The nanotechnology revolution has great potential to enhance a wide variety of products, services, and industries. This promise, however, is challenged by the concern that some manufactured nanomaterials (MNMs) have the potential to become hazardous pollutants that threaten public and environmental health. Currently, MNMs are being incorporated into a broad range of commercial products at a rapid rate, which is outpacing the development of knowledge and regulations to mitigate their potential environmental impacts.

Motivated by this concern, and recognizing an opportunity to steward nanotechnology as a tool for sustainability rather than a future environmental liability, the International Council on Nanotechnology (ICON), with financial support from the National Science Foundation, Natural Environment Research Council, and British and Science & Innovation Network, British Consulate-General Houston, recently hosted an international multidisciplinary workshop at Rice University (Houston, TX) to reflect on the state-of-the-art in nanotoxicology research and to identify the critical knowledge gaps that should be addressed to enable eco-responsible design and disposal of nanoenabled products (Figure 1). The following is a distillation of critical discussions and ideas generated by more than 50 leading experts from North America and Europe.

Critical Knowledge Gaps and Priority Research Areas. Whether MNMs could be designed to be “safe” and still display the reactivity or properties that make them useful is an outstanding and daunting question that needs urgent attention. Some scientists believe that manipulating MNM structure to suppress the properties that make them toxic might compromise their usefulness and advocate risk management primarily through exposure control. However, the modern chemical industry has demonstrated that a wide range of substances can be reengineered to create safer, greener, and yet effective products and processes. Encouraging examples include the substitution of branched alkylbenzene sulfonate surfactants, which caused excessive foaming in the environment, with biodegradable linear homologues, and the replacement of ozone-depleting chlorofluorocarbons (CFCs) by less harmful and less persistent hydrochlorofluorocarbons (HCFCs). Further...
thermore, even those MNMs whose value draws from the same chemical activity that may cause adverse biological effects could be amenable to eco-responsible life-cycle engineering. In these cases, tailored coatings, on-board packaging, or special disposal strategies are worthy of consideration.

To realize eco-responsible nanotechnology systematically requires improved understanding of how MNMs interact with environmental systems and their ultimate fate through application, reclamation, recycle, reuse, remanufacture, and disposal. The ICON workshop identified a series of critical knowledge gaps that represent the most significant barrier to achieve environmentally benign design and disposal of MNMs. The most important of these are elaborated below.

Structure—Activity Relationships for Manufactured Nanomaterials in the Environment. Modifying the chemical structure of a nanomaterial could change the way it interacts with both its physical and biological environment, ultimately affecting its mobility, reactivity, bioavailability, and toxicity. In theory, it may be possible to understand how MNM structure affects properties and behavior, and this could be used to “design away” problematic features and to incorporate environmentally benign functionalities without sacrificing performance. However, it is unclear whether the structure—activity relationships (SARS) framework developed for chemical species could be applied to nanoparticles; this is certainly a challenging issue. Thus, there is a need to delineate the merits and limitations of SARS to predict stability and function of MNMs in the environment. Particular emphasis should be placed on discerning structural properties that alter bioavailability, bioaccumulation, and toxicity, and how MNM structural transformations in different environments alter their properties, behavior, and impact.

The Nanoparticle—Environment Interface. The measurement and characterization of MNMs in environmental and biological matrices is fundamental to understanding the fate, transport, and potential impact of these materials. However, current analytical capabilities to quantify and to characterize MNMs in complex matrices are in their infancy and face great challenges in terms of separating, preconcentrating, and detecting MNMs (or surrogate “indicator” analytes) with minimal alteration of their properties. Thus, the development, standardization, and validation of a toolbox of robust analytical methodologies (and possibly new instruments) remain a very high priority. Furthermore, MNMs are often characterized in their original form prior to ecotoxicological testing, even though they will likely be transformed in the environment before reaching a receptor (Figure 2). For example, MNMs may agglomerate, acquire, or lose coatings and experience dissolution or redox reactions that alter their surface charge, reactivity, and toxicity. Thus, there is also an urgent need for rapid analyses to follow these changes and to discern the forms of MNMs that ecological receptors are exposed to, and collaborations between ecotoxicologists and analytical chemists that couple MNM dynamic characterization and toxicity testing should be promoted.

Manufactured Nanomaterial Bioavailability and Sub-lethal Effects. There is currently no consensus on preparation and testing procedures for the assessment of MNM bioavailability and related impacts on organisms. As a result, different laboratories may generate different results for the same type of MNM. This underscores the need for standardized protocols to enable comparison of results, with the recognition that such protocols need to be carefully considered to ensure that they are relevant and are likely to generate meaningful results. For example, as the scale of biological hierarchy and complexity increases (from molecular to biochemical, physiological, individual, population, and community responses), the relevance of dose—response studies increases, but so do the response time and the potential for confounding factors. Related important but unexplored areas of research include the potential for trophic transfer and biomagnification of MNMs
through food webs, including discerning likely entry points and sub-lethal impacts to ecosystem services such as primary productivity, nutrient cycling, and waste degradation. Uptake mechanisms by different organisms are also poorly understood and require consideration of reciprocal effects because the MNM may affect the living system and vice versa.

**Predictive Modeling of Multimedia Fate and Transport.** Computational models that predict the form and concentration of MNMs at the point of exposure remain an unmet high-priority challenge to enable risk assessment. Such models would be important to identify environmental compartments and ecological receptors that are most susceptible to the accumulation of different MNMs. A possible advantage may be that some MNMs may exhibit properties similar to dissolved solutes (e.g., chemical reactivity) and colloidal particles (e.g., aggregation and deposition), for which advection—dispersion—reaction models and filtration equations have respectively been developed and validated. The critical knowledge gap in multimedia modeling is primarily related to uncertainties about the applicability of existing approaches to the nanodomain and the identification/validation of the key properties and rates that define MNM transport and fate. This includes consideration of processes that transform MNMs or modify their surfaces and aggregation states (Figure 2), which may vary as a function of environmental conditions. Since we know little about the processes in type 2–4 (e.g., surface modification, physical attenuation mechanisms, degradation and transformation mechanisms; Figure 2), it should not be assumed that these mechanisms lead to loss or inactivation of the MNM. For instance, nanoparticle aggregation and precipitation in aqueous systems may lead to benthic organisms being a primary target, while disaggregation rates and processes are barely understood in these complex environments. Nevertheless, stochastic particle-tracking models might be appropriate to assess nanoparticle transport and fate. 

**Disposal Scenarios and Release Dynamics.** As a first step to predict exposure and to evaluate the need for interception or remediation technologies, it is necessary to understand source dynamics (including MNM leaching from commercial products) and the scale of discharges into various environmental compartments. This requires an inventory of the magnitude and use of MNMs within defined spatial domains. Quantification of potential fluxes to the environment from both point and nonpoint sources is also a priority that can only be accomplished after developing appropriate analytical tools or identifying sentinel species that can be monitored to detect pollution by MNMs.

**CONCLUDING REMARKS AND OUTLOOK**

The need for proactive steps toward the long-term goal of safer design and disposal of MNMs has never been clearer nor more urgent. Pertinent research to advance these efforts would greatly benefit from the development of robust analytical techniques to track MNMs in the environment and validate models. Another collective priority is to develop reference MNM libraries for sharing by different research teams.

The above research priorities could fit the traditional risk assessment framework to integrate hazard identification with dose—response and exposure assessment for evaluating and mitigating potential impacts. For example, research on SARs to discern the functionalities and properties that make MNMs harmful should be integrated with research on their release and subsequent migration and fate following disposal to determine which ecological receptors might be at a higher risk. Proactive risk assessment is also important to assess the need for institutional response, such as requiring the labeling of some products containing MNMs and the adaptation of existing regulations for their recycling and disposal.

Overall, there are many outstanding questions that provide an opportunity for knowledge exchange and collaboration between disciplines to prioritize mitigation strategies. In fact, all of the issues outlined above require multidisciplinary teams, across international boundaries, to generate useful and relevant answers that contribute to the sustainability of nanotechnology.

**REFERENCES AND NOTES**


