COMMENTARY

Safe handling of nanotechnology

The pursuit of responsible nanotechnologies can be tackled through a series of grand challenges, argue **Andrew D. Maynard** and his co-authors.

D. RAMSEY

Potential health risks from exposure to engineered nanomaterials must be understood and minimized.

When the physicist and Nobel laureate Richard Feynman challenged the science community to think small in his 1959 lecture 'There's Plenty of Room at the Bottom', he planted the seeds of a new era in science and technology. Nanotechnology, which is about controlling matter at near-atomic scales to produce unique or enhanced materials, products and devices, is now maturing rapidly with more than 300 claimed nanotechnology products already on the market[1]. Yet concerns have been raised that the very properties of nanostructured materials that make them so attractive could potentially lead to unforeseen health or environmental hazards[2].

The spectre of possible harm — whether real or imagined — is threatening to slow the development of nanotechnology unless sound, independent and authoritative information is developed on what the risks are, and how to avoid them[3]. In what may be unprecedented pre-emptive action in the face of a new technology, governments, industries and research organizations around the world are beginning to address how the benefits of emerging nanotechnologies can be realized while minimizing potential risks[4]. Yet despite a clear commitment to support risk-focused research, opportunities to establish collaborative, integrated and targeted research programmes are being missed[5]. In September, Sherwood Boehlert, chair of the US House Science Committee, commented in a hearing that "we're on the right path to dealing with the problem, but we're sauntering down it when a sense of urgency is required". And in October, Britain's Royal Society raised concerns that the UK government had not made enough progress on reducing the uncertainties surrounding the health and environmental impacts of nanomaterials[6].

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The risks

As research leaders in our respective fields, we recognize that systematic risk research is needed if emerging nano-industries are to thrive. We cannot set the international research agenda on our own, but we can inspire the scientific community — including government, industry, academia and other stakeholders — to move in the right direction. So we propose five grand challenges to stimulate research that is imaginative, innovative and above all relevant to the safety of nanotechnology.

Fears over the possible dangers of some nanotechnologies may be exaggerated, but they are not necessarily unfounded. Recent studies examining the toxicity of engineered nanomaterials in cell cultures and animals have shown that size, surface area, surface chemistry, solubility and possibly shape all play a role in determining the potential for engineered nanomaterials to cause harm[7]. This is not surprising: we have known for many years that inhaled dusts cause disease, and that their harmfulness depends on both what they are made of and their physical nature. For instance, small particles of inhaled quartz lead to lung damage and the potential development of progressive lung disease, yet the same particles with a thin coating of clay are less harmful[8]. Asbestos presents a far more dramatic example: thin, long fibres of the material can lead to lung disease if inhaled, but grind the fibres down to shorter particles with the same chemical make-up and the harmfulness is significantly reduced[9].

It is generally accepted that, in principle, some nanomaterials may have the potential to cause harm to people and the environment. But the way science is done is often ill-equipped to address novel risks associated with emerging technologies. Research into understanding and preventing risk often has a low priority in the competitive worlds of intellectual property, research funding and technology development. And yet there is much at stake in how potential nano-specific risks are understood and managed. Without strategic and targeted risk research, people producing and using nanomaterials could develop unanticipated illness arising from their exposure; public confidence in nanotechnologies could be reduced through real or perceived dangers; and fears of litigation may make nanotechnologies less attractive to investors and the insurance industry.

The science community needs to act now if strategic research is to support sustainable nanotechnologies, in which risks are minimized and benefits maximized. Our five grand challenges are chosen to stimulate such research, as well as bring focus to a range of complex multidisciplinary issues. The challenges span the next 15 years, and their successful achievement will depend on coordination, collaboration, resources and ingenuity. They are not comprehensive — there is essential research that is not covered here — but they do form a framework on which others can build.

The challenges

Develop instruments to assess exposure to engineered nanomaterials in air and water, within the next 3–10 years. Because nanotechnologies are diverse and exposures to nanomaterials will vary widely, assessing exposure and potential impacts on health or the environment will require multiple sensor types operating under different conditions. Three issues stand out as fertile ground for innovative research: monitors for airborne exposure, detectors for waterborne nanomaterials, and smart sensors that can measure both exposure and potential hazards.

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We don't yet know which aspects of airborne nanomaterials should be measured — number, surface area or mass concentration, a combination of these, or something else entirely. But people working with nanomaterials urgently need inexpensive personal aerosol samplers that are capable of measuring exposure in the workplace and environment. This universal aerosol sampler would log exposure against aerosol number, surface area and mass concentration simultaneously, and provide a historic record that can be interpreted in the light of new knowledge and new exposure monitoring paradigms. It would be portable, sufficiently inexpensive to ensure widespread use, and available commercially within the next 3 years.

Effluent from nanomanufacturing processes, use of nanoparticle-containing substances such as sunscreens, and disposal of nanomaterial-containing products, will inevitably lead to increasing quantities of engineered nanomaterials in water systems. If we cannot track these materials, it will be almost impossible to determine how benign or harmful their presence is. The second challenge therefore is to develop instruments that can track the release, concentration and transformation of engineered nanomaterials in water systems (including liquid-based nanotechnology consumer products), within the next 5 years.

Advances in information technology and sensor design are leading to the development of smart sensors that combine information on various aspects of exposure and hazard in a way that is useful for decision-making. The concept is embodied in radiation monitors and biomonitoring, but has not yet been extended to engineered nanomaterials. The final part of this challenge therefore is to develop smart sensors that indicate potential harm to human health. An example would be sensors that simultaneously detect airborne nanoparticles and determine their potential to generate reactive oxygen species — possibly providing early indications of harm. Such sensors should be available within the next 10 years.

Develop and validate methods to evaluate the toxicity of engineered nanomaterials, within the next 5–15 years. There are many aspects to evaluating nanomaterial toxicity. But there are three that we consider crucial for stimulating high-quality research and preventing the unnecessary use of hazardous nanomaterials: validated screening tests, developing viable alternatives to *in vivo* tests, and determining the toxicity of fibre-shaped nanoparticles.

The enormous diversity of engineered nanomaterials with different sizes, shapes, compositions and coatings matches, and possibly exceeds, that of conventional chemicals. High-throughput protocols that are benchmarked and validated are urgently needed to screen for potential hazards. The first part of this challenge is to reach international agreement on a battery of *in vitro* screening tests for human and environmental toxicity within the next 2 years, and to validate these tests within the next 5 years. Essential to this challenge will be the widespread and global availability of standard nanoparticle samples to allow comparison and refinement of methods across government, industry and academic laboratories.

Although testing *in vivo* will continue to provide the most relevant information on human (and other organism) hazards, there is an economic and ethical impetus to minimize the burden of animal testing. Emerging technologies — including nanotechnology — are providing new possibilities for simulating and predicting nanomaterial behaviour in living organisms. We propose that relevant and validated alternatives to *in vivo* toxicity testing of engineered nanomaterials be developed over the next 15 years.

Fibre-shaped nanomaterials possibly represent a unique inhalation hazard, and their pulmonary toxicity should be evaluated as a matter of urgency. Inhalation of a sufficient dose of asbestos fibres can lead to the malignant disease mesothelioma, the causation of which is related to the length, width and chemistry of the fibres, as well as their ability to persist in the lungs.

Although it is not clear whether fibre-shaped nanoscale particles formed from carbon and other materials will behave like asbestos or not, some materials are sufficiently similar to cause concern: any failure to pick up asbestos-like behaviour as early as possible would be potentially devastating to the health of exposed people and to the future of the nanotechnology industry. We propose that the potential health impact of high-aspect-ratio, biopersistent engineered nanotubes, nanowires and nanofibres is systematically investigated within the next 5 years.

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Nanotechnology is rapidly advancing, with more than 300 nanoproducts already on the market.

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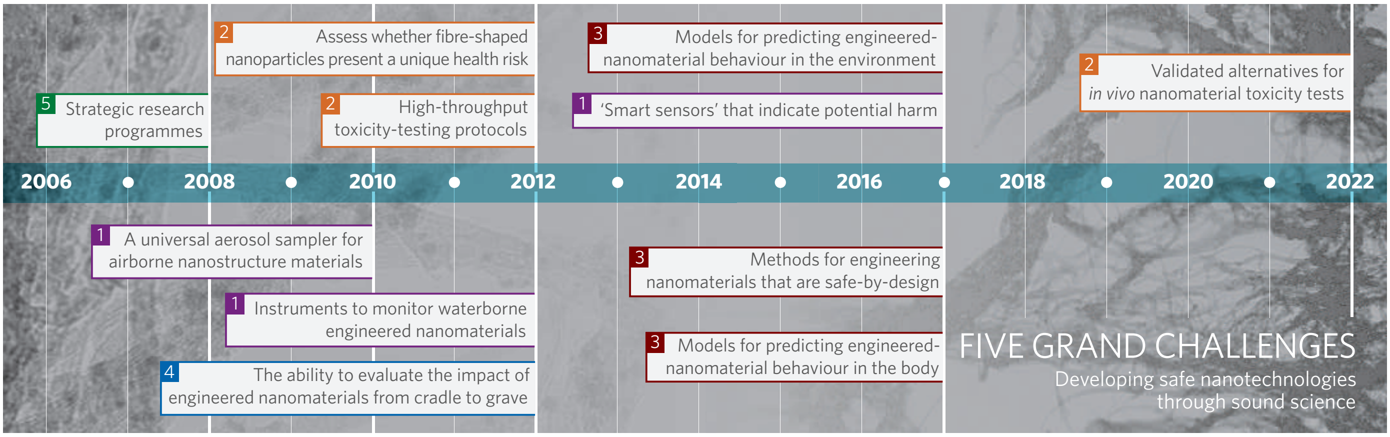

Develop models for predicting the potential impact of engineered nanomaterials on the environment and human health, within the next 10 years. To assess the safety of complex multicomponent and multifunctional nanomaterials, scientists will need systems capable of predicting the potential impact of new nanomaterials, devices and products. Once again our challenge here has three parts. First, to develop validated models capable of predicting the release, transport, transformation, accumulation and uptake of engineered nanomaterials in the environment. In parallel, validated models must be developed that are capable of predicting the behaviour of engineered nanomaterials in the body, including dose, transport, clearance, accumulation, transformation and response. These models should: relate the physical and chemical characteristics of nanomaterials to their behaviour; allow an integrated approach to predicting potential impact of engineered nanomaterials and nanoproducts; and estimate impact within susceptible populations.

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Third, to use predictive models for engineering nanomaterials that are safe by design. This might include engineering the nanomaterials in ways that enhance desired properties while suppressing hazardous ones, or creating fail-safe mechanisms that ensure a transition to benign materials upon disposal.

Develop robust systems for evaluating the health and environmental impact of engineered nanomaterials over their entire life, within the next 5 years. Thinking in terms of life cycles leads to a holistic approach to managing risks and benefits. Developing robust ways of evaluating the potential impact — good or bad — of a nanoproduct from its initial manufacture, through its use, to its ultimate disposal will stretch both scientific and policy communities, but will lead to new methodologies that are widely applicable.

Develop strategic programmes that enable relevant risk-focused research, within the next 12 months. Ultimately, systematic and organized risk research will empower industry, consumers and policy-makers to make the best decisions about the development and application of emerging nanotechnologies. As end-users of the scientific data, these communities must play a central role in shaping what is done and how. Government research strategies that systematically reduce uncertainty surrounding the potential impact of nanotechnologies and support science-based oversight are essential to the safe development of nanotechnology. But these must be complemented by, and integrated with, industry-led research. We highlight three areas that we believe are critical to the success of such risk research: collaboration, communication and coordination.

The first challenge is identifying mechanisms that enable collaborative research programmes — whether interdisciplinary, between government and industry, or between different stakeholders. Virtual interdisciplinary research centres and networks are one way of stimulating collaboration, as long as they are accompanied by adequate resources. We would also encourage joint government–industry partnerships that underpin good product stewardship and oversight, while being transparent and credible.

Communicating research on nanotechnology risks and benefits outside the scientific community is challenging, but is essential for a risk dialogue based on sound science. This means developing communication activities that enable technical information to be summarized, critiqued and ultimately synthesized for various interested parties, including decision-makers and consumers. The advent of the Internet provides an ideal venue for such activities and we encourage its use in communicating with the end-users of risk-based science.

Finally, a global understanding of nanotechnology-specific risks is essential if large and small industries are to operate on a level playing field, and developing economies are not to be denied essential information on designing safe nanotechnologies. We propose that mechanisms, networks and meetings are established that enable international information-sharing and coordination between the public and private sectors.

Nanotechnology comes at an opportune time in the history of risk research. We have cautionary examples from genetically modified organisms and asbestos industries that motivate a real interest, from all stakeholders, to prevent, manage and reduce risk proactively. We have a global research infrastructure that supports international collaboration. We also have revolutions in biotechnology, sensing and computation that are transforming how health-focused research is performed. If the global research community can take advantage of these circumstances and rise to the challenges we have set, then we can surely look forward to the advent of safe nanotechnologies. ■

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