

### What Tools are Being Used to Detect and Quantify Nanomaterial Exposures?

Both analytical and modeling tools are being used to estimate and assess nanomaterial exposures across the product life cycle. The complexity of nanomaterial detection and quantification increases across the life cycle of products and after human contact. This increase is because nanomaterials in stock solutions are fairly homogeneous, free of interferents, and at relatively high concentrations compared to finalized products. As nanomaterials are incorporated into products they may be from 0.1 to 5 % by weight of a product (e.g., CNTs in polymers [6]) down to as low as < 0.01% by weight (e.g., TiO<sub>2</sub> in foods [7]), and even lower in some consumer products (e.g., 1.5 mg of quantum dots per television [8]). Not only do low concentrations hinder detection, but also, the nanomaterials are often enmeshed in heterogeneous and complex matrices of similar elemental composition (e.g., carbon nanotubes in carbon-based polymers).

A number of adaptations to available, non-nanotechnology-specific techniques hold promise for nanoparticles. In pure solutions, simple light scattering detection systems are appropriate at > 1 mg/L in liquids. Advancements to inductively coupled plasma mass spectroscopy (ICP-MS) or time-of-flight mass spectrometry (TOF-MS) software, while using the same equipment hardware, are allowing collection of data for some nanomaterials containing metals when processed in “single-particle” mode. This adaptation allows for counting and sizing of nanomaterials at very low concentrations on the order of parts per trillion. However, this sensitivity is highly dependent upon the element (well-detected elements are silver, gold, cerium, and indium, but not titanium or silicon), and more elegant data processing holds some promise. Even minute quantities of rare earth elements (e.g., yttrium or cobalt in CNTs) hold promise for advancing these detection methods. Other methods developed for monitoring soot in the air have been adapted for CNTs.

Methods to extract, separate, and/or concentrate nanomaterials from complex matrices are under development and hold promise to separate various forms of nanomaterials (e.g., to separate ionic and nanoscale forms of metals). While electron microscopy remains the “gold standard,” there are really no methods to answer the simple question, “How many nanomaterials are in a product?” (for example, a computer), especially when information from the manufacturer is not available.

A potential strategy is to combine the availability of the analytical techniques with a tiered sampling approach, but this approach hinges upon having acceptable detection limits. Detecting ENMs among natural and/or incidental NMs with many times higher relative concentrations is challenging. It is also very difficult, and usually extremely expensive due to required access to specialized equipment, to track transformations in nanomaterial properties effectively over time or through the life cycle of a product. This challenge includes tracking transformations during human exposure (dermal, oral, or inhalation). Outside of biomedical drug delivery systems, few human studies track NM biodistribution, bioavailability, or bioaccumulation, or adverse outcomes from nanomaterials released from consumer products.

## Occupational Exposure: Current State, Challenges, and Future Research

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The introduction of engineered nanomaterials into commercial material applications continues at a rapid pace, despite the overall evolution of the technology now having moved from the initial “excitement stage” to a phase driven by more realistic market forces. High-volume manufacture and formulation of “first-generation” nanomaterials, such as nanoscale titania and ceria, continues globally. Refinement and improvement of manufacturing processes for more sophisticated and promise-filled nanomaterials, such as carbon nanotubes and graphene, are being reported almost daily. All of these indicators point to increasing

volumes of engineered nanomaterials being manufactured and an even greater number of product applications for these materials. The petrochemical industry, for instance, will be using increasing quantities of nanoscale catalysts. One of the natural outcomes of this continued rise in volumes and product applications is concern for human health and environmental damage. Whether in a research laboratory, a manufacturing facility, as part of a commercial task, or in the reuse or recycling of these materials, there are workers involved. At nearly every step along the life cycle of an engineered nanomaterial and the products that contain them, there is potential for workers to be exposed. Evaluating worker exposure, characterizing potential risks, and implementing effective controls to eliminate or minimize risk are all critical to ensuring responsible development of the technology because workers represent the first opportunity for human exposure to any new technology or the materials it produces. Often, the materials may not be completely characterized and their potential hazards not fully understood. In many ways, creating an effective worker health and safety program for a new technology or material is the first step in building a legacy of success for responsible development, sustainability, and stewardship.

To evaluate the potential risk of engineered nanomaterials in any occupational setting, it is extremely important to develop effective exposure assessment science that focuses on properties that are characteristic, if not unique, to this class of materials. Such an approach links toxicology, risk assessment, and epidemiology to create a complete picture of the potential risks and impacts. Hazard information is being generated at a rapid pace for many nanomaterials from toxicological studies. The rise of hazard data and efforts to derive occupational exposure limits (OELs) has accelerated efforts to evaluate occupational exposures. Despite progress in recent years in measurement techniques for nanomaterials, there remains much uncertainty as to the appropriate exposure metrics to use. The growing number of dose metrics proposed for toxicology evaluations, especially for inhalation studies with inhalation being the primary workplace exposure pathway, compounds this uncertainty. While metrics such as particle number, surface area, and surface charge are being explored as more advanced approaches to measure dose and exposure, mass continues to be the primary metric used in reporting results from toxicology studies. The heterogeneity of nanomaterials also complicates formulating exposure assessment strategies. Using multiple sampling, analytical, and instrumental approaches has become widespread among industrial hygiene practitioners, but methods that are more rugged are still needed. This need is particularly important for complex exposure scenarios such as mixed manufacturing facilities and construction sites. The importance of occupational exposure levels, like the National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limits for titanium dioxide and carbon nanotubes, cannot be overstated as benchmarks for evaluating exposure assessment results.

Several groups around the globe have proposed various workplace-exposure assessment strategies. Employing a multi-metric and tiered or phased approach has become one of the more effective approaches. A basic challenge continues to be potential differences between materials as measured in the workplace compared to the seemingly same materials when evaluated in toxicology studies. Efforts are underway in several research institutes to close the gap between nanomaterials encountered in the workplace or the environment and those that are evaluated in their pure (pristine) or as-manufactured state. These efforts are aimed at making the toxicology evaluations more representative of what is encountered in an actual exposure scenario. This area of research will improve workplace exposure science by linking the efforts of toxicology, exposure measurement, and epidemiology. By creating a feedback process from exposure measurements to toxicology studies, dose metrics and test materials will become more representative and risk characterizations more realistic. Combining health outcome studies into the overall strategy will

incorporate the use of biological indicators such as biomarkers for a more complete picture of the actual exposure experience. The critical challenge is to identify meaningful biomarkers.

Finally, the potential release of engineered nanomaterials from intermediate or finished products has become a growing concern. Research is underway by several groups to evaluate the overall potential for exposure to engineered nanomaterials along their complete life cycle. While the biological significance of these materials in any sort of release is not known, a prudent approach is to characterize the potential for release and explore methods to minimize or control releases. NIOSH has demonstrated that engineering controls are effective in reducing exposure to nanomaterials [9–11]. Older, proven control technologies must be considered, but new thinking is critical as well.

## Health Risk Driven Exposure Assessment for Consumers during the Life Cycle of Nanomaterial-Containing Products

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The number of consumer products containing engineered nanomaterials has increased 5–10 times over the last 5 years, among which titanium, silver, and carbon-based ENMs are the predominant materials employed [12]. This increase may affect consumers' exposure to ENMs and associated chemicals along the life cycle of these consumer products. ENMs can be found in sporting goods, appliances, home and garden wares, medicinal products, electronics and computers, food and beverages, children's toys, clothing, and personal care products [12], thereby implying potential exposures via all of the three major exposure routes of inhalation, ingestion, and dermal contact. Studies have been reported in the literature that use multiple approaches to assess consumer exposure within the context of human health risk assessment.

### Deriving Exposure from Consumer Product Data and Exposure Scenarios

A key component of this approach to exposure assessment is characterization of the consumer product for ENM contents. For example, a tiered approach has been used to characterize silver nanoparticles in selected consumer products relevant to children's potential exposure [13]. The approach first identifies all consumer products relevant to the defined exposure. Second, a select subset of the products is identified as having high exposure potential. The final step is to measure the content and form of silver in this subset of products. The analytical method commonly used to determine metal content in consumer products has been ICP-MS; the methods for determining physical forms of ENMs are scanning electron microscopy (SEM) and transmission electron microscopy (TEM). New technologies like surface-enhanced Raman spectroscopy (SERS) have also been explored for the characterization of nanoparticles in consumer products [14]. Since exposure is more closely related to the level of ENMs released from consumer products than the ENM's content, studies have been conducted to determine ENM release to the ambient air or to a relevant body organ (e.g., skin surface). Among these studies, experiments using a chamber with a well-controlled ventilation system in which spraying actions mimic consumer practices provide both release rate and physico-chemical properties of ENMs [15, 16]. For example, through characterizing the materials released during spraying of cosmetic powders, Nazarenko *et al.* found that a user would be exposed to nanomaterials predominantly through nanoparticle-containing agglomerates larger than the 1–100 nm size fraction of aerosols [17]. These agglomerated particles are different in size compared to the nanomaterials originally added to the products, resulting in deposition in a different region of the respiratory tract.



### **About the National Nanotechnology Initiative**

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

### **About the Nanoscale Science, Engineering, and Technology Subcommittee**

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

### **About the Nanotechnology Environmental and Health Implications Working Group**

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

### **About This Report**

This document is the report from a workshop sponsored by the Consumer Product Safety Commission and co-hosted by the NNI that was held on July 7 and 8, 2015. The technical workshop was designed to bring together experts from Federal, regional, State, and local governmental and nongovernmental organizations to provide an assessment of the state of understanding in nanotechnology-related exposure science. The goal of this report is to provide an impactful document that will be useful in planning the future direction of exposure science and nanomaterials environmental, health, and safety research. This workshop is one of a series of technical workshops sponsored by the NSET Subcommittee to inform long-range planning efforts for the NNI and its EHS Research Strategy. This report is not a consensus document but rather a technical report with an aim to assess the state of exposure science and the tools and methods available to characterize and quantify exposure of people and the environment to engineered nanomaterials from manufactured products.

### **About the Report Cover and Book Design**

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# Workshop Proceedings

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