there are new data on general population exposures to cerium(IV) oxide (ceria) and on consumer exposures to spray-applied nanomaterials that are of interest. Better effects and exposure data will lead to an increased ability to perform quantitative risk assessments. Longer-term research efforts of interest include the efforts of EPA and FDA on high-throughput toxicity screening of nanomaterials, European efforts to predict protein corona impacts on biodistribution and toxicity, and efforts to use category–activity and structure–activity relationship approaches to predict toxicity.

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[9] Sayre, P., S. Prothero, and J. Alwood, Nanomaterial risk assessment and management experiences related to worker health under the Toxic Substances Control Act. J . Occup. and Environ. Med., 2011. 53(6 Supplement): S98–S102.

[10] U.S. Environmental Protection Agency. *Review of OECD/OPPTS-harmonized and OPPTS ecotoxicity test guidelines for their applicability to manufactured nanomaterials,* 2009; http://nepis.epa.gov/Adobe/PDF/P100CXC2.pdf.

Given this, the charge to the workshop breakout groups was to consider Dr. Sayre's and other plenary presentations and identify the top three near–term regulatory challenges and data gaps to address these challenges; also sought were suggestions for longer-term research needs.

Breakout 1: Human Health Data Needs

***Chair*: Michael Riediker, Centre Hospitalier Universitaire Vaudois**
***Rapporteur*: Wendelyn Jones, CropLife America**

Introductory Talks

Regulatory Challenges and Data Needs: Work under the OECD Sponsorship Programme, EU Future Plans and International Cooperation Settings

Tom van Teunenbroek, The Netherlands Ministry of Infrastructure and the Environment

Dr. Tom van Teunenbroek is a nanomaterials research and policy coordinator and a country representative to the OECD WPMN. His talk, entitled "Data Needs and Research Strategy (for Nanomaterials)," summarized the next steps in the OECD WPMN process for the assessment of nanomaterials' effects and fate, and the Netherlands' roles in this process. The OECD WPMN has a number of activities underway and is now entering the second phase of the OECD Sponsorship Programme, which in part consists of testing nanomaterials using OECD protocols. The Netherlands, in conjunction with Germany, has organized three workshops that have included considerations for this next phase of the Sponsorship Programme. Recognized at all three workshops have been the importance of data fulfilling regulatory purposes; the heterogeneity of nanomaterials; the challenges of sample preparation and dosimetry; and the lack of absorption, distribution, metabolism, and excretion (ADME) data and methods. The next phase of the Programme should be based on a thorough understanding of Phase 1 results, and any further reporting should both be in a standardized format and meet clear expectations for deliverables.

To that end, the Netherlands was set to host a meeting on Phase 1 Inhalation Toxicity results and implications in October 2011. Phase 2 should also target development of an intelligent testing strategy that decreases cost, time, and animal usage to obtain base-set information; such an effort could begin with correlating nanomaterial physicochemical properties and *in vitro* and *in vivo* protocols for inhalation toxicity. Standardized exposure scenarios should be developed for nanomaterials. Finally, Dr. Van Teunenbroek described the lack of chronic toxicity data and personal monitoring data for workers that are also needed for complete risk assessments of nanomaterials, although these sorts of data may not fall immediately under the scope of Phase 2 efforts. For OECD work and for similar multinational research efforts, significant funding and cooperative work is needed, based on sound expert judgments from area experts and clear plans for implementation.

Human and Safety Data Needs

Andre Nel, University of California, Los Angeles

Prof. Andre Nel provided his perspective on the top four regulatory challenges in the field of inhalation toxicology: (1) validated and widely acceptable *in vitro* and *in vivo* screening platforms for regulatory decision making on inhalable ENMs, (2) dosimetry calculations that take into consideration hazardous material properties and also are useful for setting exposure limits, (3) personal exposure assessment, and (4) implementation of risk reduction strategies while knowledge-generation in points 1–3 is taking place. He specifically highlighted barriers to validating and harmonizing *in vitro* and *in vivo* screening platforms for regulatory decision making, including the complexity of the large number of ENMs and their properties, and the logistics, cost, and validation of testing. A stepwise approach to the formulation of nano-regulatory policy would include evidence-based decision making and sustainability decision making in future stages. He noted that the report *Nanotechnology Research Directions for Societal Needs in 2020* effectively summarizes the state of nanoEHS research in 2010/2011:[11]

> *There is greater recognition [compared to ten years ago] of the importance of nanotechnology-related environmental, health, and safety issues for the first generation of nanotechnology products, and of ethical, legal, and social implications issues. Considerable attention is now being paid to building physico-chemical-biological understanding, regulatory challenges for specific nanomaterials, governance methods under conditions of uncertainty and knowledge gaps, risk assessment frameworks, and life cycle analysis based on expert judgment, use of voluntary codes, and incorporation of safety considerations into the design and production stages of new nano-enabled products. Increased attention includes modes of public participation in decision making and overall anticipatory governance with respect to nanotechnology.*

Summary of Participant Comments

The breakout discussion focused on regulatory challenges and associated data and research needs. The topics that emerged as central to regulatory challenges were material characterization, reference materials, endpoint selection, exposure considerations, and the need for integrated, complete health-effects databases that are couched in the broader context of EHS datasets.

Participants identified material characterization challenges that could be addressed in the short term, including an adequate description of physicochemical properties, material impurities, and the sample preparation methods (including expiration dates and/or time stamps) that would allow independent verification of results. For example, a standardized set of information for carbon nanotubes would allow researchers to effectively compare findings and expand upon each others' scientific work. This links closely to the need for reference materials because they can provide benchmarks for health effects studies on untested nanomaterials in that their physicochemical characteristics are known.

[11] Roco, M.C., C.A. Mirkin, and M.C. Hersam, 2011, *Nanotechnology research directions for societal needs in 2020: Retrospective and outlook* (Dordrecht: Springer; also available online at http://wtec.org/nano2), xviii.

Additionally, participants felt a common nomenclature should be adopted for nanomaterials to aid comparison of results from different studies and from different laboratories. The common nomenclature can serve as a communication tool, too. One idea proposed was development of a "Nano Material Safety Data Sheet (NMSDS)" to allow researchers to more readily characterize and compare nanomaterials. In the interim, as dialogues are continuing, the development of a "minimum information about a microarray experiment" (MIAME)-type standard would serve to facilitate the harmonization of science studies. A MIAME-type standard would help streamline the presentation of divergent science reports and promote alignment among researchers. This would directly facilitate the development of validated screening methods and harmonized protocols for characterizing and understanding the biological impact of nanomaterials.

There was a clear recognition that positive and negative experimental controls need to be developed—specifically for nanomaterials—that can be used in various toxicology assays. These controls would help interpret across data sets and eventually allow benchmarking.

Endpoint selection was noted by several participants as another area where challenges can be met in the next two to three years. With nanosafety research, there is a need to ensure that the correct toxicology test paradigm is selected. It is further hoped that by selecting the correct paradigm, the research from various sources could then allow grouping around a specific endpoint. For example, with regard to inhalation toxicity, knowledge from generalized particulate matter studies could help inform biological "consequences" of both acute and chronic exposure. Through targeted research, it may be possible to *a priori* know when size, and not the chemical makeup, of a nanomaterial determines the EHS profile. This knowledge would facilitate predictive toxicological approaches that best utilize *in vitro* and *in vivo* testing.

Exposure should be a factor in setting priorities over the next few years, both in terms of driving risk concerns (there is no risk if there is no exposure) and testing materials that are most representative of what humans are exposed to in the workplace or elsewhere in the material's life cycle. With nanomaterials, the traditional toxicity testing paradigm in mg/kg/day may be replaced by different dose metrics that better reflect the distribution of materials being researched. In this way, the most efficient expenditures will be made for purposes of testing. This could contribute to realistic risk assessment conclusions for the material.

The breakout group also discussed data needs. Much of the discussion focused on how to get and organize data and other information sources. Participants recognized the power of the European Registration, Evaluation, Authorisation and Restriction of Chemical substances (REACH) database, and there was discussion around how to expand access to that information. A nano-registry effort by the U.S. National Institute of Environmental Health Sciences and the U.S. National Institute of Biomedical Imaging and Bioengineering could lead to integrated assessments. However, building interoperability into a database to ensure appropriate information archiving and to avoid duplicative filings is a significant knowledge management challenge.

To observe patterns that lead to more efficient and effective research and regulatory decision making, raw data is needed. The raw data allows consideration of whether there is sufficient harmony between data collection and approaches to draw broader conclusions. The group discussed how to encourage academics to publish their methods, "no response" results, and

"positive" results. There was clear recognition that negative-response-effects study results are very hard to publish, and this can lead to a publication bias in database information. With proper curation, it may be possible to include studies not published in peer-reviewed journals.

Based on the breadth of nanoEHS research, breakout session participants recognized a need to link environmental fate and transport and ecotoxicology with human health. Specifically, some participants noted the need to consider chronic versus acute toxicity and to factor in systemic responses among ecotoxicology model organisms and mammalian toxicology model organisms when considering biological pathways.

In summary, the Human Health Data Needs breakout groups engaged in an active discussion about environmental, health, and safety questions for nanotechnology-enabled products and identified efforts that would leverage resources both in the United States and the European Union by developing

- Predictive toxicological approaches that utilize the correct balance between *in vitro* and *in vivo* testing
- Validated screening methods and harmonized protocols
- Appropriate exposure metrics

Breakout 2: Environment Data Needs

***Chair*: Pedro Alvarez, Rice University**
***Rapporteur*: Flemming Cassee, The Netherlands National Institute for Public Health and the Environment**

Introductory Talks

Nano-Sized Particles in the Environment: Fate, Transport, and Potential Impacts to Ecosystem Health

Pedro Alvarez, Rice University (U.S.)

Prof. Pedro Alvarez opened his talk with the observation that publications on the EHS implications of nanotechnology are only a small fraction of all nanotechnology-related publications, emphasizing the need to be more proactive about risk assessment. He explained how the antimicrobial activity of nanoparticles can be used in risk analysis because bacteria carry out many ecosystem services and because antibacterial activity may be a fast-screening indicator of toxicity to higher-level organisms. However, assessing the hazards of nanomaterials is complicated by the fact that the mechanisms by which nanoparticles might harm cells are quite diverse. Additionally, most toxicological risk assessment studies are carried out on unmodified nanoparticles, which is not a realistic strategy because nanoparticles can have multiple fates in the environment: degradation and transformation, physical attenuation, surface modification, and persistence. Prof. Alvarez described in detail the effects of a surface coating of natural organic matter on fullerenes. As an additional example, he also noted the difference between bioavailability and toxicity in silver nanoparticles. Prof. Alvarez emphasized the fact that risk is a product of hazard and exposure, and he closed by presenting a matrix of

research priorities, which highlighted the need for metrology and analytical methods, elucidation of structure–activity relationships, and predictive models of release and exposure scenarios.

Environmental Behavior and Effects of Nanoparticles on Organisms: Research and Data Needs for Regulatory Decision Making

Richard Handy, University of Plymouth (EU)

Prof. Richard Handy's presentation was divided into three sections: environmental chemistry of nanoparticles; biological effects of nanoparticles; and regulatory needs for ecotoxicology. Each section of the talk reviewed key work done in the field and provided a list of data needs or key findings on the topic. On the subject of the fate and behavior of nanoparticles in the environment, Prof. Handy described multiple research needs and knowledge gaps, including user-friendly predictive modeling of particles in experimental media, increased detection limits, and measured rates of delivery for co-contaminants. Knowledge gaps on the biological effects of nanoparticles range from the effects of nanoparticles on specific body systems, such as the nervous system, to food chain effects. Prof. Handy closed his talk by describing a list of findings from several recent workshops and proposing a list of practical solutions to improve experimental validity.

Summary of Participant Comments

The discussion that followed focused on issues that that can be met within a few years' time. This resulted in a list of **regulatory challenges** for environmental exposures, fate, and effects:

- *Integration of existing information and action based on recommendations*: Several research recommendation reports have been published, and it is time that regulators start combining and prioritizing this information.
- *Source characterization,* including dynamics (fluxes): Where do nanomaterials enter environmental media, and what is the rate and concentration?
- *Exposure*: Where can we expect (the highest) exposures and at what levels and forms, including interactions with other (bio)substances?
- *Bioavailability*: What is the life cycle of a given nanomaterial; is there evidence for bioaccumulation; and can this lead to secondary human exposure?
- *Susceptibility*: What are the most sensitive receptors?
- *Comparability*: Where can we group nanomaterials using methods such as quantitative structure–activity relationship (QSAR)? This may be important for setting standards.
- *Metrology*: How do we detect engineered nanoparticles among the many "natural" nanoparticles?

Based on the list above, three issues were further discussed with respect to data and research needs:

- **Source characterization** including dynamics (fluxes):

  Data needs: rates of release, inventory of use, information on value chains, and metrics related to sources

  Research needs: informatics (database development), market research (social science), and actual measurements

- **Susceptibility**:

  Data needs: ascertain the most sensitive receptors (species, ecosystems, life stages)

  Research needs: determine appropriate endpoints that are valid over a wide range of species, species sensitivity distributions and what is a good set, and standardization of methodology and reference materials

- **Integration** of existing information and actions based on recommendations:

  Data needs: reports from technical workshops, etc.; also use "negative" information

  Research needs: gather information, identify common agreement, and fuse information into global databases or unify current databases

Regulatory Panel Discussion on Comments from the Two Breakout Groups on Health and Environment

Chair: Tom van Teunenbroek, The Netherlands Ministry of Infrastructure and the Environment

EU: Ken Dawson (SCENIHR), Andrej Kobe (DG ENV), Hermann Stamm (DG JRC) Alexander Pogany (BMVIT)

U.S.: Phil Sayre (EPA), Bill Jordan (EPA), Carlos Peña (FDA), Treye Thomas (CPSC), Kerry Dearfield (USDA)

The panel discussion began with a summary of the findings from the breakout session on Human Health Data Needs. In addition to the regulatory challenges emphasized in that breakout session, the panelists described additional challenges in performing exposure assessments because it may not be known if and to what extent nanomaterials are released from products. The panelists agreed with the data needs that were identified in the breakout session, and they highlighted additional needs for coordinated databases between the United States and the European Union and for studies on the absorption and bioavailability of nanomaterials. They identified the highest priorities to advance research in this field:

- Standardizing sample preparation
- Measuring relevant exposure
- Evaluating the effects of the matrix material (i.e., is the material that is tested in the lab the same as the material in the product)

For environmental research, the panelists supported the regulatory and data needs that were proposed in the breakout session. Additionally, they suggested a need to understand how the coating of a nanomaterial affects the transportation and fate of that material.

Shared research goals between human health and the environment were identified: improved nanomaterial characterization, simulation of nanoparticle release scenarios, and implementation of standardized reference materials and uniform metrics. The panelists emphasized the need to prioritize research toward these crosscutting goals and the need for collaboration among experts in human health and the environment. Finally, it was noted that enhanced communication among industry, researchers, and policymakers is essential for progress to be made.

4. Tackling the Challenges of Producing Reliable, Reproducible Data for Nanomaterials Assessment and Risk Management

Testing and Risk Assessment of Nanomaterials

Janeck J. Scott-Fordsmand, Aarhus University (EU)

Prof. Janeck Scott-Fordsmand introduced the data breakout sessions by discussing the current challenges in the testing and risk assessment of nanomaterials, especially with respect to producing reliable and reproducible data. He emphasized the need to distinguish more useful information from less useful information and to standardize while keeping relevance in sight. His talk focused on a standard ecotoxicity test and highlighted currently unresolved issues and requirements. He identified requirements for

- Reference nanomaterials, possibly "group-specific"
- Easily available, highly (and reliably) characterized nanomaterials covering groups
- Standard characterization methods (before and during a test) easily available for routine laboratory testing
- Consideration of test design based on specific nanomaterial characteristics, e.g., surface area
- Standard protocols (validated and with criteria) on how to add nanomaterials to the media
- Good characterization in regard to bioaccumulation, and second-generation toxicity studies
- Consideration of additional effect parameters; current general ecotoxicity effect measures (mortality, growth, and reproduction) are valid, but additional measures must be considered to account for different modes of nanomaterial action and to provide information for future risk assessment

Prof. Scott-Fordsmand stressed additional conclusions about the state of the science: (1) effects studies are emerging; (2) these studies are still scattered, making comparison difficult; (3) quantitative exposure characterization is missing; (4) expert collaboration is presently necessary for characterization; (5) standardization is important, with definition of acceptable ranges; and (6) information flow is vital.

Breakout Sessions on Human Health and Ecological Effects

Following Prof. Scott-Fordsmand's talk, the meeting participants were divided into six breakout groups, three groups under human health and three under ecological effects. Each breakout group addressed one of the following six questions:

Questions on Human Health

1. When do unique properties—with risk assessment implications—arise for specific nanomaterials?
2. How do surface modifications and chemical transformations affect toxicity?

3. What metrics are most scientifically accurate when relating dose to response in toxicity assessments? And how are dose–response data best extended to determining occupational exposure limits and environmentally relevant concentrations?

Questions on Exposure and Fate of Nanoparticles in the Workplace and Environment

4. How relevant are model nanoparticles to understanding exposure in the workplace? How relevant are they to recommending industrial hygiene practices?
5. What are the critical parameters and data needs for understanding the behavior of nanoparticles in environmental media?
6. What are the critical parameters and data needs relevant to understanding the behavior of nanoparticles in consumer and general population exposures?

Breakout 1: When do Unique Properties—with Risk Assessment Implications—Arise for Specific Nanomaterials?

***Chair*: Robert Hurt, Brown University (U.S.)**
***Chair*: Nigel Walker, U.S. National Institute of Environmental Health Sciences**

***Rapporteur*: Bengt Fadeel, Karolinska Institutet (EU)**
***Rapporteur*: Harry Bushong, NanoTox, Inc. (U.S.)**

Introductory Talks

A Risk-Forecasting Framework for Nanomaterials

Mark Wiesner, Duke University (U.S.)

Prof. Mark Wiesner gave a presentation entitled "A Risk Forecasting Framework for Nanomaterials." He briefly introduced the Center for the Environmental Implications of Nanotechnology, a U.S. center funded by the National Science Foundation and EPA, which also has links to European research in the field of nanosafety through the FP7 project "Risk Assessment of Engineered Nanoparticles." Prof. Wiesner presented the desirable elements of a risk forecasting framework and then focused on the issues of novel properties of nanomaterials. He argued that evidence for novel size-dependent properties alone, rather than a specific particle size, should be the primary criterion in any definition of nanoparticles when making decisions about their regulation for environmental, health, and safety reasons.[12] In other words, nanoparticles should fulfill two criteria; they should be small and have novel properties.

Carbon-Based Nanoparticles and Health Implications

Dominique Lison, Université Catholique de Louvain, Brussels (EU)

Prof. Dominique Lison discussed "Surface Defects and Respiratory Toxicity of Multi-Walled Carbon Nanotubes." The starting point for his presentation was the publication by Muller et al.

[12] Auffan, M., et al. Towards a definition of inorganic nanoparticles from an environmental, health and safety perspective. *Nat. Nanotechnol*. 2009, 4:634–641.

in 2005[13] in which respiratory toxicity of multi-walled carbon nanotubes was assessed. The central thesis of the presentation was that different material properties may drive different toxicities (of the same nanomaterial). For instance, the presence of metal impurities or the occurrence of structural defects may drive inflammation and granuloma formation following exposure to carbon nanotubes via the airways, while other features, including aspect ratios of the nanotubes, may be associated with genotoxicity and carcinogenicity.[14,15,16,17]

Summary of Participant Comments

The discussions that followed focused on how novel properties should be defined and understood and also on the possible distinction among novel intrinsic properties of nanoparticles versus novel behaviors of nanoparticles in a specific biological or environmental context. Some suggestions on how to move forward were also expressed, although the potential for other options was acknowledged.

With regard to how novel properties should be defined, the following views and questions were expressed:

- What are novel properties, and should we focus exclusively on them for purposes of determining their potential risks?
  - Do we need to care whether material properties are "novel" versus simply whether toxicological properties of concern arise?
  - A novel property should be discontinuous/nonscalable, not predicted by simple extrapolation by size (i.e., high surface area).
  - Should a property be regarded as novel only if it is quantitatively different, such as enhanced surface reactivity, or must there be wholly new effects not seen before?
- Novel properties can be categorized into two groups:
  - Properties that are intrinsic to the particle itself, such as a material property
  - Properties that are "contextual" relative to conventional materials; these properties can arise in an environmental or a biological matrix:
    - exposure or transformation in environmental media
    - translocation within an organism or cell and toxicity that are modified relative to conventional (non-nano) materials
- In many cases, the biological toxicity pathways of concern are not new but rather are being activated in a new way by nanoparticles. Therefore, focus should not be exclusively on new

[13] Muller, J., et al. Respiratory toxicity of multi-wall carbon nanotubes. *Toxicol. Appl. Pharmacol*. 2005, 207:221–231.

[14] Poland, C.A., et al. Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study. *Nat. Nanotechnol*. 2008, 3:423–428.

[15] Fenoglio, I., et al. Structural defects play a major role in the acute lung toxicity of multiwall carbon nanotubes: Physicochemical aspects. *Chem. Res. Toxicol*. 2008, 9:1690–1697.

[16] Muller, J., et al. Structural defects play a major role in the acute lung toxicity of multiwall carbon nanotubes: Toxicological aspects. *Chem. Res. Toxicol*. 2008, 21 (9):1698–1705.

[17] Muller, J. et al. Absence of carcinogenic response to multiwall carbon nanotubes in a 2-year bioassay in the peritoneal cavity of the rat.*Toxicol. Sci*. 2009, 110:442–448.

toxicity pathways because most cases of concern thus far deal with known toxicity pathways triggered in a new way.

- How do we design *out* toxic properties or manage risk if the case in question is deemed not to involve a "novel" property? Will an exclusive focus on novel properties cause us to overlook important public health issues involving nanotechnology?

With regard to the implications for risk assessment and regulation of nanomaterials, the following views were expressed:

- A different risk assessment approach is needed, e.g., should our dose metric be based on mass or surface area for some nanomaterials?
- How can high-throughput screening be useful to categorize nanomaterials, and how should appropriate *in vitro* tests be selected to assess relevant endpoints?
- How do we identify these novel/specific physico-chemical properties and their correlation to toxicity?
- Can we use the concept of "novel properties" to group nanomaterials for more rational risk assessment and regulation?
- How could materials be grouped based on novel properties that could potentially merit regulation?
- How could database(s) of nanomaterials and data related to their novel properties be developed and maintained?

Finally, mechanisms to address these questions in the global research community were addressed:

- The research community could benefit from sets of nanoparticles produced by material scientists with systematic variations in one property while holding other properties constant—a significant challenge in many cases.
- Efforts should be made to initiate online, Internet-based discussion of models and concepts to accelerate scientific interaction and to set up a method for a curated discussion and exchange of knowledge.
- Focus on novel properties, novel behaviors, or size should be considered. Can consensus be reached regarding which (set of) novel properties are needed for risk assessment of nanomaterials?

A general observation was that the phrase "novel properties" means different things depending on the context or scientific discipline. Material scientists tended to focus on intrinsic novel properties while the biologists and toxicologists suggested that new biological behavior could also be considered as a novel property if linked to the nanoscale size of the particle.

Breakout 2: How do Surface Modifications and Chemical Transformations Affect Toxicity?

***Chair*: Jay West, American Chemistry Council**
***Rapporteur*: Adrienne Sips, The Netherlands National Institute for Public Health and Environment**

Introductory Talks

The Role of the Nanoparticle Surface in Interactions with Living Organisms
Ken Dawson, University College Dublin (EU)

Environment: Ecotoxicity and Transformations
Steve Klaine, Clemson University (U.S.)

Prof. Kenneth Dawson and Prof. Steve Klaine are both experts in the field of surface modifications of nanoparticles and how that might affect, respectively, ecotoxicity or human toxicity. Although coming from different directions, their presentations addressed similar issues. They made it clear that pristine particles, whether aggregated/agglomerated or not, are unlikely to exist in the environment or in the body. Proteins or organic matter tend to cover the surface of particles. This is not a static situation but a dynamic process in which the surface is modified over time. A variety of molecules can exchange quickly or slowly on and off the surface.

These surface dynamics raise the question, "What is the biological identity of a particle?" The question is extremely relevant to address, as it is reasonable to assume that it affects dispersion in (testing) media, transport across biological barriers, uptake in cells and tissues, and interactions with living systems. No straightforward predictions can be made as to whether surface modifications affect toxicity in a positive or a negative way. Prof. Klaine demonstrated that coated carbon nanotubes are more bioavailable than uncoated CNTs, but there are also cases where the opposite has been observed. He hypothesized that organisms might "see" only the natural organic matter (comparable to proteins in human body) and not the CNTs. Further, natural organic matter–modified CNTs are more stable in aqueous media, resulting in longer exposures for pelagic organisms that may make them more amenable to absorption.

The surface of a nanoparticle changes during the life cycle of the particle. This phenomenon is called "aging" or "surface history." This history tells about the various identities of the particle in various stages of its life cycle. At this moment only limited possibilities are available for identifying such surface history.

Prof. Dawson concluded his presentation with a few key messages:

- Overall, the acute hazards of nanoparticles seem to be less than expected
- The role of pristine particles might be not so relevant for exposure (both external and internal)
- Information about the "real" *in situ* identity of nanoparticles is fundamental for hazard classification

- Surface adsorbed species give information about the life cycle and their presence in certain environmental compartments
- Research should be framed to evaluate hypotheses by characterizing those things that are essential for assessing the risks
- New tools might be needed to address the questions on surface modifications and their impact on risk assessment

Summary of Participant Comments

The group's discussion made clear that surface and surface history of nanoparticles are important for understanding their behavior and toxicity. Multidisciplinary approaches will be essential: *surface chemists* provide insights into the likelihood of certain chemical reactions and factors that will affect the surface; *analytical chemists* obtain information on the surface history; *toxicokineticists* clarify the relationship between surface history and absorption, distribution, metabolism, excretion, and toxicity; and *toxicologists* determine the interactions of particles with biological systems. In the end, the issue of surface modifications will probably need specific attention in regulatory toxicology and accompanying risk assessment.

Surfaces are dynamic systems, and it is still unclear how to deal with these dynamic systems in regulatory toxicology and risk assessment. Unresolved issues include how to deal with a consistent nomenclature for the surface; how to deal with layered particles; how to characterize the surface *in situ*; whether suitable techniques are available; and whether reference fluids and reference particles can help to structure the search, giving insight on the impact of surface modifications on toxicity.

The speakers and the attendees of this session agreed that there is solid evidence for the importance of surface and surface history in toxicity testing of nanoparticles. This, however, does not mean that the fate of nanoparticles is well understood in all cases. For example, in some situations proteins are stripped off of the nanoparticles inside lysosomes, but not always.

We know now that there is a strong indication that the surface of pristine particles might not be highly relevant for predicting behavior and toxicity. The surface of the pristine particle and the route of exposure through the environment or the body determine the initial interactions with proteins or other macromolecules and thereby determine further surface history. Understanding coatings and coating dynamics will contribute to more robust assessment of exposure (including kinetics/fate). The role of surface composition in exposure metrics should be investigated.

The role of surface modifications and transformations should receive more attention because of the potential for surface modifications to affect human and environmental health risks of nanomaterials. The topic will be complex. For that reason U.S.–EU collaboration on how to put available information in perspective relative to risk assessment might lead to more purposeful approaches to address analytical needs, risk assessment approaches, and regulatory issues that are in line with these scientific questions.

Breakout 3: What Metrics Are Most Scientifically Accurate When Relating Dose to Response in Toxicity Assessments? How are Dose–Response Data Best Extended to Determining Occupational Exposure Limits and Environmentally Relevant Concentrations?

***Chair*: Rafi Korenstein, Tel Aviv University (EU)**
***Rapporteur*: David Warheit, DuPont (U.S.)**

Introductory Talks

***In Vitro–In Vivo* Correlations of Dose-and-Response Metrics: Concepts for Occupational Exposure Limit (OEL) Extrapolation**
Günter Oberdörster, University of Rochester (U.S.)

Environment: The Effects of Carbon Nanoparticles in Aquatic Species—the Importance of Testing Across Populations and Life Cycles
Teresa Fernandes, Napier University (EU)

The session commenced with two informative and short presentations that served to stimulate the subsequent discussion. Prof. Gunter Oberdörster focused on the topic of health-effects-related dose metrics. Prof. Teresa Fernandes focused on environmental issues in her presentation.

The breakout group for Session 3 was challenged to address the following questions:

- What metrics are most scientifically accurate when relating dose to response in toxicity assessments? How are dose–response data best extended toward determining occupational exposure limits and environmentally relevant concentrations?
- Additional topics for suggested discussion (if time permitted) included
  - Implications of the responses for risk assessment, regulatory data needs, and research and technology development
  - Mechanisms to achieve consensus on this question in the global research community

Summary of Participant Comments

Following the presentations, there was a lively and wide-ranging discussion with the goal of identifying the best dose metrics for relating dose to response in toxicity assessments as well as for determining occupational exposure limits and environmentally relevant concentrations. However, it was noted during the discussion that, given current practical and scientific limitations on the accurate measurement of dose characteristics, no single dose metric should be preeminent and that all three currently accepted metrics should be included and reported when possible. The three dose metrics that are commonly utilized for nanotoxicity and nanoparticle exposure evaluations are mass, particle number, and particle surface area. There are not many studies to date, particularly ones carried out in environmental media, where a systematic assessment of these questions has been attempted. However, some studies have indicated that for certain particle types and media, results obtained are different when data are

assessed on a mass–dose basis and a surface area basis. However, often the surface area assessments carried out on dry particles use only the Brunauer-Emmett-Teller (BET) method. Similarly, it is unclear how particle numbers should and could be assessed given the tendency of particles to aggregate or agglomerate in media.

Additional suggested developmental research goals included the determination of biologically available surface area (i.e., surface area of particles or target tissues) and the need to comprehensively characterize the physicochemical characteristics of the nanomaterial being tested or measured in order to correlate the dose with any measured endpoints. Moreover, to better develop accurate dose metrics, it will be necessary to identify specific modes of actions and biokinetics, and these are likely to be different for each particle type, route of exposure, and dose. A final suggestion was that to better understand dose metrics related to environmental fate and human health indices, it will be necessary to gain insights into measurements of the surface area of particles in complex environments, for example in environmental media.

Breakout Sessions on Measuring Exposures and Fate of Nanoparticles in the Workplace and the Environment

Breakout sessions 4–6 covered questions related to measuring exposures and fate of nanoparticles in the workplace and the environment, including behavior of nanoparticles in consumer and general population exposures.

Breakout 4: How Relevant are Model Nanoparticles to Understanding Exposure in the Workplace? How Relevant are they to Recommending Industrial Hygiene Practices?

***Chair*: Chuck Geraci, U.S. National Institute for Occupational Safety and Health**
***Rapporteur*: Enrico Bergamaschi, University of Parma (EU)**

Introductory Talks

In his introductory remarks, Dr. Chuck Geraci addressed the session's topic and emphasized some critical issues surrounding the following questions: How relevant are model NPs to understanding exposure in the workplace, and how relevant are they to recommending industrial hygiene practices?

Considering the different exposure scenarios, it should be recognized that ENMs show a heterogeneous behavior along their life cycles. There is a continuum of changes, usually substantial, occurring to particles during synthesis, development, manufacture, use, and disposal. In every step, ENMs can change size (e.g., due to agglomeration), shape, functionalities, or surface characteristics due to incorporation into a formulation or matrix, and those changes can affect the exposure assessment methodology.

For many purposes related to the exposure assessment and characterization, there is the need to use reference material(s), and model NPs belong to the hierarchy of such reference materials.

Use of Model Nanoparticles to Understand Exposures in the Workplace

Laura Hodson, U.S. National Institute for Occupational Safety and Health

Ms. Laura Hodson began by reminding the group that the assessment of exposure to ENMs in the workplace poses specific challenges, and that harmonized protocols for exposure assessment and material characterization (sample collection, handling, and analysis, e.g., evaluation of chemical composition using energy-dispersive spectroscopy) are needed. These challenges will require the use of well-characterized model NPs.

Ms. Hodson then presented a case study of titanium dioxide to demonstrate how model NPs can be used for understanding workplace exposures. In the case study, TiO_2 was used for instrument evaluations and for animal inhalation studies aimed at understanding how and to what extent nanoparticles are delivered to the target organs. The instrumentation was then used in the workplace to determine exposure potentials. All of the data was subsequently used in a risk assessment leading up to proposed REL of 2.4 mg/m^3 for fine TiO_2 and 0.3 mg/m^3 for ultrafine TiO_2. The use of the model NPs can ensure compliance with the RELs and aid in assessing the effectiveness of control measures implemented. Ms. Hodson shared a list of model NPs currently available in the United States and European Union (http://www.nano-refmat.bam.de/en/), including reference materials and standard reference materials issued or under development by the U.S. National Institute for Standards and Technology (NIST).

Critical Parameters/Data Needs for Exposure Assessment in Occupational and Environmental Scenarios

Rob Aitken, Institute of Occupational Medicine (EU)

Dr. Rob Aitken discussed the most critical parameters and data needs to be considered for exposure assessment in occupational and environmental scenarios. He noted that there are several reasons for making measurements: identification of sources of nanoparticle emissions, quantification of release, assessment of efficiency and reliability of control measures for exposure containment, ensuring compliance with OELs, gathering of data for epidemiological studies, etc. However, a key factor in exposure assessment data is that exposure relies on not only the detection of airborne concentrations of nano-objects but also requires information on magnitude, route, frequency, duration, spatial distribution, and control measures. When measuring, it is important to carefully consider the characteristics of exposure, choose the appropriate metric, take into account the background aerosols and distinguish them from other nano-objects, and adopt different strategies when measuring high-aspect-ratio nanomaterials, nanofibers, and free nanoparticles. The field studies carried out to date have addressed the measurements of a limited range of nanomaterials (e.g., metal oxides) and tasks (synthesis and handling) and have been carried out mainly at laboratory facilities where it is relatively easy to control exposure determinants. For complex aerosols, some form of image analysis (e.g., electron or optical microscopy) is critical in identifying particles of interest.

Possible realistic applications of model NPs in the current practice of industrial hygiene can be summarized as follows:

- Development and calibration of instruments for air (Aerosol dispersion)
- Development and calibration of instruments for water (Liquid dispersion)
- Efficacy of control measures, e.g., respirators, filters (Aerosol dispersion)
- Efficacy of control measures, e.g., gloves (Powder or liquid dispersion)
- Simulation of work activities (Power, aerosol, or liquid dispersion)
- Dustiness testing (Powder)
- Release from composites (Surface coating or solid dispersion in composite)
- Interactions with "background" particles (Aerosol or liquid dispersion)
- Relationship between metrics (Aerosol or liquid dispersion)
- Transfer between compartments (Aerosol or liquid dispersion)
- Validation of models (Aerosol or liquid dispersion)

Summary of Participant Comments

After a constructive discussion, the session participants noted that model NPs can

- Be representative of the life cycle of nanoproducts, usually characterized by continuum of increasing complexity
- Be reliably used to model and refine the release scenario, providing a tool for standardizing the exposure assessment (that is, to "test the test," e.g., by generating a "standard aerosol" kit for measurements in different situations)
- Help to harmonize measurement approaches by providing reference and/or well-characterized nanomaterials, to assess the instrumental performance and to conduct laboratory-scale experiments that mimic workplace exposure
- Assist in discrimination of ENM exposure from environmental particles ("background"), since their identification can be easier
- Help to identify appropriate dose metrics (e.g., recognizing new metric parameters such as their *reactivity*)
- Facilitate the conducting of round-robin workplace exposure measurements

The participants recognized that responses for risk assessment and regulatory purposes should be supported by scientific evidence and, ideally, harmonization in risk assessment procedures that, at present, are lacking. In spite of a number of uncertainties about exposure, model NPs could facilitate the implementation of good industrial hygiene practices for key categories of nanoparticles by supporting an improvement in management strategies and a wider range of methods to characterize various exposure aspects. It was also suggested that model NPs will help in the development of personal and area monitoring tools, which are different but complementary goals.

Breakout 5: What are the Critical Parameters and Data Needs for Understanding the Behavior of Nanoparticles in Environmental Media?

***Chair*: Andrew Nelson, University of Leeds (EU)**
***Rapporteur*: Carolyn Cairns, Consumers Union (U.S.)**

Introductory Talks

Fullerenes in the Environment: Behavior, Bioavailability, and Effects
Pedro Alvarez, Rice University (U.S.)

Use of Modeling to Predict Environmental Concentrations of Nanomaterials
Bernd Nowack, Swiss Federal Laboratories for Material Sciences and Technology (EU)

Presenters gave an overview of various factors in nature and in commerce affecting the fate of nanomaterials in environmental media and the critical parameters that might predict their behavior. Prof. Pedro Alvarez discussed key characteristics of C_{60} (buckminsterfullerene): how certain transformations can impact fate and toxicity, the relevance of standard parameters such as reduction potential or reactive oxygen species production, and octanol–water distribution measurements commonly used to predict the fate of conventional compounds. Dr. Bernd Nowack's presentation focused on using material flow models to target critical environmental compartments and pathways, quantify releases and exposures, and anticipate possible transformations that might take place as nanomaterials flow through commerce and into the environment.

Summary of Participant Comments

Participants outlined a number of critical parameters and data needs as priorities for near-term, risk-relevant research, including the need for an appropriate framework for accurate modeling that reflects potential transformations, surface mechanisms, and aggregation properties. How nanoscale complexities impact solubility and its relationship to bioavailability was also noted as a critical research question. The need to match the modeling activity to the decision-making objective was also considered important in that models used for broad premarket predictive assessments may be different than those used to assess risks of existing commercial substances with particular commercial applications. Some suggested taking a reverse-engineering approach that defines an acceptable outcome and works backwards through the fate pathways to define critical parameters for a given nanosubstance and/or application. Some participants encouraged more effort to investigate how existing understanding of soft colloid chemistry might translate to nanoparticles. Others encouraged researchers to think broadly and consider what important factors may be overlooked, such as the importance of partial pressures of CO_2, and how to adjust models for effects that may not be fully understood at this time.

Participants recognized the implications of their responses for

- *Risk Assessment:*
  Many of the standard tools used for conventional chemical risk assessment are not fully applicable to nanoscale materials. For example, assumptions inherent in standard biotic-ligand models and transformation factors may be inappropriate for nanoscale

materials. Time scales may be very different, and the state of the receiving environment may play a vastly more critical role in the outcomes. Including uncertainty assessments with environmental fate and toxicity modeling efforts was proposed as a way to gauge the impact of uncertainty on the scope of possible risks and the range of biological interference. By distinguishing parameters associated with high mechanistic uncertainties from those safety judgments that carry a relatively lower level of uncertainty, such assessments could guide research toward activities that would leverage the greatest value for risk assessment.

- *Regulatory Data Needs:*
  The parameters discussed were considered critical to help focus regulatory decisions on the most biologically relevant factors associated with environmental release of nanomaterials and to define safety thresholds for various endpoints. It was also recognized that understanding the general fate and evolution of the surface chemistry may be more important than specifying particular mechanisms of impact. Participants speculated that knowing what types of impacts are possible may be more critical than understanding exactly how they occur, although finding unifying principles in mechanistic and surface chemistry is a long-term goal.

- *Research and Technology Development:*
  The considerable impact that environmental media and related transformations may have on nanomaterial fate and toxicity supported participants' recommendation that research move away from work on pristine particles and focus on substances and mixtures in the form in which they are used in commerce and found in the environment. Fundamental to this shift is better characterization of commercialized nanomaterials and their form in environmental media. This will depend in part on the availability of improved instrumentation for fieldwork that would enable nanoparticle dynamics to be characterized at lower detection limits.

- *Other issues (reproducibility, training, networking, etc.):*
  Three main efforts were viewed as critical to a research program that effectively supports risk assessment: developing a library of commercialized ENMs and the products in which they are utilized; instituting a program of interlaboratory calibration; and training to get researchers, technicians, and other stakeholders working under the same standards.

In addition, participants addressed the following:

- *Mechanisms to achieve consensus on this question in the global research community:*
  Several participants saw tremendous value in having U.S. and EU researchers work from a common platform that includes shared methods and joint reporting. Closer collaboration among financial administrators was recommended to eliminate "ownership" issues that inhibit coordination and drive redundancies. Participants noted separate strengths in U.S. and EU approaches, recommending changes to minimize the frequency of reporting and to allow researchers to reply to reviews. An effort to foster greater coordination among mechanistic scientists and model developers was also recommended.

- *Long-term suggestions and other ideas important to this session:*
  Many in the group recognized the value of long-term collaboration on nanotechnology risk research and proposed the creation of a joint EU–U.S. research center to foster laboratory exchange. Such action would increase awareness of and access to equipment and other resources at nanotechnology research centers. Opportunities to interface with the patent

process to create a mechanism that informs research programs of changes in products could also be explored, as well as greater coordination of academic researchers with technology developers to better understand source material and factors driving its development. A critical long-term goal was identified of holding more joint conferences, such as this EU–U.S. workshop.

Breakout 6: What are the Critical Parameters and Data Needs Relevant to Understanding the Behavior of Nanoparticles in Consumer and General Population Exposures?

***Chair*: Frédéric Schuster, French Alternative Energies and Atomic Energy Commission**
***Rapporteur*: Treye Thomas, U.S. Consumer Product Safety Commission**

Introductory Talks

What are the Critical Parameters/Data Needs to Understand NP Exposure to Consumers and the General Population?

Frans Christensen, European Commission

Mr. Frans Christensen's presentation began with an overview of the nanomaterial life cycle, nano-enabled consumer products, and the potential for human exposure. He discussed the growth in the number of products on the market that contain nanomaterials as well as the need to understand the potential forms of the nanoparticles in product matrices. The presentation stressed the importance of identifying the form of the nanoparticle released from products and developing methods to measure the size, mass, surface area, and other characteristics. The release of nanomaterials into the environment and the potential interactions with biotic and abiotic elements is a significant information gap and should be adequately addressed. Modeling was identified as a critical tool in understanding the relationships between source, release, and fate of nanoparticles in the environment. Specifically, partitioning kinetics, transformation, and bioaccumulation were identified as key components in modeling efforts.

Consumer Exposure and Life Cycle Assessment of Nanomaterials: What's Still Needed?

Todd Kuiken, Woodrow Wilson Center (U.S.)

Dr. Todd Kuiken's presentation also emphasized the growing market for nanotechnology-enabled products across the globe. He presented several graphs that demonstrated the growth in products, product categories, and the major classes of nanomaterials that are used in consumer products. Dr. Kuiken discussed the use of nanomaterials in environmental remediation and the need for information on these materials in workplace settings. Material Safety Data Sheets (MSDSs) were identified as key sources of information for workers; however, health and safety data are needed for MSDSs. The public perception of nanotechnology is slowly growing, and those who are aware of nanotechnology have expectations for greater transparency and disclosure and desire third-party testing of products. Specifically, it is important to understand the potential exposures to nanomaterials and the releases during manufacturing, product use, and disposal. Dr. Kuiken emphasized the difficulty

in answering these questions, along with the fact that 10 years after the development of the NNI, there are still a number of questions concerning measurement techniques, toxicity testing, and environmental life cycle that require substantive work to answer.

Summary of Participant Comments

The dialogue among the session attendees was robust, and despite the variety of backgrounds, viewpoints, and perspectives, several key points emerged. The participants noted that it is critical to focus the discussion on ENMs and that obtaining and sharing information on the use of these materials in products is very important. Questions included how best to obtain this information and how to provide incentives for various entities to disclose information to the public. It was stressed that nanomaterial releases from products should be distinguished from actual human exposure to nanomaterials. This led to a discussion of the need to characterize nanomaterial releases. Identified data needs included defining the forms of the release and the techniques to quantify releases. These releases may occur in different matrices. Distinctions should be made between exposures to humans that occur as a result of fate, i.e., behavior of nanomaterials in the environment, and the exposures that occur as a result of product use that occurs primarily indoors. Environmental monitoring will involve characterizing and quantifying the release and transport of nanomaterials through air and water. Analytical methods will be required for the complexity of the matrices that will contain released nanoparticles such as wastewater, soil, and other media. Thus, robust new screening and measurement techniques will be needed. Some participants felt that these new techniques should also include simple screening and measurement methods.

It was observed that predictive models will play an important role in meeting identified data gaps, and that models used to predict release and exposure should undergo some degree of validation. The product testing should occur throughout the life cycle of the material and product, and testing should be conducted to determine the effects of aging on the durability and subsequent release of nanomaterials from products. Testing to identify releases was distinguished from actual exposure assessment studies.

The risk assessment process and the uncertainty of exposure levels to the general public were identified as key data gaps. Additional data is needed regarding the behavior of various nanoparticles in the body, as is a greater understanding of the relationship between the form of the nanoparticle that an organism is exposed to, uptake, and subsequent behavior in the body and the risk of health effects. Green chemistry was identified as a means to both design a product to minimize releases and to design a material to maximize benign biological effects.

The importance of the general public having access to information on the use of nanomaterials was emphasized. Labeling of products was suggested, with industry submitting information to national government agencies. A database to provide information on these submissions was seen as a viable means to inform the public. Informatics was seen as a critical area for nanotechnology, and cloud computing and other tools could be used in information sharing and outreach to the public. The need to train scientists to have an appreciation of the unique challenges of nanotechnology was underscored.

5. Industrial Risk Management Considerations for Worker Protection

Introduction

This session of the workshop focused on the critical issues for the nanotechnology workforce. The states of the science for complex technical challenges surrounding exposure measurement and worker protection were presented by U.S. and EU stakeholders, as were methods for communicating risk to industry management and workers.

***Chair*: Daniel Bloch, French Atomic Energy and Alternative Energies Commission (EU)**
***Rapporteur*: Shaun Clancy, Evonik North America (U.S.)**

Contributed Talks

Strategies and Methods to Assess Occupational Exposures to Engineered Nanoparticles

Kai Savolainen, Finnish Institute of Occupational Health (EU)

In his talk, Dr. Kai Savolainen described some of the issues that complicate measuring workplace exposures and examples of practices intended to overcome present difficulties such as distinguishing target nanomaterials from background nanomaterials. For example, one metric felt to be important with respect to toxicity is surface area, and he described examples of methods under development for use in the workplace that can perform these measurements. There are needs for such equipment in laboratory, manufacturing, and field settings.

In his summary, Dr. Savolainen described three needs:

- A clear exposure assessment strategy
- Novel technologies that can distinguish intentionally generated materials from background nanomaterials
- Development of occupational exposure limits

Dr. Savolainen noted that risk managers need to monitor risk along the product life cycle and that ongoing research is needed to fill the data gaps.

Worker Protection and Exposure Risk Management Strategies for Nanomaterial Production, Use, and Disposal

Markus Berges, Deutsche Gesetzliche Unfallversicherung (EU)

The German insurance company Deutsche Gesetzliche Unfallversicherung (DGUV) insures other insurance companies, so its leaders have a lot of interest in workplace safety. Part of the company's work involves performing workplace surveys, and it participates in public–private partnerships such as standards setting. Its leaders are interested in state-of-the-art technologies, setting OEL benchmarks, evaluating protective measures, and participating in a nanotechnology-focused portal for information sharing.

Dr. Markus Berges of DGUV sees gaps in assessing background levels of nanomaterials, identification of appropriate size ranges, and life cycle considerations. He sees needs for standardized sampling, better understanding of the release of nanomaterials from matrices, focus on high-aspect-ratio nanomaterials, and tiered testing such that some evaluations can be done on a routine basis although others may need sophisticated experts. DGUV leadership believes the burdens of the use of protective measures should be commensurate with the risks.

Nanomanufacturing and Occupational and Environmental Health Sciences: Integrating the Science

Don Ewert, NanoTox, Inc., and OSO BioPharmaceuticals Manufacturing (U.S.)

Mr. Don Ewert reviewed the U.S. laws that provide a legal rationale for ensuring safety in the use of chemicals, including nanomaterials. He noted that many nanomaterials undergo many changes from synthesis through product manufacture and use. Thus the information about the nanomaterial at the beginning of the product life cycle is not necessarily applicable at the end, so a good understanding of data needs at various stages in the life cycle is essential to safety analysis. There is also a need to find a balance in the use of characterization information so that nothing is defined as hazardous unless it really is.

Mr. Ewert stated that if we know about ENM characteristics that affect exposure, many of them can be controlled to decrease the potential for exposure. This would assure the public that nanomaterials can be safely handled. The handling of high-potency pharmaceuticals may provide a good example of practices that generate public confidence. Finally, Mr. Ewert discussed development of a standard practice for stewardship.

A discussion ensued about the use of control banding (CB), and it was suggested that the CB practices in the pharmaceutical industry could be useful in nanotechnology industries.

Exposure and Risk Banding Models as Tools for Risk Management

Derk Brouwer, The Netherlands Organization for Applied Scientific Research (TNO) (EU)

Dr. Derk Brouwer also addressed the use of control banding concepts and remarked that banding can be considered separately for nanomaterial emissions and personal exposures. To do so, exposure sources have to be considered, including fugitive release during preparation, use as intermediates, and releases due to activities such as weathering and abrasion. Evaluation outcomes include a determination of appropriate mitigation measures such as simple ventilation for materials with low risk profiles or full body-suit protection for potentially highly hazardous nanomaterials. The band that is chosen includes an assessment about the level of certainty in the hazard information available. Scientists in Switzerland, the United States, and France have developed control banding tools based on emissions. Other scientists in the Netherlands and Denmark have developed CB tools that address emissions. The tools can include decision trees and/or scoring systems. Work is underway within ISO Technical Committee 229 on standardization of CB methods.

Communication of Risk Management Strategies to Practitioners

Bruce Stockmeier, Argonne National Laboratory (U.S.)

Mr. Bruce Stockmeier described two concepts fundamental for risk managers: exposures to agents can be measured, and there is a safe threshold. He then asked two questions: How should nanomaterials be sampled, and what is a reasonable exposure limit? He then posed a question about the usefulness of regulations and concluded that current regulations are not particularly helpful. He stated that risk managers should be wary of becoming overly confident, because nanotechnology is different from materials in their previous experiences. They should also know that nanotechnology terminology can be confusing. The problem-solving practices of the past may not be sufficient, and risk managers need to keep in mind that there may be things that they don't know that they don't know.

Mr. Stockmeier recommended that risk managers use a risk management approach that broadly considers issues such as ethical, legal, and societal implications (ELSI); stewardship; sustainability; and public perceptions.

Risk managers could benefit from asking themselves

- How did we get to this point?
- Did it happen before for another scenario?
- Could it happen again?
- Who should be engaged to obtain helpful information?

There are research needs that include

- Determining meaningful ways to estimate dose
- Determining safe exposure levels
- Validating hazard control practices

Other needs include the need to collaborate, communicate, and coordinate; develop conclusions and recommendations; and facilitate access to existing information.

Participants noted that it is also important to recognize what has been done correctly in the past and ask if industrial hygiene professionals should obtain nanomaterial-specific training. Mr. Stockmeier responded that some training is available.

6. Getting It Done Together: Establishing Scientific Themes and Mechanisms for Ongoing Interaction

Introduction

The closing session of the workshop provided an opportunity for U.S. and EU participants to integrate the findings of the previous sessions into a discussion of existing and new mechanisms for research collaboration. Speakers described several programs, existing research platforms, and new mechanisms for ongoing, focused dialogue on nanoEHS research.

Establishing Scientific Themes and Mechanisms for Ongoing Interaction

Chair: Lang Tran, Institute of Occupational Medicine (EU)
Rapporteur: Laura Hodson, U.S. National Institute for Occupational Safety and Health

Enhancing Cooperation between EU and U.S. Scientists: BILAT-USA and Link2US Projects in the U.S. & EU

Sabine Herlitschka, Austrian Research Promotion Agency (EU)

Dr. Sabine Herlitschka described two current EU initiatives that could fund research projects that support transatlantic dialogue among nanotechnology EHS researchers. The first is European BILAT-USA, funded through the FP7, which strongly emphasizes international cooperation. The BILAT-USA project will set up a sustainable, knowledge-based, and biregional dialogue platform between science and technology key players as well as stakeholders from the EU member states and associated countries and from the United States. The project's goal is to improve awareness of EU–U.S. science and technology cooperation through a comprehensive set of activities that will

- Support a transatlantic dialogue platform addressing global issues
- Provide information on science and technology cooperation activities and opportunities between the EU and the United States to facilitate new partnerships within the EU Framework Programme
- Promote excellence in cooperative research through the organization of science forums at the policy level, symposia on cross-cutting multidisciplinary issues, and workshops and linked brokerage events at the thematic level
- Facilitate networking to support cooperative activities

Currently BILAT-USA is supporting 10,500 research projects worldwide out of 61,500 proposals submitted. Key players include the EU, Russia, China, and Japan.

The second initiative, as described by Dr. Herlitschka, is Link2US. Link2US will facilitate easy access to relevant information on U.S. cooperation programs through electronic communities such as a website, e-newsletter, and virtual helpdesk, and through designated activities such as training workshops. The Link2US Project will

- Map opportunities of U.S. Federal collaborative funding schemes and rules for participation through research and analyses
- Raise awareness in the European scientific community by disseminating information about collaborative EU–U.S. programs and funding opportunities through a multifaceted network
- Identify and analyze potential obstacles to cooperation through these programs and funding schemes so that the obstacles may be avoided and/or that solutions may be found

The American Association for the Advancement of Science is the U.S. partner of Link2US. More information may be found online at http://www.EuUsScienceTechnology.eu.

Developing Communities of Research

Sally Tinkle, U.S. National Nanotechnology Coordination Office

Dr. Sally Tinkle addressed how the participants could move forward with the development of Communities of Research (CORs) that could be based on the Communities of Practice model in order to obtain maximum collaboration with minimal budget.

Using this model, a COR would have three elements: a shared concern, a community that periodically comes together, and practitioners with a shared repertoire of resources, experiences, and tools. The nanoEHS CORs may be a good way to move forward, but we need to determine if this is a good idea and if this is the right time to launch this effort. Questions to be considered include the form of the infrastructure, the number of CORs for the initial effort, and the science topics—for example, consider setting up six CORs based on the themes of the six Day 2 breakout sessions of this workshop.

The group needs to consider all avenues for communication, including use of Wiki threads, web conferencing, or video chat for meetings. There will need to be an identified group of members for each of the CORs. U.S. NNI and EC nanotechnology leaders understand that administrative support may be necessary and are prepared to assist—the United States through the NNCO and the European Commission through its Directorate-General for Research and Innovation.

Identifying Technical Platforms for Collaboration

Georgios Katalagarianakis, European Commission

Dr. Georgios Katalagarianakis discussed EU and U.S. shared values. He suggested that groups in both regions identify technical platforms for collaboration based upon a nanomaterials safety cluster. He described seven potential working groups: (1) Synthesis, (2) Hazards, (3) Exposure, (4) Databases, (5) Risk in the Workplace, (6) Modeling, and (7) Dissemination.

Dr. Katalagarianakis went on to discuss how important it is to move the science into practice and that these technology platforms are needed to bring stakeholders together. He recognized the need to develop strategic programs that will enable risk-focused research through ongoing dialogue that includes meetings, joint actions, databases, and working groups.

Next Steps and Growing the Effort

Workshop participants acknowledged that cooperation between the European Union and the United States in nanoEHS research is expected to deliver faster and more integrated progress of

obvious societal value. The two sides already commit significant resources in their public programs to support safety-oriented research and networking activities. Bridging these networks is a high priority. Participants identified several mechanisms that may help create these bridges:

- A workshop organized annually could provide the possibility of face-to-face meetings among researchers.
- CORs could be established to enhance scientific collaborations between the United States and the EU. These CORs would be composed of scientists with common concerns who periodically come together to share resources, experience, and tools. In the context of nanoEHS, a COR provides a communication platform for specific research themes, for example, materials, hazards, exposure, and risk control. These groups would decide how best to organize the scientific scope for each community.
- Activities such as publication of common compendia for test methods and protocols, data management, etc., would support the CORs or other bridging efforts. Such supporting activities could address development of mechanisms for cross-validation of research results, exchange of information, benchmarking, training, pre-standardization research, etc. Long-term issues such as education and intelligent testing methods could be given attention through elaboration of common research strategies and roadmaps.
- For specific research priorities, publication of joint calls for research proposals might be envisaged. The cooperation effort could include projects financed by EU member states and FP7 associated states on a voluntary basis. The cooperation is open to researchers from other countries, and where applicable, intellectual property rights will be discussed and agreed upon.

This session, and the workshop, closed with an enthusiastic agreement by many attendees to participate in collaborative dialogue that will advance the science of nanoEHS for sound regulatory and policy decision making, and by the government organizers to continue a monthly dialogue to develop the mechanisms for improved collaboration.

The U.S. organizers agreed to develop a website for ongoing discussions,[18] and the EC workshop organizers offered to host the second U.S.–EU workshop on collaborative nanoEHS research efforts, in Helsinki, Finland, in late 2012.

[18] [Editor's note:] The website has since been established: http://us-eu.org.

Appendices

Appendix A. Workshop Agenda

Thursday, March 10, 2011

George Washington University
Elliott School of International Affairs
1957 E Street NW, 7th Floor, City View Room
Washington, DC 20052

8:00 – 9:00 Registration and Continental Breakfast

9:00 - 9:20 Welcoming Remarks
Daniel Clune, Principal Deputy Assistant Secretary, U.S. Department of State
Herbert von Bose, Director, European Commission, DG Research & Innovation

9:20 - 9:30 Purpose and Goals of the Workshop
Sally Tinkle, Deputy Director, U.S. National Nanotechnology Coordination Office

9:30 - 9:45 Research to Regulation Transition Needs
Elke Anklam, Director, European Commission, DG Joint Research Center – IHCP (Institute for Health and Consumer Protection)

Part 1: Understanding Perspectives and Programs

9:45 - 10:00 Overview of the EC EHS Research Plans and Perspective
Georgios Katalagarianakis, European Commission, DG Research & Innovation

- FP7 and Future FP8 Research Needs
- Most Recent Calls for Proposals, and Those Anticipated

10:00 - 10:15 Overview of U.S. 2011 EHS Research Strategy and Perspective of the Government in Developing the Plan
Sally Tinkle, Deputy Director, National Nanotechnology Coordination Office

- NNI 2011 Research Strategy
- Recent and Anticipated RFAs

10:15 - 10:30 The OECD Working Party of Manufactured Nanomaterials: Latest Developments and Outlook for the Future
Alexander Pogany, Federal Ministry for Transport, Innovation and Technology

10:30 - 10:45 Break

10:45 - 11:00 Standardization for Nanosafety: ISO Plans and Perspective
Daniel Bernard, Arkema

11:00 - 11:30 Examples of EU National Efforts

NanoCare and NanoGEM – Large Integrated Projects within the German NanoEHS Initiative of the BMBF
Thomas Kuhlbusch, Institute of Energy and Environmental Technology

Example of National EU Efforts in the Field of EHS Research Connected to N&N
Alexander Pogany, Federal Ministry for Transport, Innovation and Technology

11:30 - 12:00 Example of U.S. Efforts

Nanotechnology Research in NIOSH
Vince Castranova, National Institute for Occupational Safety and Health

NIEHS/NTP Activities Evaluating the Safety of Nanoscale Materials
Nigel Walker, National Institute of Environmental Health Sciences

12:00 - 12:30 Working Lunch

12:30 - 12:45 Research in Support of Consumer Protection Legislation
Hermann Stamm, Head of Nanobiosciences Unit, DG Joint Research Center – IHCP (Institute for Health and Consumer Protection)

12:45 - 1:15 Industry Perspective

Safety Research as an Integral Part of the Industrial Innovation Strategy
Peter Kruger, Bayer

Defining Research Needs & Crop Protection Products
Wendelyn Jones, CropLife

1:15 – 1:30 NGO Perspective

The Consumer Protection Imperative in Nanotech Research
Carolyn Cairns, U.S. Consumers Union

Part 2: Data Needs for Regulatory Decision Making

1:30 – 2:00 Overview of General Components of Regulatory Decision Making and Data Needs; Charge to the Breakout Groups
Phil Sayre, U.S. Environmental Protection Agency

2:00 – 2:15 Break

2:15 – 3:45 **Concurrent Breakout Sessions**

Session 1: *Human Health Data Needs*
Chair: Michael Riediker, Centre Hospitalier Universitaire Vaudois
Rapporteur: Wendelyn Jones, CropLife

EU Presentation: Regulatory Challenges and Data Needs: Work under the OECD Sponsorship Programme, EU Future Plans and International Cooperation Settings
Tom van Teunenbroek, Ministry of Infrastructure and the Environment

U.S. Presentation: Human and Safety Data Needs: The U.S. Nano2 Report
Andre Nel, University of California, Los Angeles

Session 2: *Environment Data Needs*
Chair: Pedro Alvarez, Rice University
Rapporteur: Flemming Cassee, National Institute for Public Health and the Environment

U.S. Presentation: Nano-Sized Particles in the Environment: Fate, Transport and Potential Impacts to Ecosystem Health
Pedro Alvarez, Rice University

EU Presentation: Environmental Behavior and Effects of NPs on Organisms: Research and Data Needs for Regulatory Decision Making
Richard Handy, University of Plymouth

3:45 – 4:15 Break

4:15 – 5:15 **Regulatory Panel**

Moderator: Tom van Teunenbroek, OECD

EU: Tom van Teunenbroek (OECD), Ken Dawson (SCENIHR), Andrej Kobe (DG ENV), Hermann Stamm (DG JRC), Alexander Pogany (AT)

U.S.: Phil Sayre (EPA), Bill Jordan (EPA), Carlos Peña (FDA), Treye Thomas (CPSC), Janet Carter (OSHA), Kerry Dearfield (USDA)

5:15 – 5:30 **Closing Remarks**

Georgios Katalagarianakis, European Commission, DG Research & Innovation

Sally Tinkle, Deputy Director, U.S. National Nanotechnology Coordination Office

FRIDAY, MARCH 11, 2011

American Association for the Advancement of Science (AAAS)
1200 New York Avenue
Washington, DC 20005

Part 3: Tackling the Challenges of Producing Reliable and Reproducible Data for Nanomaterials Assessment and Risk Management

8:00 – 8:30 Registration and Continental Breakfast

8:30 – 8:40 Overview of Day 2: Focusing on Science and Identifying of Areas of Cooperation and Leveraging
Phil Sayre, U.S. Environmental Protection Agency

8:40 – 9:10 Tackling the Challenges: Producing Reliable and Reproducible Data for Nanomaterials Assessment and Risk Management
Janeck Scott- Fordsmand, EU National Environmental Research Institute

9:10 – 9:20 Charge to the Breakout Sessions
Chris Cannizzaro, U.S. Department of State

9:20 – 9:30 Break

9:30 – 10:45 **Concurrent Breakout Sessions**

Session1*: When do Unique Properties - with Risk Assessment Implications - Arise for Specific Nanomaterials?*
Chair: Scott McNeil, Nanoscale Characterization Laboratory
Rapporteur: Bengt Fadeel, Karolinska Institutet

U.S. Presentation: A Risk Forecasting Framework for Nanomaterials
Mark Wiesner, Duke University

EU Presentation: Health: on Carbon-based NPs and Health Implications
Dominique Lison, Université Catholique de Louvain

***Session 2**: How do Surface Modifications and Chemical Transformations Affect Toxicity?*
U.S. Chair: Jay West, American Chemistry Council
EU Rapporteur: Adrienne Sips, RIVM

EU Presentation: The Role of the Nanoparticle Surface in Interactions with Living Organisms
Ken Dawson, University College Dublin

U.S. Presentation: Environment: Ecotox and Transformations
Steve Klaine, Clemson University

***Session 3**: What Metrics Are Most Scientifically Accurate When Relating Dose to Response in Toxicity Assessments? How are Dose-Response Data Best Extended to Determining Occupational Exposure Limits and Environmentally relevant concentrations?*
Chair**:** Rafi Korenstein, Tel Aviv University
Rapporteur: David Warheit, DuPont

U.S. Presentation: *In Vitro–In Vivo* Correlations of Dose-and-Response Metrics: Concepts for OEL Extrapolation
Günter Oberdörster, University of Rochester

EU Presentation: Environment: The Effects of Carbon Nanoparticles in Aquatic Species – the Importance of Testing Across Populations and Life Cycles
Teresa Fernandes, Napier University

***Session 4**: How Relevant are Model Nanoparticles to Understanding Exposure in the Workplace? How Relevant are they to Recommending Industrial Hygiene Practices?*
Chair: Chuck Geraci, National Institute for Occupational Safety and Health
Rapporteur: Enrico Bergamaschi, University of Parma

U.S. Presentation: Use of Model Nanoparticles to Understand Exposures in the Workplace
Laura Hodson, National Institute for Occupational Safety and Health

EU Presentation: Critical Parameters / Data Needs for Exposure Assessment in Occupational and Environmental Scenarios
Rob Aitken, Institute of Occupational Medicine

***Session 5**: What are the Critical Parameters and Data Needs for Understanding the Behavior of Nanoparticles in Environmental Media?*
Chair: Andrew Nelson, University of Leeds
Rapporteur: Carolyn Cairns, Consumers Union

U.S. Presentation: Fullerenes in the Environment: Behavior, Bioavailability and Effects
Pedro Alvarez, Rice University

EU Presentation: Use of Modeling to Predict Environmental Concentrations of Nanomaterials
Bernd Nowack, Swiss Federal Laboratories for Material Sciences and Technology

***Session 6:** What are the Critical Parameters and Data Needs Relevant to Understanding the Behavior of Nanoparticles in Consumer and General Population Exposures?*
Chair: Frédéric Schuster, CEA, Commissariat à L'Energie Atomique et aux Energies Alternatives
Rapporteur: Treye Thomas, Consumer Product Safety Commission

EU Presentation: What are the Critical Parameters/ Data Needs to Understanding NP Exposure to Consumers and the General Population?
Frans Christensen, European Commission

U.S. Presentation: Consumer Exposure and Life Cycle Assessment of Nanomaterials: What's Still Needed?
Todd Kuiken, Woodrow Wilson Center

10:45 – 11:00 Break

11:00– 12:30 Key Conclusions from the Breakout Sessions

12:30 – 2:00 Lunch (On your own)

2:00 – 3:15 Industrial Risk Management Considerations for Worker Protection
Chair: Daniel Bloch, Commissariat à L'Energie Atomique et aux Energies Alternatives
Rapporteur: Shaun Clancy, Evonik North America

EU: Worker Protection and Exposure Risk Management Strategies for Nanomaterial Production, Use and Disposal
Markus Berges, Deutsche Gesetzliche Unfallversicherung

EU: Strategies and Methods to Assess Occupational Exposures to Engineered Nanoparticles
Kai Savolainen, Finnish Institute of Occupational Health

U.S.: Nano Manufacturing & OEHS; Integrating the Science
Don Ewert, NanoTox, Inc, and OSO BioPharmaceuticals Manufacturing

EU: Exposure and Risk Banding Models as Tools for Risk Management
Derk Brouwer, Nederlandse Organisatie Voor Toegepast Natuurwetenschappelijk Onderzoek

U.S.: Communication of Risk Management Strategies to Practitioners
Bruce Stockmeier, Argonne National Laboratory

Part 4: Getting It Done Together

3:15 – 4:15 Establishing Scientific Themes and Mechanisms for Ongoing Interaction
Chair: Lang Tran, Institute of Occupational Medicine
Rapporteur: Laura Hodson, National Institute for Occupational Safety and Health

Enhancing Cooperation between EU and U.S. Scientists - BILAT-USA and Link2US Projects U.S. & EU
Sabine Herlitschka, Austrian Research Promotion Agency (FFG)

Developing Communities of Research (CORs)
Sally Tinkle, Deputy Director, National Nanotechnology Coordination Office

Identifying Technical Platforms for Collaboration
Georgios Katalagarianakis, European Commission, DG Research & Innovation

4:15 – 4:30 Next Steps and Growing the Effort
Travis Earles, Office of Science and Technology Policy, Executive Office of the President

Appendix B. Workshop Participants[i]

Rob Aitken, Institute of Occupational Medicine

Harri Alenius, Finnish Institute of Occupational Health

Pedro Alvarez, Rice University

Elke Anklam, European Commission

Hans Bakker, Royal Netherlands Embassy

Diego Basset, Veneto Nanotech S.C.p.A.

Tammie Bell, FDA

Enrico Bergamaschi, University of Parma Medical School

Markus Berges, Deutsche Gesetzliche Unfallversicherung

Lynn L. Bergeson , Bergeson & Campbell, P.C.

Daniel Bernard, Arkema

Sofie Björling, Swedish Embassy

Kimberly Blatz, University of Virginia

Daniel Bloch, French Atomic Energy and Alternative Energies Commission

Meta Bonner, U.S. EPA

Diana Boraschi, Italian National Research Council

Christopher Bosso, Northeastern University

Derk Brouwer,The Netherlands Organization for Applied Scientific Research

Robert Bursey, Ajinomoto Corporate Services, LLC

Harry Bushong, nanoTox, Inc.

Giulio Busulini, Embassy of Italy

Raul Cachau, SAIC-Frederick, National Cancer Institute at Frederick

Anthony Cadene, French Agency for Food, Environmental and Occupational Health & Safety

Carolyn Cairns, Consumers Union

Richard Canady, Research Foundation of the International Life Sciences Institute

Chris Cannizzaro, Department of State

Elias Carayannis, George Washington University

Janet Carter, OSHA

Flemming R. Cassee, National Institute for Public Health and the Environment

Vince Castranova, NIOSH

Gary Casuccio, RJ Lee Group, Inc.

Richard Cavanagh, NIST

Hoshing Chang, U.S. FDA

Hongda Chen, USDA/National Institute of Food and Agriculture

Frans Møller Christensen, European Commission, Joint Research Centre, Institute for Health and Consumer Protection

Shaun Clancy, Evonik North America

Edmond Claude, Université de Montréal

Jed Costanza, U.S. EPA

Kristy Davis, University of Virginia

Ken Dawson, University College Dublin

Kerry Dearfield, USDA

Bart Deelen, Embassy of Belgium

Katya Delak, American Chemical Society

Kapal Dewan, U.S. FDA

Samantha Dozier, People for the Ethical Treatment of Animas

Kevin Dreher, U.S. EPA

Albert Duschl, University of Salzburg, Austria

Josef Dvoracek, Embassy of the Czech Republic

Travis Earles, U.S. Office of Science and Technology Policy

Anita Eisenstadt, Department of State

Michael Ellenbecker, University of Massachusetts Lowell

Britt Erickson, Chemical & Engineering News

Heather Evans, NIST

Donald Ewert, nanoTox, Inc.

[i]Affiliations are as of March 2011.

Bengt Fadeel, Karolinska Institutet

Howard Fairbrother, Department of Chemistry, Johns Hopkins University

Cathy Fehrenbacher, U.S. EPA

Teresa Fernandes, Herio-Watt University

Anthony R. Flambard, Juelich Project Management Organisation, Berlin Bureau

Martin Fritts, SAIC-Frederick

Russell Furr, University of Maryland

Sharon Gaheen, Science Applications International Corporation

Keshab Gangopadhyay, NEMS/MEMS Works LLC

Shubhra Gangopadhyay, University of Missouri

Antonietta Gatti, University of Modena and Reggio Emilia

Charles Geraci, NIOSH

Anna Gergely, Steptoe & Johnson LLP

Francesc Giralt, Universitat Rovira i Virgili

Joseph Giunta, U.S. Department of Commerce, Bureau of Industry and Security

Robert Goozner, Young & Thompson

Justin Gorham, NIST

Andrea Haase, German Federal Institute for Risk Assessment

Richard Handy, University of Plymouth, UK

Bob Hannah, GlaxoSmithKline

Irene Hantman, University of Maryland School of Law

Graham Harrison, National Science Foundation

Liesl Heeter, National Nanotechnology Coordination Office

Sabine Herlitschka, Austrian Research Promotion Agency

Angela Hight Walker, NIST

Laura Hodson, NIOSH

Dave Holbrook, NIST

Geoff Holdridge, National Nanotechnology Coordination Office

Robert Hurt, Brown University

Noela Invernizzi, Woodrow Wilson International Center for Scholars

Matthew Jaffe, Crowell & Moring LLP

Ajit Jillavenkatesa, NIST/U.S. Department of Commerce

Christian Joergens, Embassy of the Federal Republic of Germany

Helinor Johnston, Heriot Watt University

Kerri-Ann Jones, Assistant Secretary, U.S. Department of State

Wendelyn Jones, CropLife America

Bill Jordan, U.S. EPA

Jim Kadtke, National Nanotechnology Coordination Office

Debbie Kaiser, NIST

Tshanda Kalombo, U.S. Department of Commerce

Georgios Katalagarianakis, European Commission

Lindsey Kayman, Counsel on Occupational and Environmental Health

Fred Klaessig, Pennsylvania Bio Nano Systems, LLC

Steve Klaine, Clemson University

Andrej Kobe, European Commission, DG Environment

Astrid Koch, Delegation of the European Union to the USA

Kamilla Kohn Radberg, Swedish Embassy

Rafi Korenstein, Tel-Aviv University

Zofia Kosim, U.S. EPA

Peter Krueger, Bayer

Sharon Ku, National Institutes of Health

Thomas Kuhlbusch, German Institute of Energy and Environmental Technology

Todd Kuiken, Woodrow Wilson International Center for Scholars

David Lai, U.S. EPA

Robert Lainsdale

Anjali Lamba, U.S. EPA

Carole LeBlanc, U.S. Department of Defense

Wen-hsiung Lee, U.S. EPA

Stephen Lehrman, Office of Senator Mark Pryor

Michelle Limoli, U.S. FDA

Igor Linkov, U.S. Army Engineer Research and Development Center

Bruce Lippy, The Lippy Group, LLC

Dominique Lison, Catholic University of Louvain

H. Haven Liu, University of California, Los Angeles

Rong Liu, University of California, Los Angeles

Laurie Locascio, NIST

Kristen Loughery, U.S. EPA

Del Lyon

Yinqing Ma, U.S. FDA

Neil Macdonald, Federal Technology Watch

Marc Magaud, Embassy of France

Berges Markus, Institute for Occupational Safety and Health of the German Social Accident Insurance

Annette McCarthy, U.S. FDA

Breeann McCusker, Department of State

Jennifer McLain, U.S. EPA

Scott McNeil, SAIC-Frederick, National Cancer Institute at Frederick

Gian Paolo Meneghini, EU Parliament

Vitaly Minchenko, Russian Embassy

John Monica, Porter Wright Morris & Arthur LLP

Sergio Moya, Centre for Cooperative Research in Biomaterials

Vladimir Murashov, NIOSH

Sri Nadadur, U.S. National Institute of Environmental Health Sciences

Ritu Nalubola, U.S. FDA

Andre Nel, University of California, Los Angeles, Center for Environmental Implications of Nanotechnology

Andrew Nelson, University of Leeds

Bryant Nelson, NIST

Bernd Nowack, Swiss Federal Laboratories for Material Sciences and Technology

Gunter Oberdörster, Rochester University

Agnes Oomen, The Netherlands National Institute for Public Health and the Environment

Kazeem Akinloye Oyelakin, Physics Department, Federal University of Technology, Akure, Nigeria

Halyna Paikoush, National Nanotechnology Coordination Office

Sue Pan, SAIC

Charalampos Papadopoulos, Embassy of Greece

Stephanie Papia, American Association for the Advancement of Science

Carlos Peña, U.S. FDA

Elijah Petersen, NIST

Diana Petreski, National Nanotechnology Coordination Office

Martin Pizinger, Embassy of the Czech Republic

Alexander Pogány, Policy Expert

Leah Proffitt, U.S. FDA

Scott Prothero, U.S. EPA

David Pui, University of Minnesota

Robert Rallo, BioCenit; Universitat Rovira i Virgili; Catalunya, Spain

Kalpana Ramakrishnan, EPA

Bakhtiyor Rasulev, Interdisciplinary Center for Nanotoxicity, Jackson State University

Rudolf Reuther, NordMiljö O. Grahn AB

Keith Rickabaugh, RJ Lee Group

Michael Riediker, Institute for Work and Health

Pat Rizzuto, Bloomberg BNA, Inc.

Mihail Roco, National Science Foundation

Solveig Roschier, Tekes at the Embassy of Finland

Rowena Dasig Rowena Dasig, Reddwall Solutions

Kristin Roy, National Nanotechnology Coordination Office

Tind Shepper Ryen, Government Accountability Office

Nora Savage, U.S. EPA

Kai Savolainen, Finnish Institute of Occupational Health

Phil Sayre, U.S. EPA

Frédéric Schuster, Commissariat à l'énergie atomique et aux énergies alternatives

Janeck J. Scott-Fordsmand, Dept Terrestrial Ecology, National Environmental research institute, Aarhus University

Juan Serrano, Embassy of Spain

Prabodh Shah, U.S. EPA

Gwyneth Shaw, New Haven Independent

Deborah Sherer, U.S. EPA

Adrienne Sips, National Institute for Public Health & the Environment

Lew Sloter, Department of Defense

Aires Soares, Delegation of the European Union to the USA

Hermann Stamm, European Commission - Joint Research Centre

Jeff Steevens, U.S. Army Engineer Research and Development Center

Bruce Stockmeier, Center for Nanoscale Materials at Argonne National Laboratory

Larry Tarnacki, Roswell Park Cancer Institute

Clayton Teague, National Nanotechnology Coordination Office

Nathalie Theriet, French Agency for Food, Environmental and Occupational Health & Safety

Treye Thomas, CPSC

Scott Thurmond, U.S. FDA

Sally Tinkle, National Nanotechnology Coordination Office

David Tobias, American Association for the Advancement of Science

Jan Topinka, Senior Scientist

Brown Torrey, IntralytixIgnace Lang Tran, Institute of Occupational Medicine

Eugenia Valsami-Jones, Natural History Museum

Tom van Teunenbroek, Ministry of Infrastructure and the Environment

Ashok Vaseashta, Institute for Advanced Sciences Convergence

Herbert Von Bose, European Commission, Directorate-General for Research & Innovation

Michael Vorlaender, German Embassy

William Waissmann, Brazil

Nigel Walker, National Institute of Environmental Health Sciences

Tom Wang, American Association for the Advancement of Science

David Warheit, DuPont Haskell Global Centers

Chris Weis, National Institutes of Health

Jay West, American Chemistry Council

Robert Wiacek

Hans-Jürgen Wiegand, Evonik Industries

Mark Wiesner, Duke University

Eva Wong, U.S. EPA

Dee Woodhull, Mercer

Nigel Walker, National Institute of Environmental Health Sciences

Ronald Ziolo, Research Center for Applied Chemistry

Appendix C. Links to Presentations

Presentation titles and links to the presentations are given in chronological order below. The presentations also are available athttp://us-eu.org/workshop/presentations/.

March 10, 2011

Part 1: Understanding Perspectives and Programs

Overview of the EC EHS Research Plans and Perspectives, Georgios Katalagarianakis, European Commission, Directorate-General for Research & Innovation

Overview of U.S. 2011 EHS Research Strategy & Perspective of U.S. Government in Developing the Plan, Sally Tinkle, U.S. National Nanotechnology Coordination Office

OECD Working Party on Manufactured Nanomaterials: Latest Developments and Outlook, Alexander Pogany, Austrian Federal Ministry for Transport, Innovation and Technology

Standardization for Nanosafety: ISO Plans and Perspective, Daniel Bernard, Arkema

NanoCare & NanoGEM–Large Integrated Projects within the German NanoEHS Initiative of the BMBF, Thomas Kuhlbusch, German Institute of Energy and Environmental Technology

Example of National EU Efforts in the Field of EHS Research Connected to N&N, Alexander Pogany, Austrian Federal Ministry for Transport, Innovation and Technology

Nanotechnology Research at NIOSH, Vince Castranova, U.S. NIOSH

NIEHS/NTP Activities Evaluation the Safety of Nanoscale Materials, Nigel Walker, U.S. National Institute of Environmental Health Sciences

Research in Support of Consumer Protection Legislation, Hermann Stamm, Nanobiosciences, Directorate-General Joint Research Center, Institute for Health and Consumer Protection

Safety Research as an Integral Part of the Industrial Innovation Strategy, Peter Kruger, Bayer

Defining Research Needs & Crop Protection Products, Wendelyn Jones, CropLife

The Consumer Protection Imperative in Nanotech Research, Carolyn Cairns, U.S. Consumers Union

Part 2: Data Needs for Regulatory Decision Making

Overview of General Components of Regulatory Decision Making and Data Needs, Phil Sayre, U.S. EPA

Session 1

Regulatory Challenges & Data Needs: Work under the OECD Sponsorship Programme, EU Future Plans and International Cooperation Settings, Tom van Teunenbroek, The Netherlands Ministry of Infrastructure and the Environment

Human and Safety Data Needs: The U.S. Nano2 Report, Andre Nel, University of California, Los Angeles

Session 2

Health, Pedro Alvarez, Rice University

Environmental Behavior and Effects on NPs on Organisms: Research and Data Needs for Regulatory Decision Making, Richard Handy, University of Plymouth

March 11, 2011

Part 3: Tackling the Challenges of Producing Reliable and Reproducible Data for Nanomaterials Assessment and Risk Management

Overview: Focusing on Science and Identifying Areas of Cooperation and Leveraging, Phil Sayre, U.S. EPA

Appendix C. Links to Presentations

Session 1

A Risk Forecasting Framework for Nanomaterials, Mark Wiesner, Duke University

Carbon-Based NPs and Health Implications, Dominique Lison, Université Catholique de Louvain

Session 2

The Role of the Nanoparticle Surface in Interactions with Living Organisms, Ken Dawson, University College, Dublin

Environment: Ecotox and Transformations, Steve Klaine, Clemson University

Session 3

In vitro-In vivo Correlations of Dose-and-Response Metrics: Concepts for OEL Extrapolation, Gunter Oberdörster, University of Rochester

The Effects of Carbon Nanoparticles in Aquatic Species: The Importance of Testing Across Populations and Life Cycles, Teresa Fernandes, Napier University

Session 4

Use of Model Nanoparticles to Understand Exposures in the Workplace, Laura Hodson, U.S. NIOSH

Critical Parameters/Data Needs for Exposure Assessment in Occupational and Environmental Scenarios, Rob Aitken, Institute of Occupational Medicine

Session 5

Fullerenes in the Environment: Behavior, Bioavailability, and Effects, Pedro Alvarez, Rice University

Use of Modeling to Predict Environmental Concentrations of Nanomaterials, Bernd Nowack, Swiss Federal Laboratories for Material Sciences and Technology

Session 6

What are the Critical Parameters/Data Needs to Understand NP Exposure to Consumers and the General Population, Frans Christensen, European Commission

Consumer Exposure and Life Cycle Assessment of Nanomaterials: What's Still Needed?, Todd Kuiken, Woodrow Wilson Center

Industrial Risk Management Considerations for Worker Protection

Worker Protection and Exposure risk Management Strategies for Nanomaterial Production, Use, and Disposal, Markus Berges, Deutsche Gesetzliche, Unfallversicherung

Strategies and Methods to Assess Occupational Exposures to Engineered Nanoparticles, Kai Savolainen, Finnish Institute of Occupational Health

Nano Manufacturing & OEHS: Integrating the Science, Don Ewert, NanoTox, Inc; OSO BioPharmaceuticals Manufacturing

Exposure and Risk Banding Models as Tools for Risk Management, Derk Brouwer, The Netherlands Organization for Applied Scientific Research

Communication of Risk Management Strategies to Practitioners, Bruce Stockmeier, Argonne National Laboratory

Part 4: Getting It Done Together

Enhancing Cooperation between U.S. and EU Scientists- BILAT-USA and Link2US Projects, Sabine, Herlitschka, Austrian Research Promotion Agency

Development Communities of Research, Sally Tinkle, U.S. National Nanotechnology Coordination Office

Identifying Technical Platforms for Collaboration, Georgios Katalagarianakis, European Commission, Directorate-General for Research & Innovation

Appendix D. Templates for Breakout Groups

Summary Report for Day 1 Breakout Session on the Environment Data Needs

Instructions: There are three products from this breakout session. 1) Please respond to the actual questions below; 2) Prepare a 4-5 slide presentation with key conclusions and recommendations for the report out (10 min max); 3) Compose a 1-2 page summary of the information to be included in the final report.

I. What are the top three regulatory challenges for environmental exposures, fate, and effects that can be met in the next two to three years? Consider beginning with challenges to assessing the bioavailability of nanomaterials in environmental media. Please provide details on at least one regulatory challenge in response to remaining questions below. What are the data needs to address these regulatory challenges?

1.

2.

3.

4.

II. What do these data needs imply for the research needs? What are the barriers to producing these data?

1.
2.
3.
4.

III. What do these data needs imply for networking and data management?

1.
2.
3.
4.

IV. What priorities and research integration concepts would maximize research time and efficiency, e.g. modeling studies, networking mechanisms, etc?

1.
2.
3.
4.

V. What are the potential areas for near-term collaboration (2 – 3 years)?

1.
2.
3.
4.

VI. Are there additional long-term research needs (8-10 years) and other ideas important to regulatory oversight of nanomaterials with regard to environmental research?

1.
2.
3.
4.

Summary Report for Day 1 Breakout Session on the Human Health Data Needs

Instructions: There are three products from this breakout session. 1) Please respond to the actual question below; 2) Prepare a 4-5 slide presentation with key conclusions and recommendations for the report out (10 min max); 3) Compose a 1-2 page summary of information to be included in the final report.

I. What are the top three regulatory challenges for human health (covering both effects and exposures) that can be met in the next two to three years? Consider beginning with challenges to inhalation toxicology, as conducted in animal models. Please provide details on at least one regulatory challenge in response to remaining questions below.

What are the data needs to address these regulatory challenges?

1.
2.
3.
4.

II. What do these data needs imply for the research needs? What are the barriers to producing these data?

1.
2.
3.
4.

III. What do these data needs imply for networking and data management?

1.
2.
3.
4.

IV. What priorities and research integration concepts would maximize research time and efficiency, e.g. epidemiology studies, modeling studies, and networking mechanisms?

1.
2.
3.
4.

V. What are the potential areas for near-term collaboration (2 – 3 years)?

1.
2.
3.
4.

VI. Are there additional long-term research needs (8-10 years) and other ideas important to regulatory oversight of nanomaterials with regard to environmental research?

1.
2.
3.
4.

Summary Report for Day 2 Breakout Session_____

Instructions: There are three products from this breakout session. 1) Please respond to the actual questions below; 2) Prepare a 4-5 slide presentation with key conclusions and recommendations for the report out (10 min max); 3) Compose a 1-2 page summary of information to be included in the final report.

I. Responses to the breakout session question on the agenda:
1.
2.
3.
4.

II. Implications of the responses for:

Risk assessment:
a)
b)
c)
d)

Regulatory data needs:
a)
b)
c)
d)

Research and technology development:
a)
b)
c)
d)

Other (standardization, training, networking, and etc):
a)
b)
c)
d)

III. Mechanisms to achieve consensus on this question in the global research community:
1.
2.
3.
4

IV. Long term suggestions and other ideas important to this session are:
1.
2.
3.
4.

Appendix E. Post-Workshop Survey

The following survey was provided to workshop participants through the U.S.–EU website (http://us-eu.org/) after the meeting. The goal of the survey was to continue the dialogue on Communities of Research.

Survey to Solicit Interest in Communities of Research (COR) Topic Areas

- Please identify yourself, your scientific discipline, and your institution
  _____, _____, _____

Are willing to have your identity released to other workshop participants in connection with your responses to the survey Yes___, No___? Released to the general public. Yes ___ No___?

- Would you be interested in having a follow-on workshop in 2012? Yes ___ No____

Special topics of interest for the next workshop?_____
Suggested changes in format?_____

- What U.S.–EU collaborations you are currently participating in?
  _____
  _____

- What future areas of collaboration are you interested in? The following topic areas encompass the science discussed at the workshop and the interests of the U.S.–EU planning team. Please identify those topic areas for which you would participate in a Community of Research.

_____ Human Health

- collaborations and protocols
- *in vitro* to *in vivo* correlations/protocols for toxicity assessments
- positive and negative controls for toxicity testing

_____ Ecotoxicology

1. collaborations and protocols
2. *in vitro* to *in vivo* correlations/protocols for toxicity assessments
3. positive and negative controls for toxicity testing

_____ Exposure metrics and dose metrics

- product life cycle
- exposure/fate/transport

- methods to measure these parameters for toxicity tests

_____ Modeling and simulation, Databases to include all data (from 1): both positive and negative data, ontology and nomenclature

_____ Development and sharing of a standard set of nanoparticles, with variation of a single property across a range on a particle type basis

_____ Workplace exposure measurements: round robin of exposure measurements techniques, discriminating ENMs from background particles.

_____ Material characterization and standards

_____ Risk reduction (engineering controls, personal protective equipment, control banding, etc.)

_____ Training, or exchanges of people, around any of the issues noted above.

If so, which issues?_____

Other _____

- How can the U.S. and the EC help in furthering the collaborations you view as important?_____ _____ _____

Appendix F. List of Abbreviations and Acronyms

ADME	absorption, distribution, metabolism, and excretion
BET	Brunauer-Emmett-Teller method to calculate the surface area of solids
BMVIT	Austrian Federal Ministry of Transport, Innovation and Technology
CB	control banding
CNT	carbon nanotube
COR	Communities of Research
CPSC	U.S. Consumer Product Safety Commission
DG ENV	Environment Directorate-General of the European Commission
DG JRC	Joint Research Centre Directorate-General of the European Commission
DGUV	Deutsche Gesetzliche Unfallversicherung (insurance company)
EC	European Commission
EHS	environment(al), health, and safety
ELSI	ethical, legal and societal implications (of nanotechnology)
ENM	engineered nanomaterial(s)
EPA	U.S. Environmental Protection Agency
EU	European Union
FDA	U.S. Food and Drug Administration
FP7	7th Framework Programme of the European Commission
ISO	International Organization for Standardization
MIAME	minimum information about a microarray experiment
MNP	model nanoparticles
MSDS	Material Safety Data Sheet
nanoEHS	nanotechnology-related environment(al), health, and safety
NGO	non-governmental organization
NIOSH	U.S. National Institute for Occupational Safety and Health
NIST	U.S. National Institute for Standards and Technology
NNI	U.S. National Nanotechnology Initiative
NP	nanoparticle
NSET	Nanoscale Science, Engineering, and Technology Subcommittee of the U.S. National Science and Technology Council's Committee on Technology
NSF	U.S. National Science Foundation

NTRC	Nanotechnology Research Center within NIOSH
OECD	Organisation for Economic Co-operation and Development
OEL	occupational exposure limit
OPPT	EPA's Office of Pollution Prevention and Toxics
OSHA	Occupational Safety and Health Administration in the U.S. Department of Labor
REACH	European Registration, Evaluation, Authorisation and Restriction of Chemical substances database
REL	recommended exposure limit
SCENIHR	European Commission Scientific Committee on Emerging and Newly Identified Health Risks
SSA	specific surface area
USDA	U.S. Department of Agriculture
WPMN	Working Party on Manufactured Nanomaterials of the OECD