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U. S. federal perspective on critical research issues in nanoEHS

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This article discusses critical issues and opportunities going forward in nanotechnology environmental, health, and safety (nanoEHS) research from the perspective of Federal Government Agency participants in the United States (U.S.) National Nanotechnology Initiative (NNI) interagency Nanotechnology Environmental and Health Implications Working Group (NEHI). NEHI is responsible for coordination of Federal Science Agency nanoEHS research. As participants in NEHI, we examine these critical issues from an integrated, transdisciplinary perspective, noting examples of impactful research efforts that are advancing knowledge in these areas. Major themes identified include detection, measurement, and characterization of real-world nanomaterial exposures, understanding the biological transformation of nanomaterials and their potential (eco) toxicological implications, understanding the landscape of nanotechnology-enabled products in commerce, and advancing the EHS knowledge infrastructure related to nanomaterials and nanotechnology. Significant investments in nanoEHS research over two decades have led to establishment of a unique and diverse multidisciplinary, multisector community of practice. These investments must be leveraged and adapted not only to future nanotechnology, but also to use as a model for accelerating acquisition of safe and reliable risk information for tomorrow's emerging technologies for a more sustainable and competitive world.

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Environmental significance

This federal perspective provides a framework of critical research needs to address potential nanotechnology-related environmental, health, and safety (nanoEHS) issues. A robust nanoEHS framework is essential for safe, responsible development of nanomaterials and nanotechnology-enabled products (NEPs)—a key goal of the U.S. Government's National Nanotechnology Initiative. NanoEHS research is essential to establishing the public confidence and regulatory certainty needed for the commercial success of NEPs, which is evolving at a rapid and accelerating pace. Evolving NEPs require continuously refining and advancing methods to detect, measure, and assess NEPs behavior in settings that reflect realistic workplace, consumer, and environmental exposures for developing effective management strategies. Moreover, a robust scientific framework for evaluating nanomaterial applications promotes productivity and manufacturing.

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Introduction

Nanomaterials, incorporated into new technologies and platforms, promise "lighter, stronger, and more functional materials, new ways to store and manipulate information, and early detection of diseases".[1] While exploiting beneficial aspects of the nanoscale properties of these engineered nanomaterials (ENMs), a significant body of research in the last two decades has expanded our understanding of how ENMs behave in the environment and in biological systems. These endeavors have laid a strong foundation for evaluating potential nanotechnology environmental, health, and safety (nanoEHS) risks to the environment, workers, and consumers.[2] At the same time, nanotechnology is enabling a growing range and complexity of materials and products incorporating nanoscale systems, structures, and devices. The diversity and evolution in applications and products using nanotechnology has prompted consideration of how the United States (U.S.) nanoEHS research agenda should adapt to continue to support robust safety assessment of these materials.

Identifying challenges, gaps, and emerging nanoEHS research needs is essential to meeting the U.S. NNI's (National Nanotechnology Initiative) goal of responsible development. Responsible nanotechnology development aims to address the societal dimensions of new technologies while accelerating research and developing the infrastructure to support commercialization.[1] The NNI represents the formal mechanism for the U.S. Government (USG) to realize "the NNI vision of a future in which the ability to understand and control matter at the nanoscale leads to ongoing revolutions in technology and industry that benefit society".[1] The authors, federal scientists and program managers integrally associated with the USG's intra- and extramural nanoEHS research programs, herein present our collective appraisal and vision of key nanoEHS research directions. As participants in the NNI's NEHI (Nanotechnology Environmental and Health Implications) Working Group, we examine these issues from an integrated, transdisciplinary perspective, citing examples of current research efforts shaping the path forward in each of the areas discussed. We summarize the research areas identified in the NNI's 2011 Environmental, Health, and Safety Research Strategy[3] that remain important and envision emerging priority topics.

NEHI began the process of revisiting its nanoEHS strategy by looking back at the progress and lessons learned in a series of public webinars[4] and identifying highlights of the NNI interagency collaboration.[5] While certain specific classes of nanomaterials—metals, metal oxides, carbon nanotubes, and others—have been studied using medium- to high-throughput screening approaches, methodological and data challenges remain. NanoEHS risk assessments continue to be hampered by the limited availability of data, including information on statistically non-significant findings, and investigators not making their data accessible to the wider community. Considerations for refreshing the NNI's 2011 strategy are framed around maintaining confidence in U.S. nanotechnology innovation pathways, and we signal to the NNI community and international collaborators areas of interest and broad themes that the USG nanoEHS community will pursue in the near term.

Thus, maintaining confidence in the capacity of the nanoEHS safety assessment and regulatory framework to handle the logarithmic growth of new materials and hybrid nanostructures (including nano-bioelectronic systems and devices being developed for biosensor, nanomedical, and environmental applications, among others) remains a fundamental task. It is strategically important now to outline the health and safety research targets as the NNI broadens the framework for achieving its responsible development goal. This work describes complementary elements to actions aimed at implementing the NNI's most recent strategic plan. We contend that further research and consensus building around these topics will yield additional opportunities to understand and minimize potential risks and find control strategies (Fig. 1).

Critical issues and opportunities going forward

Detection, characterization, and measurement

The infrastructure to detect, measure, and characterize ENMs is the foundation for robust and reproducible nanoEHS research. Since 2011, NNI agency research and development (R&D) activities in this area have focused on the goals of (1) developing measurement tools to detect, identify, and determine the physicochemical properties of ENMs in products and complex matrices; and (2) determining biological response and enabling hazard and exposure assessment of products, throughout all stages of their life cycles.[6] As noted in the NNI's 2014 nanoEHS progress report, "Federal agencies will continue to invest in tools and share information essential to assess and manage potential risks of current and anticipated ENMs and nanotechnology-enabled products throughout their life cycles".[7]

Progress towards both goals has been significant and steady. Researchers have transitioned from investigating pristine ENMs in simple matrices, to real-world forms at levels that reflect environmentally relevant exposures, and to examining interactions in more complex matrices (*e.g.*, soil, sediment, biological tissues). For example, a framework for understanding ENM transitions and actions in environmental or biological media was developed.[8] However, more reliable and reproducible standards, assays, and guidance documents are needed to study degradation byproducts and releases from consumer products.[9,10] While the development of standards, guidance documents, and test methods is underway,[11] more work is needed. NNI agencies will continue to bolster efforts to understand the full range of factors influencing the reliability and reproducibility of nanomaterial measurements in complex environments.[12] For instance, the National Institute of Environmental Health Sciences (NIEHS)-

Fig. 1 Overview of U.S. federal perspective for addressing critical issues in nanoEHS research.

funded consortium program performed two phases of *in vitro* testing with selected ENMs in an effort to identify and minimize sources of variability.[13]

The tools, technologies, and knowledge gained over the past two decades of nanoEHS support by NEHI participating agencies will be expanded to further study substances of emerging concern, including incidental nanomaterials in the environment such as nanoplastics and emissions from low-cost 3D printers, which are becoming common. Work continues on assessing their unique polymer aerosols, life cycle assessment, and the contributions of these materials to exposure and health effects. The tools and methods available to detect incidental nanomaterials and ultrafine particulates —nanoplastics, 3D printing matrices and emissions, cigarette smoke and electronic cigarettes—are continually improved by research on ENMs.[14–16] Evaluating materials such as nanoscale plastic fragments that are not precisely engineered will require greater consistency in application of nanometrology terminology and definitions, and new and enhanced analytical capabilities and approaches to address nanoplastics behavior and reactivity. Such developments are important steps towards answering fundamental questions about the human health risks of nanoplastic exposure.[17] The U.S. federal nanoEHS community will leverage the capabilities and expertise of multiple agencies to jointly conduct research to fully exploit and build on the capabilities, infrastructure, and expertise within the different agencies to address these questions. Expanding support for extramural research and international partnerships, such as the NIST and European Commission Joint Research Centre collaboration on micro- and nanoplastics characterization, would be an important path forward.[18]

Internationally recognized documentary consensus standards will play an increasingly important role in nanoEHS due to their regulatory impact and their role in ensuring accurate and comparable measurements critical to assessing risk and facilitating international trade.[59] In short, standards address the need for validated methods, guidance, and specifications that underpin the measurement infrastructure as envisioned by the 2011 NNI EHS Research Strategy.[3] NNI agencies have been actively engaged in the development of documentary standards through International Organization for Standardization (ISO) Technical Committee 229 (Nanotechnologies) and ASTM International (formerly known as American Society of Testing and Materials) Committee E56 (Nanotechnology) since these committees were formed in 2005. Agency representatives continue to hold leadership positions and to provide critically needed technical expertise. As of March 29, 2023, ISO TC 229 has published 74 standards and 28 technical reports covering a broad spectrum of materials, applications, and products, including a comprehensive 13-part terminology series.[60] Similarly, ASTM International Committee E56 has published 32 active standards, including 12 standard test methods and a 6-part series focusing on workforce education in nanotechnology.[61] It is noteworthy that development of all existing ASTM test methods in committee E56 were led or co-led by NNI agency experts, including the Food and Drug Administration (FDA), the National Institutes of Health (NIH), the National Institute of Standards and Technology (NIST), and the National Institute for Occupational Safety and Health (NIOSH). In both committees there is a growing emphasis on product- and measurand-specific standards, including analytical test methods and material specifications in response to the continuing evolution of measurement technology, industry needs, and the regulatory landscape.

NNI agencies play a considerable role in the development of Organization for Economic Cooperation and Development (OECD) guidance documents (GDs) that help improve (eco) toxicological and environmental fate testing of ENMs using OECD test guidelines. For example, the 2022 OECD GD 317 details recommendations for aquatic and sediment toxicological testing of nanomaterials.[19] However, some topics such as quantitative methods for the concentration and potential transformation of ENMs in soils and sediments[20–22] and organism tissues[23] will require additional research. Quantification of ENMs is most straightforward in simple aqueous samples, and becomes substantially more challenging when other matrices, some of which may contain naturally occurring nanoparticles, are evaluated. In addition, the potential for alternative test methods, such as *in silico* or *in vitro* tests, to supplement and potentially replace fish acute toxicity[24] and bioaccumulation tests of ENMs is currently under evaluation.[25]

Lastly, the need for reference standards (artifacts) to develop and validate measurement methods, quantify accuracy of measurements, and serve as benchmarks for intercomparison studies and in applications, remains a substantial roadblock to progress. In 2013, Stefaniak *et al.*[26] provided a critical assessment of these needs for the nanoEHS field, but progress has been slow due to multiple factors, including a lack of consensus on prioritization and the need for greater interagency cooperation. For instance, in the emerging nanoplastics area, collaborative efforts across agencies (*e.g.*, NIST, Environmental Protection Agency (EPA), FDA) and with international partners are speeding up the development of urgently needed reference standards and representative test materials.

Understanding biological transformations

A wealth of information exists regarding the effects of pristine ENMs with defined physicochemical properties on biological systems. However, ENM interactions with biotic and abiotic environments are varied and undergo dynamic spatial and temporal transformation. These interactions have been studied using a broad range of animal models and *in vitro* cell culture systems representing diverse primary and secondary target organs.[27] Investigating these interactions and the complex interactions that occur between the human body's physiological processes and various types of nanoparticles, nanostructured materials, and nanoengineered surfaces remains an important avenue for research, and advanced methods and instrumentation offer new opportunities in this area.[28] Importantly, microbial transformations in the environment (*e.g.*, in sediment, soil, water bodies, and landfills) have been shown to transform carbon-based and metal-based ENMs.[3,80]

Of course, the ultimate health and safety assessment for ENMs requires evaluating effects in human populations exposed to ENMs. Workers are generally the first in society to be exposed and at greater levels, to a new technology and assessment of exposure to occupational cohorts to ENMs should be assessed. This is especially important when animal studies have shown effects of exposure.[62,63] For future epidemiological studies there is a need to overcome current barriers such as identifying appropriately sized cohorts, obtaining representative exposure data, and developing studies with adequate latency.[64–67] In 2012, a roadmap was developed for a globally harmonized approach for occupational health surveillance and epidemiological study of nanomaterial workers, and to date some progress has been achieved.[65,68–70] Cross-national collaboration following the roadmap may be fruitful in developing epidemiologic studies on workers with potential exposure to nanomaterials. NIOSH has established an exposure registry developed from a cross-sectional epidemiological study of workers at U.S. facilities manufacturing, distributing, or using carbon nanotubes or carbon nanofibers.[71] Reviews of other nanomaterials, many in commercial use, concluded that epidemiological studies are warranted and more research and monitoring of exposed workers is needed.[63,65,72,73]

Other important topics for future work should involve improving *in vitro* predictivity of corresponding *in vivo* exposures and effects, and evaluating the role of alternative testing strategies for ENM risk analysis.[29,30] Research on nanomaterial behavior in biological systems should be expanded and include transformed nanomaterials. Studies representing biologically or environmentally relevant exposure scenarios are needed to identify key mechanistic pathways that facilitate response prediction. The USG nanoEHS community seeks innovative *in vitro* methodologies (*e.g.*, organ-on-a-chip,[74] 3D biological constructs)[75] and tools to better predict *in vivo* outcomes,[76] and to evaluate whether this knowledge is translatable to investigations on nano- and microplastics.

Gauging the utility of different metrics for toxicity assessment (*e.g.*, body burden, size distribution of particles in tissues/organs, number concentration) in test media is critical for robust risk assessment,[31] and data and tools to support comparative analytical approaches are needed.[32] Research to date has allowed for some extrapolation between materials, although more extensive read-across (and potentially other methods to estimate toxicity) is needed for advanced materials and new hybrid structures. An emerging area is the evaluation of co-exposures to mixtures of nanomaterials with other chemicals. Mixtures and their interactions have been examined extensively in pharmacology, and more recently in nanomedicine. Extending those methods, such as isobologram analysis, can provide valuable approaches for assessing the impact and potential risk from aggregate exposures associated with environmental toxicology and emerging and more complex nanomaterials and nanotechnology-enabled products.[33]

Moreover, additional research is needed to understand the implications of chronic exposure, particularly chronic low-dose exposures, and to advance the development of more predictive models for complex emerging hybrid nanomaterials.[34] This work would support the development of more sophisticated tools and new approach methods, including adverse outcome pathway (AOP) models that could support the design of tiered testing strategies to evaluate the safety of nanomaterials or advanced materials.[35–37] The AOP concept links molecular perturbations (*e.g.*, molecular initiation events) and cellular responses (*e.g.*, key events) with adverse outcomes to organisms and populations. High-throughput toxicity testing (HTT) and screening (HTS)[38] can be used to evaluate these key events for a broad range of particles. HTS and computational models are vital to the goals of reducing animal testing and addressing the exponential growth in the number of materials that require evaluation.[39,40] However, it is important to note that environmental and biological transformations (including microbial transformations) can significantly change particle toxicity, and that these methods should also evaluate such transformed particles.

Lastly, there is a need for improved modeling and simulation of ENM transformations that can occur in aquatic, soil, and atmospheric media.[30] These *in silico* approaches potentially can be used to link experimental results across different experimental scales such as from bench experiments to mesocosms (*i.e.*, an outdoor experimental system that examines the natural environment under controlled conditions). Achieving this objective is tied to informatics and modeling goals of making data FAIR (Findable, Accessible, Interoperable, and Reusable), discussed in more detail in subsequent sections.

Understanding the landscape of nanotechnology-enabled products in commerce

The sheer number and diversity of ENM-containing products, systems, and devices have brought nanotechnology applications into everyday use by millions of consumers, making it difficult to gain detailed awareness of nanotechnology in the marketplace.[41] Understanding the commercial presence of ENMs will enable a more complete assessment of where exposures may occur and is fundamental to life-cycle assessments. Developing decision support tools and methods that regulatory agencies can use for risk assessment of nanomaterials in food and environmental media and then funding research to develop data as needed would represent a novel approach.[42] Moreover, advances in emerging technology areas such as 3D printing have facilitated the rise of distributed product manufacturing and home manufacturing (do-it-yourself) activities, which has led to a blurring of end uses and users (*e.g.*, worker, consumer, general population). This introduces complexity into assessing community and home-based consumer and workplace exposures, and thus poses challenges for the design and conduct of epidemiological surveillance. NNI agencies have extensive information on control and risk management measures that can be adapted for and communicated to targeted community-based locations such as educational institutions, medical point-of-care sites, and small businesses. Extending the current R&D efforts to integrate field, simulated worker, and lab assessments could pave the way towards portable direct reading sampling devices (by providing real-time measurements) that provide *in situ* measures of biological endpoints in any environment. Working to strengthen the connection between 3D printing nanoEHS researchers, community stakeholders, and manufacturing communities is an advantageous route to accelerate this work.

Diverse physicochemical and biological properties of ENMS makes their risk assessment difficult. It is important to establish how existing test protocols and indicators account for the various environmental health and safety risks that such novel technologies pose.[43] Deriving objective benchmarks provides boundaries around uncertainty values and allows greater transparency in setting risk tolerance limits for the engineering and safe use of various nanomaterials and their products. Such robust analytical frameworks are dependent on the availability of quality data. Pilot risk-prioritization tools are available, however the accuracy of the depiction of the potential risk will be boosted if data on the actual composition of the released nanomaterials is available as an input parameter.[44] Significant progress in this area includes the development of NanoPHEAT (Nano Product Hazard and Exposure Assessment Tool), which integrates toxicity and exposure data on composite releases.[45] NanoPHEAT was developed through an interagency collaboration between NIST, the Consumer Product Safety Commission (CPSC), and the Army Engineer Research and Development Center (ERDC), and agreements with the Duke University Center for Environmental Implications of NanoTechnology.

The concept of risk governance encompasses the entirety of the risk-related decision-making process—tools, instruments, actors, and institutions—considering historical and legal contexts, guiding principles, value systems, and perceptions.[46] Issues of accuracy, privacy, and safety need to be addressed and balanced as next-generation nanotechnology-enabled products enter the market. National and international frameworks on risk governance are designed to foster more sustainable and scientifically driven efforts to shape institutional handling of emerging technologies, including nanotechnology.[47] Additional approaches *via* risk governance help bridge nanomaterial risk uncertainty (*e.g.*, deficits in knowledge regarding toxicity and bioaccumulation), as well as overcome gaps where regulatory benchmarks have not been assigned or affirmed regarding safe use of nanomaterials.[48] Significant weight should be given to accelerating the development of decision analysis tools.[49] This work should be accompanied by activities to minimize risk by embracing a holistic systems approach, and by comparative evaluation of different manufacturing/use alternatives.[50] Developing and implementing the methods and tools of decision analyses and value-of-information analyses are crucial steps forward.[51]

Particularly important for use in risk governance are occupational exposure limits. While a few have been developed, it is not feasible to apply detailed risk assessments for the myriad of engineered nanomaterials in commerce. Therefore, there is a need for research on categorical approaches that could be used.[77] Meanwhile, it is important to evaluate and update occupational exposure limits for mass-based airborne particles to ensure good continuing precautionary practices.

Advancing the knowledge infrastructure

The usefulness and accuracy of nanoEHS tools for nanotechnology assessment and governance are dependent upon the range of material properties and characterization data that is entered into transferrable and analyzable databases. Activities furthering *in silico* data access and retrieval, or informatics, are necessary to accelerate the assessment of ENMs and decrease the per-unit cost of such assessments.

Leveraging high-quality data on nanomaterial properties and functions requires that informatics tools and computational modeling efforts be used to synthesize such data and extract meaningful biological interpretations. Deepening the infrastructure—the development of interoperable, curated datasets, *in silico* tools and approaches, and a nanoEHS research community knowledgeable about modern informatics approaches—will be necessary to predict EHS effects and support safer and sustainable materials synthesis. In 2012, the NNI launched a Nanotechnology Signature Initiative (NSI) to foster and support a Nanotechnology Knowledge Infrastructure (NKI) community.[52] The NSI mechanism was designed to spotlight key areas of national priority such as water technologies, nanosensors, and solar energy collection and conversion where nanotechnology was poised to make significant impacts, and to stimulate enhanced collaboration across the federal NNI community. The NKI helped establish a vibrant and effective nanoinformatics community with strong U.S. and international linkages. For example, the National Cancer Informatics Program Nanomaterial Data Curation Initiative was set up to explore the critical aspect of data curation within the development of informatics approaches to understanding nanomaterial behavior.[53]

Pooling datasets from multiple sources facilitates more comprehensive meta-analyses, development of quantitative structure/property activity relationships (QSAR/QPAR), and read-across risk assessment approaches.[54] A long-term vision for nanoEHS is establishing a predictive framework that would improve the ability to design safer and more sustainable ENMs. Generating high-quality datasets, including information on negative (non-toxic) findings, is critical for the development of predictive modeling and simulations. Other important factors include read-across and QSAR/QPAR approaches, artificial intelligence, and machine learning/deep learning models. These tools and methods should be applicable to nanomaterials in the environment and in complex media, including nanomaterial-containing consumer products. One significant challenge with regards to linking among ENM fate and toxicity studies is that the media can be quite complex (*e.g.*, mesocosms) and often varies among studies. Therefore, recommendations have been made for harmonized media to help enable comparisons among studies and computational analyses.[78]

Developing an informatics framework that can provide a roadmap to risk governance in other areas of interest (*e.g.*, synthetic biology, predictive toxicity tools) would provide a valuable platform for tackling novel technologies. The U.S.-EU NanoEHS CORs (Communities of Research) provide a forum for information exchange and learning across diverse scientific communities and institutions. This transatlantic collaboration has generated valuable scientific outputs within the nanoEHS community. For example, the databases and computational modeling COR played a key role in creating the EU-U.S. Roadmap Nanoinformatics 2030.[55] The EU-U.S. Roadmap has identified three main nanoinformatics challenges: (1) limited datasets; (2) limited data access; and (3) regulatory requirements for validating and accepting computational models. Within that roadmap, the COR community conducted a case study that examined dissolution, a frequent target of computational modeling, and its use in regulatory testing.

Limited data and limited access challenges outlined in the EU-U.S. Roadmap are being addressed by individual agencies and through a consortia of USG agencies that maintain nanoEHS data. NNI agencies are pursuing semantic web approaches to end the "siloing" of agency-held nanoEHS data and to make the data interoperable across databases.[79] EPA has provided a use-case examples for the NNI's nanoinformatics community, applying these approaches to facilitate the integration of its AOP database (EPA AOP-DB) with other toxicologically relevant datasets.[56] By identifying mechanisms to support the use and reuse of data generated with USG support, NNI agencies are also working to make the federally held nanoEHS data FAIR and will continue to build a collaborative informatics structure to strengthen research integrity and secure long-term sustainability for nanoinformatics databases and platforms. These are not trivial tasks,[57] and will require a sustained nanoinformatics infrastructure community of interest.[58] Data that link environmental release of materials in commerce; exposure of workers, consumers, and members of the public; and toxicity are key requirements for life cycle assessments. The generation and availability of these data depend on building public-private collaborations. The federal nanoinformatics community values the connection with the broader research data management community in the United States and internationally, and plans further information exchange and dialogue. The U.S. federal effort can further benefit from advanced international efforts such as The nanodatabase (accessible at **https://nanodb.dk/**). Documenting the experience of using semantic approaches for USG nanoEHS data will lead to the generation of best practices and frameworks for managing and curating data. This will also serve as an entry point for engaging with innovators, developers, and academics, and other holders and managers of nanoEHS data outside of the Federal Government (Table 1).

Conclusion

The dynamic and complex nature of nanomaterial interactions and transformation in the environment and in biological organisms—and the exponential growth of diverse hybrid and multidimensional novel ENMs, nanostructures, and devices—stimulate numerous research questions. To ensure that the environment, workers, and consumers are not exposed to unacceptable risks, the following questions will need to be answered: first, how should hazards be identified, characterized, and assessed? Second, what mechanisms and approval processes for premarket and post-market review should be mandated or recommended? Third, what data and informatics infrastructure are needed to maximize the capacity of federally supported data to inform robust and transparent risk analysis and decision making? Fourth, how do we ensure the safety of researchers, workers, consumers, and the environment in the face of increasing use and complexity of ENMs and nanotechnology-based

Table 1 Key take-aways from U.S. federal perspective on nanoEHS research strategy

Key points/takeaways	
The U.S.G. has taken an integrated, transdisciplinary approach to conducting nanoEHS research which has facilitated advancements in the field of nanoEHS research	
The U.S.G. will continue to foster a unique, diverse multidisciplinary, multisector community of practice/research	Continued investment in the nanotechnology ecosystem: enhance research and lab-to-market infrastructure, educational facilities; broaden partnership networks
The U.S.G. is seeking to identify and fill critical issues, opportunities, gaps in current research portfolio	Periodic re-evaluation of the state-of-science
	Utilize and leverage existing knowledge from nanomedicine, continue to build on 20+ years of nanoEHS research
	Address limitations regarding characterization, assessment, and governance of potential risk of nanotechnology
	Continue to develop advanced tools for characterization, transformation, evaluation, quantification of ENMs for improved risk determinations
	Adapt to societal needs and priorities on emerging challenges (*e.g.*, nanoplastic management, addressing sustainability issues, addressing climate change)
The U.S.G. is leveraging an extensive collective knowledge base to advance understanding of interactions between nanomaterials, humans, and the environment	

products? These and other questions are core motivations for nanoEHS research and risk management going forward, where risk to human health and the environment are characterized, assessed, and managed in an objective and data-driven manner.

Overall, a core trend has emerged: while nanoEHS knowledge continues to advance, limitations remain regarding the characterization, assessment, and governance of the potential risks of nanotechnology. Addressing these challenges requires further investment not only in advancing the nanotechnology ecosystem—research and lab-to-market infrastructure, educational facilities, and broad partnerships and networks—but also in research on the technology's societal implications. Collaboratively, the goal is to develop tools and approaches that are robust and appropriate for new and advanced materials, and which can be translated into rules, regulations, operating procedures, and protocols for academia, industry, and product developers. These goals will not be easily achieved and will likely require a continued and extended commitment over the coming years to transition nanotechnology from an "emerging technology" into the new era of core commodities and composite products. The intended results, however, will be to contribute to accelerated market growth, further improvement of many essential products, and the development of novel products across multiple industries to raise the standard of living.

The nanoEHS community has leveraged the collective knowledge base to significantly advance understanding of nanomaterial human and environmental impacts. Nevertheless, we need to maximize the benefits of more than two decades of research and apply our knowledge appropriately to emerging contaminants and advanced materials. While there has been a considerable amount of progress, there remains a need to continue to work collaboratively and strategically with related disciplines such as nanomedicine, data science, and human exposome research. Such strategic cooperation is vital for a path forward in many areas, including micro- and nanoplastics pollution, other incidental or naturally occurring nanoparticles, nanoinformatics, and the validation of alternative testing approaches for risk and regulatory decision support, among others. The federal community will continue to use interagency forums and work groups as needed to respond dynamically and effectively to emerging, thorny, and multidisciplinary nanoEHS challenges.

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Conflicts of interest

There are no conflicts to declare.

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