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Data dialogues: critical connections for designing and implementing future nanomaterial research

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Abstract Individuals and organizations in the engineered nanomaterial (ENM) community have increasingly recognized two related but distinct concerns: (1) Discordant data due to differences in experimental design (e.g., material characteristics, experimental model, and exposure concentration) or reporting (e.g., dose metric and material characterization details), and (2) a lack of data to inform decisions about ENM environmental, health, and safety (EHS). As one way to help address these issues, this Commentary discusses the important role of "data dialogues" or structured discussions between ENM researchers in EHS fields (e.g., toxicology, exposure science, and industrial hygiene) and decision makers who use the data researchers' collect. The importance of these structured discussions is examined here in the context of barriers, solutions, and incentives: barriers to developing research relevant for human and ecological risk assessments; potential solutions to overcome such barriers; and incentives to help implement these or other solutions. These barriers, solutions, and incentives were identified by a group of expert stakeholders and ENM community members at the December 2013 Society for Risk Analysis panel discussion on research needed to support decision making for multiwalled carbon nanotubes. Key topics discussed by experts and ENM community members include: (1) The value of researchers collaborating with EHS decision makers (e.g., risk analysts, product developers, and regulators) to design research that can inform ENM EHS-related decisions (e.g., occupational exposure limits and product safety determinations), (2) the importance of funding incentives for such collaborative research, (3) the need to improve mechanisms for data sharing within and between sectors (e.g., academia, government, and industry), and (4) the critical need to educate the "next generation" of nanotechnology researchers in EHS topics (e.g.,

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risk assessment, risk management). In presenting these outcomes, this Commentary is not intended to conclude the conversation that took place in December 2013 but rather to support a broader dialogue that helps ensure important risk assessment questions are answered for ENMs.

Keywords Engineered nanomaterials · Research planning · Health and environmental risk assessment · Risk management · Communication

1 Introduction

1.1 Problem statement

After more than a decade of research, the science of environmental, health, and safety (EHS) for engineered nanomaterials (ENMs) resembles a patchwork of information that often leaves decision makers (e.g., risk analysts, regulators, and product developers) uncertain about how to proceed with decisions related to ENM EHS (e.g., setting occupational exposure limits and determining potential human exposure from an ENM product). Laboratory research on ENM EHS, in general, has progressed in a series of disconnected efforts that offer parallel evaluations of ENM environmental behavior, exposure potential, hazard identification, or safety assessment. ENM research findings are thus often difficult to compare due to differences in experimental design (e.g., material characteristics, experimental model type, exposure concentration, and analytical methods) (Liu et al. 2013), or reporting (e.g., one dose metric, such as number of particles, without sufficient detail to convert to other metrics, like surface area or mass volume). In addition, available ENM data are often not directly applicable to decisions about ENM EHS. For instance, laboratory research generally includes ENMs with different physicochemical characteristics than those used in commercial products and the state-of-the-science does not currently support confidence in extrapolations between ENMs with distinct characteristics. The related, but distinct, issues of incongruent data and research disconnected from decisions about ENM EHS have been recognized by several organizations (NRC 2012, 2013; OECD 2012; PCAST 2012). Indeed, several large-scale collaborative efforts are underway in Europe (EU) and the United States of America (USA) (e.g., in EU: the "Nanosciences, Nanotechnologies, Materials and new Production Technologies (NMP)" theme of Seventh Framework Programme (FP7) and "Nanotechnologies, advanced materials and advanced manufacturing and processing" group in Horizon 2020; in the USA: the National Nanotechnology Initiative EHS research strategy implementation, and National Institutes of Environmental Health Centers for Nanotechnology Health Implications Research (NCNHIR) Consortium; in both the USA and EU: the collaborative nanoEHS communities of research). However, an intentional and proactive approach is still needed to ensure continued progress by the ENM EHS community (i.e., researchers, research funding organizations, regulators, product developers) in coordinating research efforts that can inform ENM EHS decisions. As an example of such an approach, this Commentary discusses the important role of "data dialogues" or structured discussions between researchers across several EHS disciplines (e.g., toxicology, exposure science, and industrial hygiene) and decision makers who use the data that researchers collect (e.g., risk analysts, regulators, and product developers).

1.2 Background: comprehensive environmental assessment applied to ENMs

A gap or disconnect between data gathered by researchers and the information needed by product developers, regulators, and/or others to make risk management or other policy decisions is an issue relevant to ENMs and other chemicals, technologies, or even broader topics [e.g., criminal justice and traffic policy (Oliver et al. (2014)]. The United States Environmental Protection Agency (U.S. EPA) and others have applied a Comprehensive Environmental Assessment (CEA) approach to help address such disconnects in ENM research. The CEA approach offers a process to structure available information within a framework[1] and to consider stakeholder input in EHS decisions (Powers et al. 2012). The

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[1] For any substance considered in a CEA application, stakeholders review information in the CEA framework, which includes: the product life cycle; environmental transport, transformation, and fate; exposure and dose in human, ecological, and abiotic receptors; impacts in human and ecological health, as well economic, environmental resource, and societal impacts. The term product life cycle refers to the processes that take place for a particular product related to: raw material extraction, production, transport, storage, use, and disposal and/or recycling. The term abiotic receptors includes inanimate objects such as cars or buildings that may also be impacted by exposure to environmental contaminants (e.g., effects of sulfur in the form of acid rain on structures).

U.S. EPA has applied CEA to inform research planning for future risk assessment and management of select ENMs. As a part of this process, the U.S. EPA developed a series of case studies and structured workshops that incorporate "data dialogues" on selected ENM in particular applications (i.e., nanoscale titanium dioxide in sunscreen and water treatment, nanoscale silver in disinfectant spray, multiwalled carbon nanotubes [MWCNTs] in flame-retardant coatings applied to upholstery textiles) (ICF 2011; RTI International 2012; U.S. EPA 2010a, b, 2012, 2013). The outcome of each ENM CEA was a set of research priorities identified by expert stakeholders representing diverse technical expertise and sector perspectives. More information on the CEA approach, its applications to ENM research planning and potential utility in this or other contexts is available (Davis 2013; ICF 2011; Painter et al. 2014; Powers et al. 2012, 2014; RTI International 2012; U.S. EPA 2010a, b, 2012, 2013).

1.3 Background: December 2013 Society for Risk Analysis symposium

A CEA on MWCNTs in flame-retardant coatings applied to upholstery textiles was conducted in 2012, with a final summary report outlining research priorities for MWCNTs released in September 2013 (U.S. EPA 2013). To build on the MWCNT CEA, a panel discussion was conducted at the Society for Risk Analysis (SRA) Annual Meeting in December 2013 (Baltimore, MD). Four experts in the fields of MWCNT research, risk assessment, and risk management provided brief presentations on some of the specific MWCNT research priorities identified through the CEA process (see Supplementary Information [SI] Table 1 and (RTI International 2012; U.S. EPA 2013) for more information on the identified research priorities). These presentations provided a foundation for an interactive discussion, or "data dialogue" with audience members who represented a spectrum of perspectives in the ENM community (e.g., federal regulatory organizations, academic institutions, and industrial organizations). In brief, each expert presenter reflected upon a subset of the research priorities identified during the 2012 MWCNT CEA workshop process to discuss the following questions:

- What research related to (the selected MWCNT research question in SI Table 1) is currently underway?
- Who is doing that research?
- What are the barriers to continuing research related to this question?
- What incentives could encourage more research related to this question?

Through the above questions, each presenter attempted to connect research gaps for future MWCNT risk assessment and management that were identified in the 2012 workshop and the implementation of research to address those gaps. A summary of information presented to symposium participants is provided in SI Tables 1–4. These presentations provided a foundation for an interactive discussion, or "data dialogue," with an audience having diverse roles, expertise, and affiliation types. This Commentary focuses on and expands upon key points raised during that interactive conversation. Specifically, panelists and discussants identified a series of barriers, possible solutions to overcoming each barrier, and incentives to implement these or similar solutions (Table 1). While the symposium discussion was initially focused on MWCNTs, the recommendations that emerged are likely applicable to other ENMs.

2 Key barriers and potential solutions: improving connections between research, risk assessment, and risk management for MWCNTs

2.1 Starting with the end in mind: design research for a specific decision context

Currently, research managers and others in academic, federal, or private organizations generally develop ENM research plans without consideration of their pertinence to a specific decision context (e.g., plans to inform exposure assessments, hazard identification in risk assessment, and dose–response analyses) (NRC 2012). For example, an individual researcher may be more interested in advancing the scientific knowledge of a particular field, with the goal of publishing papers or acquiring grant funding, rather than in supporting a particular decision (e.g., dose–response analysis in risk assessment). This disconnect in research plans from decision contexts was one of the first barriers that panelists and discussants in the December 2013 SRA symposium identified for moving forward with MWCNT research priorities to support future risk assessment and management. Several discussants suggested using a product focus, similar to the use of flame-retardants in the CEA MWCNT case study, to address the lack of data clearly related to ENM EHS decisions noted above. As expanded on below, discussants noted that individuals planning research could utilize an example ENM product to structure the development of specific research questions. The resulting data may subsequently provide specific input to risk managers and others making EHS-related decisions across the product life cycle (e.g., setting occupational exposure limits during manufacturing).

Multiple factors may currently inhibit individual researchers (e.g., principle investigators and postdoctoral fellows) and research managers (e.g., individuals directing research for multiple laboratories or investigators within

Table 1 Summary of barriers, solutions, and incentives panelists and discussants identified in December 2013 symposium

Barriers	Solutions
Lack of decision context or product focus in ENM research planning	Funding organizations and other institutions that guide ENM research planning (e.g., NRC, NNI) increase emphasis on applied and basic ENM research proceeding in parallel
	ENM researchers continue to incorporate a product life cycle view into research planning
	ENM community members (e.g., researchers, risk analysts, product developers, and regulators) engaging in more collaborative research planning
Difficulty focusing on existing research priorities	Funding organizations and other institutions that guide ENM research planning develop performance measures, targets, and time frames to address EHS research priorities for ENM
Lack of avenues to publish negative results	ENM EHS community develops a journal specifically intended to inform sustainable ENM design through the publication of negative data
Lack of centralized public information on ENM applications or products on the market	Develop a new database for manufacturers and researchers to contribute aggregated data
	Build on existing databases to develop ENM-specific information; examples of existing databases:
	Nanomaterial Registry (NR) (https://www.nanomaterialregistry.org/ https://www.nanomaterialregistry.org/)
	National Institute of Environmental Health Sciences (NIEHS) Chemical Effects in Biological Systems (CEBS) (http://www.niehs.nih.gov/research/resources/databases/cebs/)
	National Institute of Standards and Technology (NIST) Materials Genome Initiative (MGI) (http://www.nist.gov/mgi/)
	The Nanodatabase (http://nanodb.dk)
	eNanoMapper (http://www.enanomapper.net/enm)
	Project on Emerging Nanotechnologies, Consumer Products Inventory (http://www.nanotechproject.org/cpi/)
Incentives	
Opportunities for dialogues between individuals planning research and those interested in the resulting data (e.g., a symposium at an established scientific meeting, workshop process to identify research priorities, and collaborative efforts to test methods)	
Additional funding for collaborative research (e.g., private–public partnerships initiated by investigators, and agency Requests for Proposals that specify multidisciplinary and multi-sector requirements, respectively)	
New educational programs in nanotechnology that focus on risk assessment, uncertainty characterization, and risk management concepts and applications relevant to evolving ENM as well as "traditional" research methods (e.g., ENM synthesis, ENM toxicology)	

EHS environmental health and safety, *ENM* engineered nanomaterial, *NNI* National Nanotechnology Initiative, *NRC* National Research Council

companies, research organizations, universities, and government agencies) from using an example ENM product to structure research. These factors include: (1) A lack of validated, centralized, and publicly available information on ENM products currently on the market and (2) differences in incentives for researchers compared to ENM product developers, regulators or other decision makers. Related to the first factor, the large number of ENM products and potential manufacture, use, or disposal scenarios for each one results in an intractable number of potential decision contexts to focus research on. Thus, some prioritization or categorization of decision contexts may be necessary for effectively planning research specific to particular ENM products or EHS decision contexts. Efforts to develop categories for ENM testing were the topic of a recent workshop hosted by the Organisation for Economic Cooperation and Development (OECD) Scientific Committee on Consumer Safety (SCCS 2013). Efforts to increase publicly available information on ENM products and develop incentives for collaborative research between researchers and individuals in EHS fields are discussed further below in Section III. The remainder of this section focuses on the potential solutions that panelists and discussants identified to better align research efforts with the goal of informing risk related decision making.

One solution is an increased emphasis on both applied and basic ENM research proceeding in parallel from funding organizations and other institutions that guide ENM research planning (e.g., the National Research Council [NRC] and National Nanotechnology Initiative). Basic research to understand fundamental ENM properties or behavior is unlikely to be designed to inform a particular decision and therefore may necessarily proceed outside a decision-specific context (i.e., applied research). For instance, a recent project under a joint EPA and National Science Foundation (NSF) program aims to develop sustainable catalysts for synthesizing organic building blocks, but the project has not yet defined the range of applications that could follow (NSF 2014a; b). Outcomes of this basic research may inform applied research related to improving production practices for a variety of ENM products in the future; yet, the growth of the market for ENM products suggests that parallel efforts to pursue applied research on currently available products would benefit EHS decision makers (e.g., risk analysts, product developers, regulators). EHS decision makers might consider working with funding organizations and others in the ENM community to develop appropriate incentives for researchers to pursue research designed to inform a specific decision context. Incentives for collaborative research are discussed in subsequent sections.

A second solution to this barrier includes ENM EHS community members expanding upon current efforts to incorporate a product life cycle view into research planning (Bauer et al. 2008; NNI 2011; Walser et al. 2011; Wardak et al. 2008). The product life cycle view benefits both basic research, exemplified in the EPA-NSF program noted above, and research developed around specific products. The difference between researchers who use a product life cycle perspective in basic versus applied research is in how much either knows about possible future uses of the data (e.g., basic researchers may develop ENM synthesis methods applicable to a variety of ENM product types, while applied researchers may focus on potential human exposures associated with "off-label" or unforeseen uses of ENM products). To that end, investigators who plan applied research with a product life cycle perspective may be able to collect data relevant to questions for a particular product that are not evident when looking at ENMs outside the context of a product. For example, researchers studying MWCNTs in general may not identify research questions specific to how the materials are used (e.g., is there environmental release of MWCNTs incorporated into textiles when the textile is exposed to fire?). In addition, because ENM properties (e.g., surface coating, tube diameter) commonly vary across product types, when researchers design experiments with a product focus, they can collect data more specific to the ENM physicochemical properties, and potential hazard or exposure, of that particular ENM product. Moreover, the product life cycle perspective can help researchers develop data relevant to how the product matrix (i.e., other chemical components of the product) may react with ENMs, and thus influence the potential for ENM release and subsequent behavior in the environment or biological systems (El Kazzouli et al. 2012; Fukumori and Ichikawa 2006; Nowack et al. 2012). Therefore, when researchers design investigations to evaluate ENMs in a specific product system [e.g., (Sooresh et al. 2012; Wohlleben et al. 2013)], they can produce particularly important data for EHS decision makers to understand potential ENM exposure or hazard in human or ecological populations. Yet, these types of investigations are only beginning to become available in the literature. The product life cycle perspective can help researchers and funding organizations develop additional basic and applied research by encouraging connections across (1) disciplines, (2) the phases of a product's life cycle, and (3) the many parties who have a need for or interest in the information (e.g., members of the public making a personal decision regarding use of a specific product or treatment).

Related to the potential utility of using the product life cycle to establish a variety of connections across the ENM community is a third solution that involves ENM community members engaging in more collaborative research planning. Specifically, ENM community members will need to work across technical disciplines and institutional sectors (e.g., academia and industry) in order to help identify and address research questions applicable to particular ENM products or decision contexts. For example, researchers and EHS decision makers could collaborate to identify a common set of experimental design (e.g., material physicochemical characteristics, exposure concentrations and duration, and experimental model) and reporting parameters (e.g., material and dose characterization). Researchers could then use these parameters when developing experiments, such as animal bioassays or higher-throughput assays (e.g., in vitro screens). EHS decision makers could use the resulting data to support tasks such as deriving toxicity values for allowable public exposures, or targeting exposure measurements to inform the development of recommended exposure levels for the workplace [e.g., see (NIOSH 2013a, b)]. Examples of these types of collaborative research planning efforts are included in a subsequent section, along with a discussion on the need to create incentives to encourage more support for cross-disciplinary, cross-sector collaborations from funding organizations and other institutions that guide ENM research planning (U.S. GAO 2012).

To facilitate the development of collaborative research plans that incorporate applied and basic research as well as the product life cycle, research managers could utilize one or more of the following example approaches to inform ENM research planning: Value of information (Linkov et al. 2011a), multi-criteria decision analysis (MCDA) (Subramanian et al. 2014), structured decision making (Gregory et al. 2012), or hypothesis mapping (Masinter et al. 2014). MCDA is a variety of decision-support methods used to select from alternative options based on user-defined criteria. MCDA can incorporate the views of multiple stakeholder groups and can be used to produce a set of ranked or prioritized options, hence providing value as a tool for research planning (Linkov et al. 2011b). The use of MCDA has gained attention in recent years for its utility in ranking the relative risks of various ENMs and selecting the 'best' synthesis process for ENMs (Canis et al. 2010; Tervonen et al. 2009). Structured decision making is a primarily deliberative form of multi-attribute analysis, focused on engaging stakeholders in identifying objectives and performance measures for evaluating options, generating alternative approaches (e.g., alternative research strategies) that meet these objectives, analyzing trade-offs between alternatives, and ultimately identifying suitable strategies and/or priorities (Gregory et al. 2012). In addition, value of information (VOI) analysis provides a tool for evaluating the benefits of acquiring new or additional knowledge on a particular problem in comparison with the costs of acquiring this knowledge (Back et al. 2007). VOI can be utilized on its own, or in combination with multi-attribute analysis, to aid in evaluating the value of alternative research strategies. Finally, research managers might combine MCDA and VOI approaches with other structured stakeholder engagement procedures, such as Nominal Group Technique, to develop research priorities (Powers et al. 2012). A recent review discusses other frameworks that incorporate a product life cycle perspective and may be useful for connecting ENM research planning with risk analyses and management efforts (Grieger et al. 2012).

2.2 Finding focus: systematically plan research to address identified priorities

Following efforts to develop research questions with a specific decision context in mind, researchers and research managers need to develop clear plans to carry out timely investigations in the identified priority areas. Yet, panelists and discussants in the December 2013 SRA symposium noted that a significant barrier to ENM research planning is a tendency to develop additional research questions rather than develop specific plans to address identified priority areas. Time and effort spent discussing new research questions can deplete resources research managers need to plan research that addresses priority areas identified through the collaborative planning approaches discussed above. To be clear, though, the scientific community recognizes the value of identifying new research questions; this practice is a cornerstone for the advancement of the science of nanotechnology and, by extension, the science of EHS for ENMs. The development of new research questions by researchers needs *management*, not *elimination*. Researchers' interest in developing new research questions for ENMs is understandable given the seemingly endless applications and unique properties of ENMs (Tolaymat et al. 2010); yet, a lack of focus on specific questions that include common experimental design factors (e.g., particular materials, test systems, and test methods) has resulted in discordant experimental results for toxicological and other parameters for most ENMs, as illustrated for silica nanoparticles (Schug et al. 2013) and MWCNTs (Liu et al. 2013). Examples of recent efforts to effectively coordinate the use of specific materials, test systems, and methods across laboratories are discussed further below (ILSI 2013; Schug et al. 2013). As highlighted in a recent evaluation of federally funded ENM EHS research in the USA, a solution to overcoming this barrier is to develop performance measures, targets, and time frames to address EHS research priorities for ENMs (U.S. GAO 2012). These three elements may be particularly useful in helping researchers and decision makers (including regulators) determine when the information is sufficient to move forward with interim risk analyses for particular ENM categories or products. The recent NRC reports on a research strategy for ENMs are clear examples of ongoing efforts to focus on identified priority areas (NRC 2012, 2013). The first report identified key research areas for supporting decisions about ENM EHS, such as the development of risk assessments and risk management plans and included a number of recommendations on how to address the identified research gaps (NRC 2012). The most recent report evaluates progress in the identified areas (NRC 2013). The scope of the NRC effort is quite broad, covering all ENM types. In contrast, as outlined above, discussants in the December 2013 SRA symposium highlighted that a focus on specific ENM-decision contexts may be particularly useful in producing data that could inform ENM EHS decisions. Future collaborative efforts between organizations with ENM interests might apply the model provided by the NRC reports to specific ENM products. Examples of these types of focused collaborative efforts are offered in subsequent sections.

2.3 Publishing negative data: develop venues to share findings that did not show ENM toxicity or exposure

Planning, implementing, and tracking research progress to inform risk assessment and management of ENMs would benefit from a more complete understanding of existing data. To that end, panelists and discussants identified a lack of scientific journals or other appropriate means to publish negative results (i.e., data indicating a lack of biological or environmental reactivity) as a key barrier for moving forward with MWCNT research (Hankin et al. 2011; Nanotechnology 2013). Although many publications have reported low or no toxicity for certain ENMs, negative results are generally presented only in the context of positive results (i.e., significant changes in a subset of endpoints or with a subset of ENM types included in the study).

Reasons for a lack of negative data in the literature vary [e.g., see (ter Riet et al. 2012)], and this barrier impacts research progress in at least two ways. First, a lack of negative data in the literature may impede research managers in efficiently using resources to implement research plans that address identified priority areas. Specifically, if individuals planning research are not aware of negative results in a particular test system or for a particular type of ENM (e.g., carboxylated MWCNTs), then they may utilize resources to conduct a redundant study. In contrast, if negative data are published, then researchers could design studies with the intent to test the reproducibility of results or the impact of small differences in experimental design. Second, a lack of negative data in the literature may also impede researchers and product developers' progress in designing sustainable ENMs. Sustainability may be defined in a variety of ways, but for ENM, it generally denotes materials for which data indicate low levels of human and ecological toxicity, environmental persistence, bioaccumulation, and/or other relevant parameters (Subramanian et al. 2014). Negative data can help inform the design of MWCNTs or other types of ENMs with a favorable cost–benefit ratio (i.e., minimal impacts on human and environmental health coupled with a clear benefit to human health or welfare, or other parameters, via the product system).

Discussants in the December 2013 SRA symposium suggested that one way to encourage the publication of negative data in the literature is to develop a journal specifically intended to inform sustainable ENM design through the publication of such data. While several journals are available for publishing negative results (e.g., Journal of Negative Results in Biomedicine (http://www.jnrbm.com/) for scientists and physicians, the Journal of Negative Results—Ecology and Evolutionary Biology (http://www.jnr-eeb.org/index.php/jnr), the Journal of Articles in Support of the Null Hypothesis (http://www.jasnh.com/) for psychological studies), they do not focus on ENMs and are not generally utilized by researchers in nanotechnology-related fields. As such, a journal specific to negative ENM-related data might help facilitate collaborative research across sectors. For example, academic researchers might work to publish with industry colleagues to present their negative findings in the context of future material or product design efforts. A new journal from Nature—*Scientific Data* (http://www.nature.com/scientificdata/about/)—that is focused on publishing datasets across multiple scientific domains may provide a valuable model for the development of the type of journal that discussants identified as important for ENMs. The development of a journal focused on negative ENM data may also help spur existing journals to publish negative ENM data more frequently.

2.4 Finding data relevant to products on the market: develop mechanisms to share

According to panelists and discussants in the December 2013 SRA symposium, future risk assessment and management efforts will benefit not only from improved access to negative data, but also from access to data on currently available MWCNT products. Some existing resources provide helpful information on this topic [e.g., production quantity estimates of select ENM types (Hendren et al. 2011), databases of manufacturer-identified nanotechnology-enabled consumer products currently on the market (Project on Emerging Nanotechnologies 2014) and of ENMs produced by various companies worldwide (Nanowerk 2014)]. However, researchers need more verified and centralized information to develop a clear understanding of specific ENM products and formulations currently available to consumers. As noted above, product characteristics (e.g., intended use, polymer composition) and the particular properties of the MWCNTs used in the product (e.g., surface coating, length, and diameter) influence the potential for environmental release of MWCNTs and their subsequent behavior in the environment or in specific biological systems (e.g., estuaries, agricultural soil, and human digestive tract) (Nowack et al. 2012). In order for researchers to collect data relevant to assessing the potential risks and benefits of MWCNT products, they need access to information on the specific types of MWCNTs, and other ENM types, used in products on the market. An inherent complication is that manufacturers may be reluctant to share data on products under development or on the market with researchers in academia or other sectors because of concerns about proprietary information (NNCO 2012).

According to panelists and discussants, one way that the ENM EHS community could address this barrier is to develop a database of aggregated information on MWCNT products. Information in the database would not be attributable to any particular manufacturer but would allow researchers to design experiments based on the types of materials and product specifications that are likely relevant to products available on the market. Moreover, if researchers subsequently added their experimental results to the shared database, researchers and product developers could evaluate results from across different laboratories or disciplines that may not normally work together. Thus, sharing information via a common database could benefit both manufacturers (e.g., early identification of material toxicity by outside researchers) and researchers (e.g., enhanced funding opportunities by demonstrating a clear need for proposed research). In pursuing this approach, the ENM EHS community would likely need to carefully consider a variety of database design questions (e.g., whether or not to require that users to contribute data in order to use the database). An alternative approach to developing a new database could be to build from existing database resources with MWCNT-focused data and thereby leverage existing infrastructures and prior investments. Potential partners could include the Nanomaterial Registry (NR) funded by the National Institutes of Health (NIH) (https://www.nanomaterialregistry.org/), the National Institute of Environmental Health Sciences (NIEHS) Chemical Effects in Biological Systems (CEBS) (http://www.niehs.nih.gov/research/resources/databases/cebs/), the National Institute of Standards and Technology (NIST) Materials Genome Initiative (MGI) (http://www.nist.gov/mgi/), and the newly launched eNanoMapper (http://www.enanomapper.net/enm). As discussed below, funding mechanisms or other incentives are needed to support the development of databases and other collaborative approaches.

3 Incentives for implementing solutions to identified barriers

As discussed above, panelists and discussants identified several solutions to the barriers that impede the development of research that informs future MWCNT risk assessment and management. They also recognized the potential value of developing clear incentives for researchers and others in the scientific community to work toward implementing these solutions. These incentives and examples of ongoing work that might serve as models for their implementation are outlined below.

3.1 Opportunities for data dialogues

Panelists and discussants recognized the potential value of mechanisms that encourage more cross-disciplinary, cross-sector research planning for specific decision contexts (e.g., setting occupational exposure limits during manufacturing, measuring human or ecological exposure potential from an ENM product). While the importance of multidisciplinary research is not a new concept (Anastas 2012; Rapport 1997), implementing research that crosses the boundaries of technical disciplines (e.g., material design, toxicology, and exposure science) and sectors (e.g., academia and industry) generally requires additional time and effort by the individuals involved, including those who carry out the research and those who develop the research announcements for contracts and grants at the individual and especially the center level (Harris et al. 2012; National Academy of Sciences 2004). The extra time and effort that collaborative research requires suggests that researchers and others involved in planning this type of research may need incentives that are different from those typically associated with research (e.g., peer-review publications and funding that support tenure or other career development opportunities) (Grieger et al. 2013). A series of opportunities that facilitate dialogues between individuals with diverse technical and sector perspectives may help incentivize researchers and others to invest the necessary time and effort by providing an environment for idea generation and increased understanding of alternative viewpoints.

The recent application of CEA to MWCNTs in flame-retardant coatings applied to upholstery textiles is one example of an effort to use a specific product focus to inform multidisciplinary research planning (U.S. EPA 2013). This and related CEA applications all used a case study document and structured workshop process to engage experts across a variety of technical disciplines and sector perspectives (U.S. EPA 2010b, 2012). Another example of a product-focused approach to research design and implementation for MWCNTs is the International Life Sciences Institute (ILSI) Nano Release project (ILSI 2013). Similar to the CEA approach, the ILSI NanoRelease project engages multidisciplinary experts representing several sectors; this work focuses on detection methods for MWCNTs. The NanoRelease project is now in the initial stages of implementing the methods research that experts engaged in the process identified.

Incentives for participants involved in both the CEA and NanoRelease work include establishing or enhancing connections with fellow experts engaged in the process, and recognition in the peer-reviewed or gray literature (e.g., review papers, white papers, and workshop summary reports). Both examples may serve as a foundation for future efforts to develop opportunities for dialogues between individuals planning research and those interested in the resulting data. Such opportunities might include additional sessions at scientific meetings (e.g., Society for Risk Analysis, Society of Toxicology, Society of Environmental Toxicology and Chemistry) that provide a forum for discussions among researchers and decision makers (e.g., risk analysts, regulators, and product developers) about research priorities for particular ENM types and key considerations for experimental designs intended to address priority areas. The resources needed to support these opportunities will likely range from relatively minimal (e.g., a symposium at an established scientific meeting) to substantial (e.g., a workshop process to identify research priorities or collaborative efforts to test methods). Yet, if research institutions, federal agencies, or other organizations in the scientific community provide these opportunities, then they may facilitate a more cost-effective use of resources in subsequent research (e.g., resulting data may be more easily utilized in risk analyses or other evaluations that inform risk management efforts). Notably, organizations could provide these opportunities at a lower cost by utilizing tools to support discussions without face-to-face interactions (e.g., webinar discussions, web-based rating forums such as IdeaScale, http://ideascale.com/) (Powers et al. 2014). The importance of funding these and other collaborative efforts is discussed further below.

3.2 Structured funding mechanisms for collaborative research

In addition to providing opportunities for increased engagement among individuals gathering data on ENMs and those potentially using the information, the panelists and discussants recognized the potential value of additional funding for collaborative research that emerges from such discussions. Both bottom-up and top-down mechanisms (e.g., private–public partnerships initiated by investigators, and agency Requests for Proposals that specify multidisciplinary and multi-sector requirements, respectively) could provide funding for projects that engage experts in research design, risk assessment, and risk management of ENMs. In addition to incentivizing greater collaboration across disciplines and sectors, such funding mechanisms could also promote trust to improve data sharing both within and among sectors (e.g., between different academic research labs or academic and industry organizations). A recent evaluation of federally funded ENM EHS research also identified the lack of tangible incentives (e.g., funding) as an important obstacle in cross-disciplinary and multi-stakeholder collaborations for responsible nanotechnology development (U.S. GAO 2012).

Funding efforts similar to those suggested by panelists and discussants include the joint EPA/NSF networks program (NSF 2014a) that includes ENMs, as well as the ENM-targeted Nanotechnology Characterization Laboratory (NCL) and NIEHS Centers for Nanotechnology Health Implications Research (NCNHIR) Consortium. The NCL represents a joint effort between the National Cancer Institute, the U.S. Food and Drug Administration, and NIST to provide the infrastructure and characterization services for nanomaterials used in cancer diagnostic or treatment technologies (see http://ncl.cancer.gov/). Industry partners agree to the release of the characterization information developed by the NCL. In exchange, the NCL runs a suite of expensive assays at no cost to the manufacturer. The NCL model could potentially be applied to the development and sharing of other types of ENM data (e.g., environmental transformation and fate studies). The NCNHIR represents a funding model in which researchers in several laboratories work collaboratively to develop data on an agreed-upon set of ENMs in order to better understand how the physicochemical properties of ENMs influence their behavior in biological systems and subsequent human health effects (Schug et al. 2013). Recent publications from this consortium identified key considerations for comparing results across test models, characterization approaches, and materials (Bonner et al. 2013). Additional examples of funding structures that encourage collaborative work on ENMs are available in Europe (NRC 2013). For instance, the European Commission recently funded several projects (e.g., SUN and GUIDENANO under the 7th framework program [http://www.sun-fp7.eu/ and http://www.guidenano.eu/.]) (EC 2013) that highlights the expectation of close collaboration with stakeholders and different industries to produce realistic models and tests. Anticipated outcomes of these types of projects include: (1) Better understanding and quantification of ENM release from manufacturing, use, and end-of-life stages; (2) a framework that can guide generation of data for modeling environmental transport and transformation; (3) better understanding of interrelationships among transformation, transport, and aging mechanisms in determining environmental exposure; and (4) better harmonization via more standardized characterization metrics. Additional calls are expected from the EC for research proposals that incorporate close collaboration between scientists, industry representatives, regulators, and insurance representatives.

3.3 Expanded educational programs for the next generation of ENM researchers

While resources for increased communication and collaboration between individuals currently carrying out work related to nanotechnology (e.g., material development, toxicology research, and product safety management) are important, panelists, and discussants also recognized the value of investing in incentives for the next generation of ENM researchers. Specifically, funding organizations such as the NSF or NIH could create training grants for academic institutions to develop new educational programs in nanotechnology that focus on risk assessment, uncertainty characterization, and risk management concepts and applications relevant to ENMs, in addition to "traditional" research methods (e.g., ENM synthesis and ENM toxicology). A similar approach is already underway in the medical field to train investigators in regulatory science (e.g., safety assessment and clinical trial development). This existing approach could provide a model from which to develop programs for ENM regulatory training (see http://publichealth.uams.edu/academics/certificates/certificate-in-regulatory-science/). Incentives to participate in these types of educational programs might include scholarships, career opportunities (e.g., internships in federal or industrial institutions), and recognition in the scientific community (e.g., certification in regulatory nanotoxicology). Finally, the development of ENMs is just one of many emerging technologies. To reap the benefits of these emerging technologies while simultaneously ensuring their safe and responsible use, traditional approaches to risk assessment and risk management may benefit from better integration of complex and often value-laden decisions that arise when working under conditions of extreme uncertainty. To this end, education and training programs could adopt a forward-looking approach to risk and sustainability for ENMs and other emerging technologies that include important aspects such as setting the decision context and addressing both variability and uncertainty (Subramanian et al. 2014). Such educational efforts could also produce a collateral benefit of greater understanding of emerging technologies in the broader community via the networks of those next-generation students. Greater public understanding of ENMs and other emerging areas of science could lead to a more informed foundation for evolving policies and regulatory requirements related to emerging technologies or materials [concern about a lack of public understanding about ENMs was part of a recent food labeling debate and illustrates the importance of public education and communication on ENM, see Europarl (2014)].

4 Closing remarks

Nanotechnology research has produced numerous exciting applications for ENMs in various consumer and industrial products, but a clear understanding of ENM EHS issues is only beginning to come into focus (NRC 2013; Schrurs and Lison 2012). To continue making progress toward more informed ENM EHS decisions, there is a pressing need for increased dialogue and collaboration among the many researchers gathering data in diverse fields (e.g., material characterization, environmental behavior, exposure, and toxicity) and the large number of people interested in using those data to inform their decisions, particularly regarding environmental and human health (e.g., risk analysts, regulators, and product developers). This Commentary highlights outcomes of one such dialogue in a December 2013 SRA Symposium that included researchers working in several technical disciplines as well as individuals involved with informing regulatory decisions and other risk management efforts. The discussion identified a series of (1) barriers to the development of research that informs future ENM risk assessment and management, (2) potential solutions to overcome such barriers, and (3) incentives to facilitate implementation of those solutions.

Key barriers identified by participants in the symposium included (1) a lack of decision context or product focus in ENM research design, (2) difficulty in switching focus from the development of new questions to the implementation of research to address existing priorities, (3) a lack of negative data in the published literature, and (4) a lack of publicly available information on product specifications for ENMs used in applications and products on the market. Specific solutions to overcome these barriers are discussed above, and each solution might benefit from efforts to develop incentives for greater communication and collaboration among individuals gathering the data and those interested in using the information. These incentives relate to (1) opportunities for data dialogues, (2) structured funding mechanisms for collaborative research, and (3) expanded educational programs for current and future ENM researchers.

Importantly, this Commentary is not intended to be an "end" to the conversation that took place in December 2013, but rather a part of a broader dialogue that helps ensure important risk assessment questions are answered for ENMs. This dialogue will be facilitated through actions such as those outlined above. Moving toward greater communication and collaboration on ENM research to inform future risk assessment and management will require not only enhancing opportunities for dialogue, but also acting on the outcomes of such dialogues.

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