serve research, regulatory and commercial knowledge needs[31].

## Bridging interdisciplinary communities

Nanotechnology by its very nature is interdisciplinary. This interdisciplinarity certainly holds true in the area of nanoEHS research, and a vibrant community has developed. While in the early days of nanoEHS research toxicologists and exposure scientists largely worked independently, there are many examples of collaboration among these communities to inform dosing, for example. One area where these researchers come together is through the international nanoEHS CORs (Fig. 2). Established in 2012, these informal groups provide a platform for researchers to collaboratively identify and address key research needs through a variety of community-led activities such as telecons, webinars, workshops, publications and annual in-person meetings. There are currently seven nanoEHS CORs focused on characterization, databases and computational modelling, ecotoxicity, human toxicity, exposure through product life, risk assessment, and risk management and control. There are also collaborations developing between related communities focused on implications and applications. For example, there are considerable synergies between nanoEHS and nanomedicine. Furthermore, the use of nanotechnology in agriculture, water and environmental remediation continues to grow. Lessons learned and continued engagement of the nanoEHS community will be critical to success in these areas.

## Expanding nanoEHS knowledge

Over the past fifteen years, nanotechnology research and development has led to a wide variety of applications in areas as diverse as electronics, textiles, sporting goods, energy, infrastructure, automotive, water purification and medicine, and nanotechnology continues to be an active area of research the world over. As new nanomaterials, manufacturing methods and applications are discovered and developed, the international nanoEHS research community is well positioned to build upon the strong collaborations and scientific foundation they have developed to continue to expand understanding and ensure responsible development of nanotechnology into the future. ❐

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# Best practices from nano-risk analysis relevant for other emerging technologies

The experiences gained from the past 15 years of nanomaterial risk analysis may be useful for the risk analysis efforts of other emerging technologies.

Khara Grieger, Jacob L. Jones, Steffen Foss Hansen, Christine Ogilvie Hendren, Keld Alstrup Jensen, Jennifer Kuzma and Anders Baun

It has been 15 years since the first wave of international research programmes were launched to understand the potential health, environmental and societal impacts of nanotechnologies and engineered nanomaterials[1]. Among other areas, investigations into the adequacy of the chemical risk assessment framework for nanomaterials soon became a keystone research effort[2]. While great strides have been made[3], including key work by national and international research consortia (for example, the Organisation for Economic Co-operation and Development's Working Party on Manufactured Nanomaterials, the EU NanoSafety Cluster and the US National Nanotechnology Initiative)[4–6], uncertainty still significantly impedes nanomaterial risk evaluations. Today, concrete conclusions regarding the health and environmental risks of most nanomaterials and products in which they are contained are lacking, and regulations struggle to keep pace with the rapidly evolving science and data developments that underpin nanomaterial risk assessment[6,7]. Moreover, the reliance on risk assessment for informing oversight and decision making for nanomaterials has not only led to numerous challenges due to the complexities and uncertainties involved in characterizing nanomaterials and associated risks[6,8,9], but has also illuminated several underlying and unresolved tensions regarding the use of specific, existing test methods and risk assessment frameworks for decision making[10].

Given the experiences, challenges and lessons learned over the past 15 years, it is now an opportune time to reflect on the field of nanomaterial risk assessment and analysis and, perhaps even more importantly, identify best practices that may be applicable to other emerging and disruptive technologies (for example, advanced materials, synthetic biology, quantum technologies, artificial intelligence and machine learning, three-dimensional printing and climate engineering). We have identified five best practices from nanomaterial risk analysis that, in our view, could help advance risk analysis and responsible innovation relevant for other emerging technologies.

## Research for decision making

While the difficulty of drawing concrete conclusions from risk assessments of nanomaterials and nano-enabled products is partly due to technical and analytical challenges[3,7], there are also more fundamental issues at play: nano-risk research has largely been directed towards understanding the science rather than meeting decision making and regulatory needs[6,11]. In this context, a distinction may be made between 'traditional science' (that is, hypothesis, discovery-based science that is not necessarily relevant for regulation, but highly relevant in scientific terms) and 'regulatory-relevant science' (that is, science designed to support regulatory decision making). Numerous authors have previously highlighted the challenge of supporting decision making needs while also developing the scientific areas of nanomaterial risk analysis and nanosafety[6,8,9]. While it is possible to link evolving nanosafety data to decision and policy-relevant needs using 'bottom-up' strategies[7], the initiation of strategic, purposeful regulatory-relevant science programmes (that is, using 'top down' strategies) at the start of major risk and safety efforts for emerging technologies could help target research more effectively towards regulatory decision making, at least for near- and medium-term decisions. This would also help to address the so-called pacing problem often experienced between new technological innovation, efforts to understand their potential impacts and subsequent regulatory responses[12].

## Time and cost estimates

Further refinements of risk assessment strategies, including the development of robust testing procedures and datasets for diverse nanomaterials, will likely continue to be an evolving process. In addition, the diversity of nanomaterial types, sizes, coatings, functionalizations and products in which they are used only exacerbates existing challenges and amplifies the time, resources and complexities involved. Although it may be disappointing that after almost two decades of research and significant investments in nanomaterial risk analysis (that is, estimated at several hundred million to a billion US dollars/euros[13,14]), additional time and resources are needed to comprehensively understand potential impacts of nanomaterials, this may not be entirely surprising upon reflection. For comparison, it took over three decades to develop robust chemical risk assessments[15], two decades to develop quantitative microbial risk assessments in food[16] and similar timelines in other risk assessment fields[17]. In fact, early estimates anticipated that it would cost US$249 million to US$1.18 billion and take 24–53 years to develop and complete quantitative risk assessments for nanomaterials and products[18].

The process of identifying risks, adapting or developing assessment protocols and procedures, and testing, validating and harmonizing risk assessment methods for other emerging technologies are also likely be complex, time-consuming and expensive. This may especially be the case if this process is based on the traditional approach of relying on experimental evidence and knowledge-based assessments for risk evaluations[17]. Therefore, it may help prepare and align stakeholder expectations early on to have realistic estimates of the time, costs and degrees of complexities involved to derive concrete conclusions regarding risks. These estimates may help prepare industry, policymakers and other decision-makers so that they can prioritize research efforts and funding programmes directed at near-term methods, policy or decision-making while the underlying safety science is developed. Estimates also need to factor in the often-iterative process between industry, regulators and other stakeholders when submitting safety data and information on new materials or technologies to ensure the current state-of-science is reflected in submissions.

## Uncertainties

Scientific uncertainty — defined here as all types and forms of knowledge deficits in evaluations[19,20] — has been one of the main obstacles in nanomaterial risk analysis[3,21]. In response, additional nanosafety research was called for and launched in accordance[2,22,23]. While many knowledge gaps have been reduced, new research challenges and areas of uncertainty have also arisen[6]. To help overcome these challenges related to the prevalence of extensive uncertainties in nanomaterial data and risk analysis, various alternative approaches have been proposed (for example, risk screening, prioritization, control banding and decision-support tools)[24]. However, a core issue of how best to deal with uncertainties in diverse nano-risk evaluations has not yet been addressed head on, despite several calls[11,21,25,26].

In general, standard approaches to handle uncertainties in risk assessment (for example, probabilistic analysis) may not be well suited for emerging technologies characterized by deep and extensive uncertainties in potential risk evaluations[17]. Risk assessment efforts for nanomaterials and other emerging technologies would benefit from including or being complemented by uncertainty assessments that identify and describe different scientific uncertainties and communicate how they may impact overall risk estimates[27]. Dynamic risk evaluation and management processes also allow for adaptive responses to quickly evolving scenarios or in light of new information[28]. Adaptive and responsible risk governance frameworks that account for uncertainty in risk evaluations[26], incorporate stakeholder perspectives and include procedural robustness may also be useful to proactively deal with uncertainty in risk analysis and decision support involving emerging technologies[29].

## Data and privacy

Concrete conclusions regarding the potential risks of nanomaterials have also been hampered by challenges related to data management and harmonization, along with issues of privacy, confidentiality and intellectual property. Integrating diverse data sets without harmonized data production, collection and management approaches has led to mismatched datasets[30] and varying levels of completeness, quality, transparent documentation and use of discrete data[6,31]. Data access and sharing across projects and consortia have also been an obstacle, although some projects have started to implement findable, accessible, interoperable and reusable (FAIR) principles in response[6,7]. There have also been challenges to obtaining confidential or intellectual property-comprised information from industry[31], with modest results obtained thus far[31,32].

Moving forward, having more harmonized, multi-scale and even decision-directed approaches may help to avoid challenges related to data harmonization and integration. It is recognized, however, that it may be difficult to develop harmonized data management, data access and ontologies in a quickly evolving field across research consortia. Future risk assessment and management efforts could rely on robust communication mechanisms between researchers and, with appropriate funding, integrate risk research efforts with respect to curation functionality, infrastructure and communication processes from the onset. To help foster data sharing from industry and other stakeholders, key initiatives should focus on establishing strong relationships to build trust and increase communication as well as providing clear incentives for data sharing[7].

### Fit-for-purpose risk analysis tools

To understand and quantify potential risks of nanomaterials for use in regulatory contexts, the chemical risk assessment framework was selected as the starting point, as highlighted above. This decision was made amidst early calls for broader risk governance approaches[33] and without significant or extensive stakeholder dialogue specifically focused on identifying and selecting appropriate and fit-for-purpose evaluation approach(es). While the use of the chemical risk assessment framework for nanomaterials was a logical step, given its use for chemicals, stakeholders may have benefited from being involved in an initial process that critically evaluated a range of tools, frameworks and methods to evaluate risks and make subsequent decisions. A thorough and critical evaluation of robust, fit-for-purpose risk analysis tools or frameworks could have improved stakeholders' understanding and expectations on their utility, limitations and outcomes, as well as helped illuminate the expected time, cost and degrees of complexity that may be expected to eventually complete assessments. For example, probabilistic risk analysis, microbial risk analysis and pest risk analysis have been proposed for active nanomaterials that interact with and respond to biological systems[34]. Further, not all decisions regarding potential risks need to be made from quantitative estimates, as other options include the selection of alternatives[35,36]. Finally, entirely new ways of thinking about risks for emerging technologies may also be warranted in some cases, such as the utilization of 'risk innovation' that incorporates risk appraisals within evolving innovation processes[37].

While pursuing and deriving a (quantitative) risk assessment for nanomaterials and other emerging technologies is clearly worthwhile in some cases (for example, following 'traditional science' processes), it may also be a lengthy and time-consuming endeavour, and there may be other risk evaluation approaches that could be more applicable for a given decision. A process that critically evaluates diverse evaluation frameworks and approaches followed by a transparent selection process for an emerging technology could be beneficial early on to ensure that the most fit-for-purpose risk analysis framework is selected for utilization, further exploration, or to ultimately produce outcomes that meet decision-makers' needs. Convergence and team science methodologies may offer identification of useful approaches and methodologies and even derive new procedures for solving complex and emerging risks with greater societal relevance, including issues raised by nanomaterials, advanced materials and other emerging technologies. ❐

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